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(54) SUBSTITUTED PYRIMIDINES FOR THE TREATMENT OF DISEASES SUCH AS CANCER

SUBSTITUIERTE PYRIMIDINE ZUR BEHANDLUNG VON KRANKHEITEN WIE KREBS

PYRIMIDINES SUBSTITUÉES POUR LE TRAITEMENT DES MALADIES COMME LE CANCER

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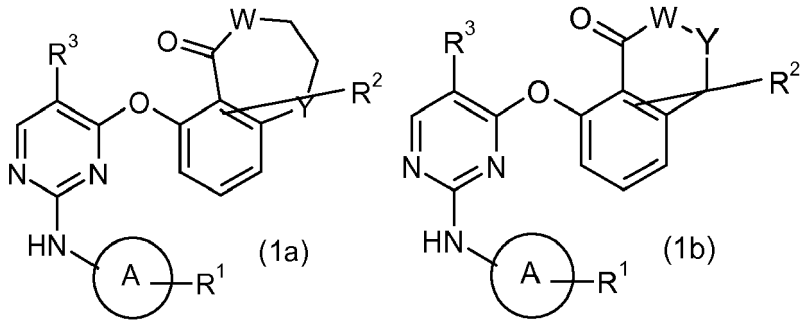
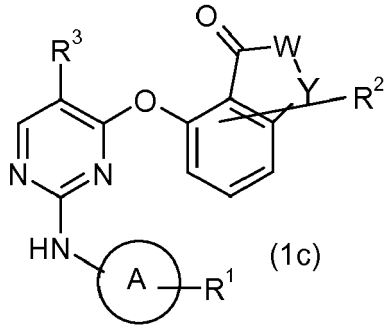
Description

[0001] The present invention relates to new pyrimidines of general formula **(1a)**, **(1b)** and **(1c)**





wherein the groups **A**, **R1** to **R3**, **W** and **Y** have the meanings given in the claims and specification, processes for preparing these pyrimidines and their use as medicaments.

Background to the invention

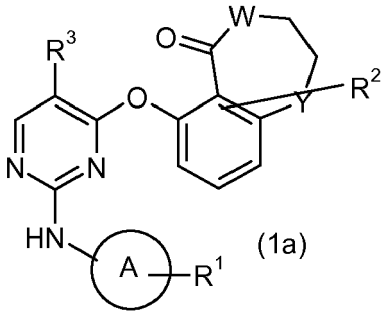
[0002] Tumour cells that acquire the properties for invasion and metastasisation require specific survival signals. These signals allow them to overcome special apoptosis mechanisms (anoikis) which are triggered, inter alia, by the loss of cell adhesion. In this process, focal adhesion kinase (FAK/PTK2) is one of the essential signal molecules which on the one hand controls cell-matrix interactions through so-called 'focal adhesions' and on the other hand imparts anoikis resistance. Interference with these mechanisms by inhibiting PTK2 may lead to the apoptotic cell death of tumour cells and limit the invasive and metastasising growth of tumours. In addition, focal adhesion kinase has major significance for the growth, migration and survival of tumour-associated endothelial cells. An anti-angiogenic activity may therefore also be achieved by inhibiting PTK2.

[0003] Pyrimidines are generally known as inhibitors of kinases. Thus, for example, International Patent Application WO 2008038011 describes pyrimidines as aurora kinase inhibitors, these pyrimidines having, as substituents, an oxymethyl-piperidine group in the 4 position and fluorine in the 5 position. US 2008/255172, WO 01/64655 and WO 2006/021457 describe substituted pyrimidines and their use for the treatment of proliferative diseases. The aim of the present invention is to indicate new active substances which can be used for the prevention and/or treatment of diseases characterised by excessive or abnormal cell proliferation.

Detailed description of the invention

[0004] It has been found that, surprisingly, compounds of general formula **(1a)**, **(1b)** and **(1c)** wherein the groups **A**, **R1** to **R3**, **W** and **Y** have the meanings given below, act as inhibitors of specific tyrosine-kinases. Thus, the compounds according to the invention may be used for example for treating diseases connected with the activity of specific tyrosine-kinases and characterised by excessive or abnormal cell proliferation.

[0005] In one aspect the invention relates to compounds of general formula **(1a)**,



(1a)

wherein

A denotes a group, optionally substituted by one or more identical or different **R1**, selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;

R1 and **R2** each independently of one another denote hydrogen or a group selected from among **Ra, Rb** and **Ra** substituted by one or more identical or different **Rc** and/or **Rb; R3** denotes a group selected from among hydrogen, halogen, -ORc, $-OCF_3$, -SRc, -NRcRc, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

W and **Y** independently of one another represent CH_2, O, N-Re or N-ORe;

each **Ra** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **Rb** is a suitable group and is independently selected from among =O, -ORc, C_{1-3}haloalkyloxy, $-OCF_3$, =S, -SRc, =NRc, =NORc, =NNRcRc, =NN(Rg)C(O)NRcRc, -NRcRc, -ONRcRc, -N(ORc)Rc, -N(Rg)NRcRc, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, -S(O)Rc, -S(O)ORc, $-S(O)_2$Rc, $-S(O)_2$ORc, -S(O)NRcRc, $-S(O)_2$NRcRc, -OS(O)Rc, $-OS(O)_2$Rc, $-OS(O)_2$ORc, -OS(O)NRcRc, $-OS(O)_2$NRcRc, -C(O)Rc, -C(O)ORc, -C(O)SRc, -C(O)NRcRc, -C(O)N(Rg)NRcRc, -C(O)N(Rg)ORc, -C(NRg)NRcRc, -C(NOH)Rc, -C(NOH)NRcRc, -OC(O)Rc, -OC(O)ORc, -OC(O)SRc, -OC(O)NRcRc, -OC(NRg)NRcRc, -SC(O)Rc, -SC(O)ORc, -SC(O)NRcRc, -SC(NRg)NRcRc, -N(Rg)C(O)Rc, $-N[C(O)R^c]_2$, -N(0Rg)C(O)Rc, -N(Rg)C(NRg)Rc, -N(Rg)N(Rg)C(O)Rc, -N[C(O)Rc]NRcRc, -N(Rg)C(S)Rc, -N(Rg)S(O)Rc, -N(Rg)S(O)ORc, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, -N(Rg)C(O)ORc, -N(Rg)C(O)SRc, -N(Rg)C(O)NRcRc, -N(Rg)C(O)NRgNRcRc, -N(Rg)N(Rg)C(O)NRcRc, -N(Rg)C(S)NRcRc, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, -N(Rg)C(NRg)ORc, -N(Rg)C(NOH)Rc, -N(Rg)C(NRg)SRc and -N(Rg)C(NRg)NRcRc;

each **Rc** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **Rd** and/or **Re** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **Rd** is a suitable group and is independently selected from among =O, -ORe, C_{1-3}haloalkyloxy, $-OCF_3$, =S, -SRe, =NRe, =NORe, =NNReRe, =NN(Rg)C(O)NReRe, -NReRe, -ONReRe, -N(Rg)NReRe, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, -S(O)Re, -S(O)ORe, $-S(O)_2$Re, $-S(O)_2$ORe, -S(O)NReRe, $-S(O)_2$NReRe, -OS(O)Re, $-OS(O)_2$Re, $-OS(O)_2$ORe, -OS(O)NReRe, $-OS(O)_2$NReRe, -C(O)Re, -C(O)ORe, -C(O)SRe, -C(O)NReRe, -C(O)N(Rg)NReRe, -C(O)N(Rg)ORe, -C(NRg)NReRe, -C(NOH)Re, -C(NOH)NReRe, -OC(O)Re, -OC(O)ORe, -OC(O)SRe, -OC(O)NReRe, -OC(NRg)NReRe, -SC(O)Re, -SC(O)ORe, -SC(O)NReRe, -SC(NRg)NReRe, -N(Rg)C(O)Re, $-N[C(O)R^e]_2$, -N(ORg)C(O)Re, -N(Rg)C(NRg)Re, -N(Rg)N(Rg)C(O)Re, -N[C(O)Re]NReRe, -N(Rg)C(S)Re, -N(Rg)S(O)Re, -N(Rg)S(O)ORe $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, -N(Rg)C(O)ORe, -N(Rg)C(O)SRe, -N(Rg)C(O)NReRe, -N(Rg)C(O)NRgNReRe, -N(Rg)N(Rg)C(O)NReRe, -N(Rg)C(S)NReRe, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, -N(Rg)C(NRg)ORe, -N(Rg)C(NOH)Re, -N(Rg)C(NRg)SRe and -N(Rg)C(NRg)NReRe;

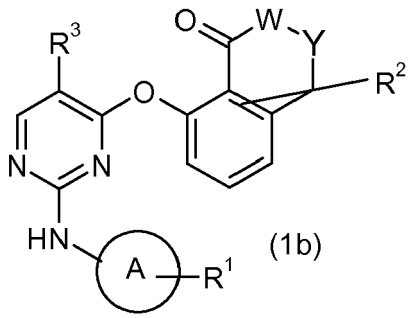
each **Re** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **Rf** and/or **Rg** selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **Rf** is a suitable group and is independently selected from among halogen and $-CF_3$; and

each **Rg** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

[0006] In another aspect the invention relates to compounds of general formula (**1b**),



(1b)

wherein

A denotes a group, optionally substituted by one or more identical or different $\mathbf{R^1}$, selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;

$\mathbf{R^1}$ and $\mathbf{R^2}$ each independently of one another denote hydrogen or a group selected from among $\mathbf{R^a}$, $\mathbf{R^b}$ and $\mathbf{R^a}$ substituted by one or more identical or different $\mathbf{R^c}$ and/or $\mathbf{R^b}$;

$\mathbf{R^3}$ denotes a group selected from among hydrogen, halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

W and **Y** independently of one another represent CH_2, O, N-R^e or N-OR^e;

each $\mathbf{R^a}$ is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each $\mathbf{R^b}$ is a suitable group and is independently selected from among =O, $-OR^c$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$;

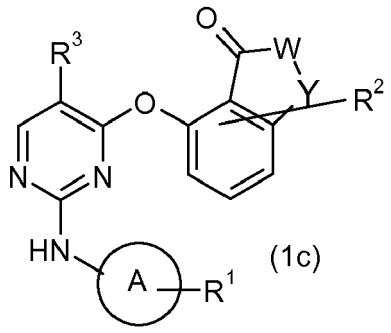
each $\mathbf{R^c}$ independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^d}$ and/or $\mathbf{R^e}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each $\mathbf{R^d}$ is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ and $-N(R^g)C(NR^g)NR^eR^e$;

each $\mathbf{R^e}$ independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^f}$ and/or $\mathbf{R^g}$ selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heter-

oaryl and 6-18 membered heteroarylalkyl;
each $\mathbf{R^f}$ is a suitable group and is independently selected from among halogen and $-CF_3$; and
each $\mathbf{R^g}$ independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;
optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

[0007] In another aspect the invention relates to compounds of general formula **(1c),**



(1c)

wherein
A denotes a group, optionally substituted by one or more identical or different $\mathbf{R^1}$, selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;
$\mathbf{R^1}$ and $\mathbf{R^2}$ each independently of one another denote hydrogen or a group selected from among $\mathbf{R^a}$, $\mathbf{R^b}$ and $\mathbf{R^a}$ substituted by one or more identical or different $\mathbf{R^c}$ and/or $\mathbf{R^b}$;
$\mathbf{R^3}$ denotes a group selected from among hydrogen, halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;
W and Y independently of one another represent CH_2, O, N-R^e or N-OR^e;
each $\mathbf{R^a}$ is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;
each $\mathbf{R^b}$ is a suitable group and is independently selected from among =O, $-OR^c$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$;
each $\mathbf{R^c}$ independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^d}$ and/or $\mathbf{R^e}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;
each $\mathbf{R^d}$ is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$,

$-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ and $-N(R^g)C(NR^g)NR^eR^e$;

each **R^e** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^f** and/or **R^g** selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

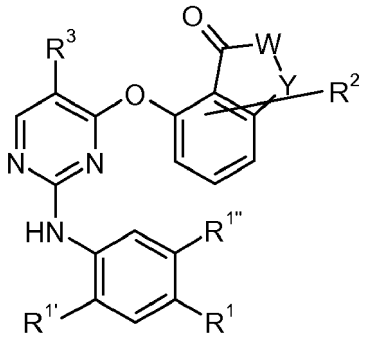
each **R^f** is a suitable group and is independently selected from among halogen and $-CF_3$; and

each **R^g** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

[0008] In another aspect the invention relates to compounds of general formula **(1a)**, **(1b)** or **(1c)**, wherein **A** is phenyl.

[0009] In another aspect the invention relates to compounds of general formula **(1d)**,



(1d)

wherein

W and **Y** each independently of one another represent CH_2, O, N-R^e or N-OR^e, and

R^1 denotes hydrogen or a group selected from among **R^a, R^b** and **R^a** substituted by one or more identical or different **R^c** and/or **R^b**,

each **R^a** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^b** is a suitable group and is independently selected from among =O, $-OR^c$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$,

each **R^c** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different R^d and/or R^e selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^d** is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$,

$-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ and $-N(R^g)C(NR^g)NR^eR^e$,

each **R^e** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different R^f and/or R^g selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^f** is a suitable group and is independently selected from among halogen and $-CF_3$; and

each **R^g** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, and **$R^{1'}$** and **$R^{1''}$** each independently of one another denote a group selected from among hydrogen, halogen and $-OR^c$, and

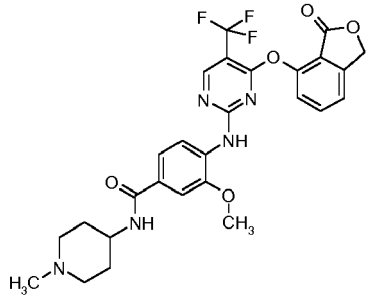
R^2 denotes hydrogen or a group selected from among **R^a, R^b** and **R^a** substituted by one or more identical or different **R^c** and/or **R^b,** and

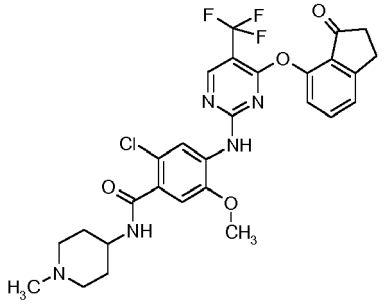
R^3 denotes a group selected from among hydrogen, halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

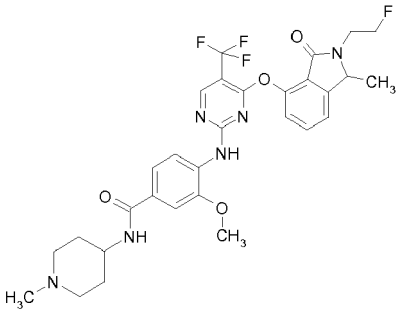
optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

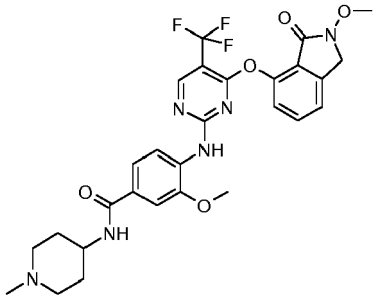
[0010] In another aspect the invention relates to compounds of general formula **(1a)**, (**1b**), **(1c)** or **(1d)**, wherein **R^3** is Cl or CF_3.

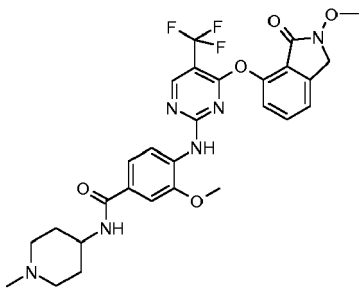
[0011] In another aspect the invention relates to a compound selected from the group consisting of,

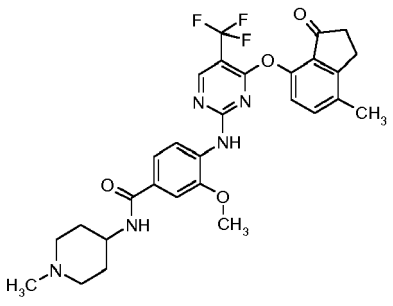


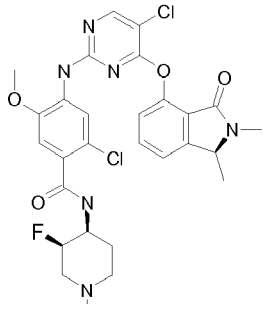


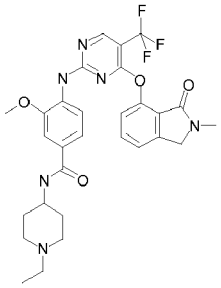


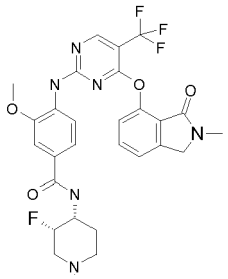


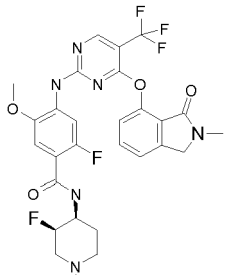


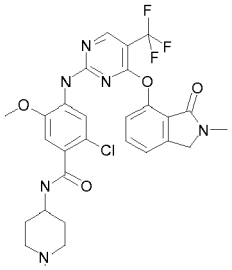


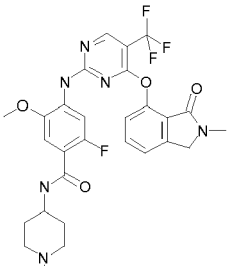


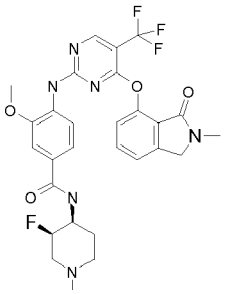


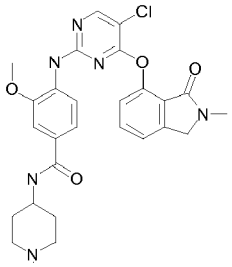


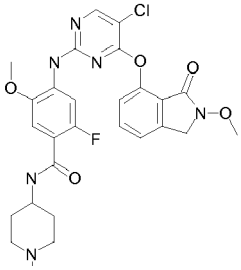


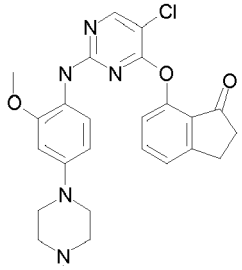


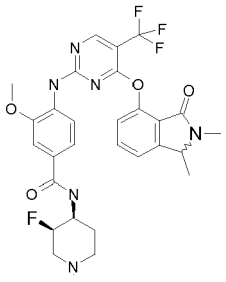


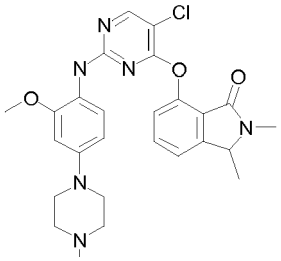


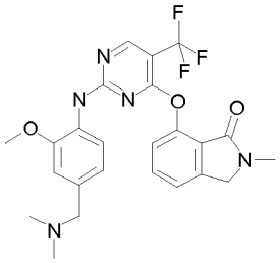


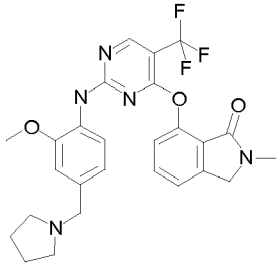


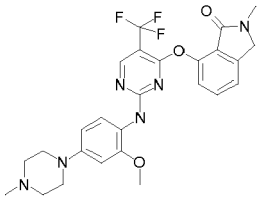


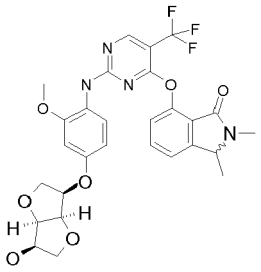


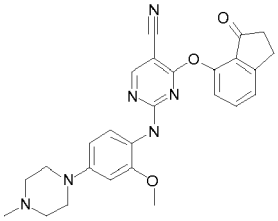


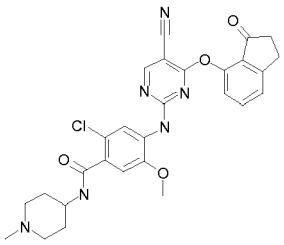


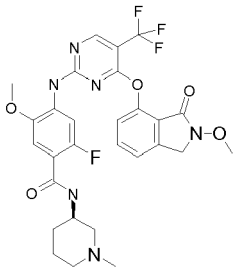


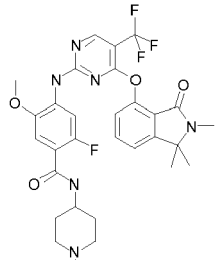


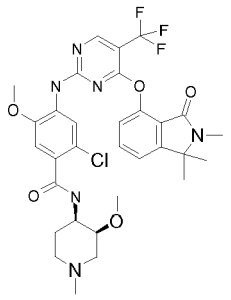


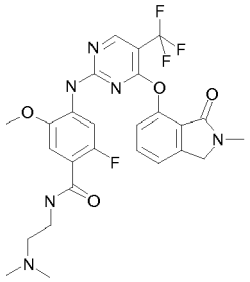


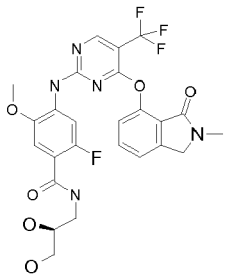


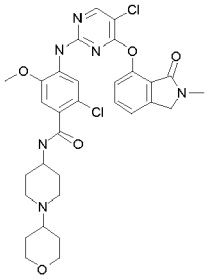


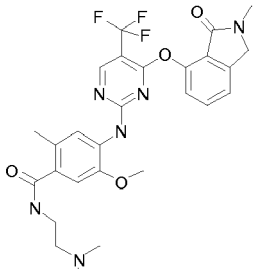


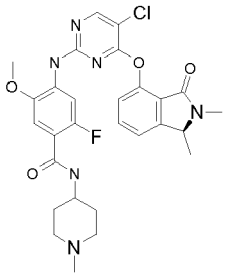


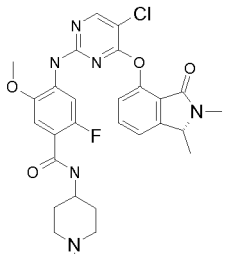


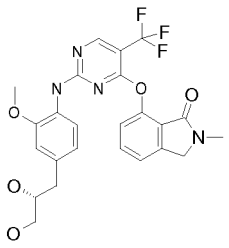


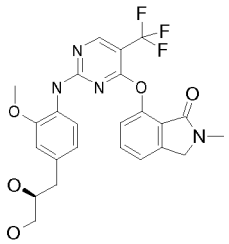


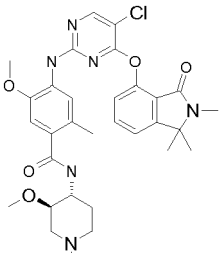












[0012] In another aspect the invention relates to compounds, or the pharmaceutically effective salts thereof, of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** for use as medicaments.

[0013] In another aspect the invention relates to compounds, or the pharmaceutically effective salts thereof, of general

formula **(1a)**, **(1b)**, **(1c)** or **(1d)** for preparing a medicament with an antiproliferative and/or pro-apoptotic activity.

[0014] In another aspect the invention relates to pharmaceutical preparations containing as active substance one or more compounds of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** or the physiologically acceptable salts thereof optionally in combination with conventional excipients and/or carriers.

[0015] In another aspect the invention relates to the use of compounds of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** for preparing a medicament for the treatment and/or prevention of cancer, infections, inflammations or autoimmune diseases.

[0016] In another aspect the invention relates to pharmaceutical preparations comprising a compound of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** and at least one further cytostatic or cytotoxic active substance, different from formula **(1a)**, **(1b)**, **(1c)** or **(1d)**, optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

Definitions

[0017] As used herein, the following definitions apply, unless stated otherwise:

Alkyl is made up of the sub-groups saturated hydrocarbon chains and unsaturated hydrocarbon chains, while the latter may be further subdivided into hydrocarbon chains with a double bond (alkenyl) and hydrocarbon chains with a triple bond (alkynyl).

Alkenyl contains at least one double bond, alkynyl contains at least one triple bond. If a hydrocarbon chain were to carry both at least one double bond and also at least one triple bond, by definition it would belong to the alkynyl sub-group. All the sub-groups mentioned above may further be divided into straight-chain (unbranched) and branched. If an alkyl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon atoms, independently of one another.

[0018] Examples of representatives of individual sub-groups are listed below.

Straight-chain (unbranched) or branched saturated hydrocarbon chains:

[0019] methyl; ethyl; *n*-propyl; isopropyl (1-methylethyl); *n*-butyl; 1-methylpropyl; isobutyl (2-methylpropyl); *sec*.-butyl (1-methylpropyl); *tert.* -butyl (1,1-dimethylethyl); *n*-pentyl; 1-methylbutyl; 1-ethylpropyl; isopentyl (3-methylbutyl); neopentyl (2,2-dimethyl-propyl); *n*-hexyl; 2,3-dimethylbutyl; 2,2-dimethylbutyl; 3,3-dimethylbutyl; 2-methyl-pentyl; 3-methylpentyl; *n*-heptyl; 2-methylhexyl; 3-methylhexyl; 2,2-dimethylpentyl; 2,3-dimethylpentyl; 2,4-dimethylpentyl; 3,3-dimethylpentyl; 2,2,3-trimethylbutyl; 3-ethylpentyl; *n*-octyl; *n*-nonyl; *n*-decyl etc.

Straight-chain (unbranched) or branched alkenyl:

[0020] vinyl (ethenyl); prop-1-enyl; allyl (prop-2-enyl); isopropenyl; but-1-enyl; but-2-enyl; but-3-enyl; 2-methyl-prop-2-enyl; 2-methyl-prop-1-enyl; 1-methyl-prop-2-enyl; 1-methyl-prop-1-enyl; 1-methylidenepropyl; pent-1-enyl; pent-2-enyl; pent-3-enyl; pent-4-enyl; 3-methyl-but-3-enyl; 3-methyl-but-2-enyl; 3-methyl-but-1-enyl; hex-1-enyl; hex-2-enyl; hex-3-enyl; hex-4-enyl; hex-5-enyl; 2,3-dimethyl-but-3-enyl; 2,3-dimethyl-but-2-enyl; 2-methylidene-3-methylbutyl; 2,3-dimethyl-but-1-enyl; hexa-1,3-dienyl; hexa-1,4-dienyl; penta-1,4-dienyl; penta-1,3-dienyl; buta-1,3-dienyl; 2,3-dimethyl-buta-1,3-diene etc.

Straight-chain (unbranched) or branched alkynyl:

[0021] ethynyl; prop-1-ynyl; prop-2-ynyl; but-1-ynyl; but-2-ynyl; but-3-ynyl; 1-methyl-prop-2-ynyl etc.

[0022] By the terms propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl etc. without any further definition are meant saturated hydrocarbon groups with the corresponding number of carbon atoms, all the isomeric forms being included.

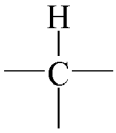
[0023] By the terms propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl etc. without any further definition are meant unsaturated hydrocarbon groups with the corresponding number of carbon atoms and a double bond, all the isomeric forms, i.e. (*Z*)/(*E*) isomers, being included where applicable.

[0024] By the terms butadienyl, pentadienyl, hexadienyl, heptadienyl, octadienyl, nonadienyl, decadienyl etc. without any further definition are meant unsaturated hydrocarbon groups with the corresponding number of carbon atoms and two double bonds, all the isomeric forms, i.e. (*Z*)/(*E*) isomers, being included where applicable.

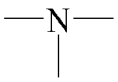
[0025] By the terms propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl etc. without any further definition are meant unsaturated hydrocarbon groups with the corresponding number of carbon atoms and a triple bond, all the isomeric forms being included.

[0026] By the term heteroalkyl are meant groups which can be derived from the alkyl as defined above in its broadest

sense if, in the hydrocarbon chains, one or more of the groups $-CH_3$ are replaced independently of one another by the groups -OH, -SH or $-NH_2$, one or more of the groups $-CH_2-$ are replaced independently of one another by the groups -O-, -S- or -NH- , one or more of the groups



are replaced by the group



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one or more of the groups =CH- are replaced by the group =N-, one or more of the groups $=CH_2$ are replaced by the group =NH or one or more of the groups =CH are replaced by the group =N, while overall there may only be a maximum of three heteroatoms in a heteroalkyl, there must be at least one carbon atom between two oxygen atoms and between two sulphur atoms or between one oxygen and one sulphur atom and the group as a whole must be chemically stable.

[0027] It is immediately apparent from the indirect definition/derivation from alkyl that heteroalkyl is made up of the sub-groups saturated hydrocarbon chains with heteroatom(s), heteroalkenyl and heteroalkynyl, and one further subdivision may be carried out into straight-chain (unbranched) and branched. If a heteroalkyl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying oxygen, sulphur, nitrogen and/or carbon atoms, independently of one another. Heteroalkyl itself may be linked to the molecule as a substituent both via a carbon atom and via a heteroatom.

Typical examples are listed below:

[0028] dimethylaminomethyl; dimethylaminoethyl (1- dimethylaminoethyl; 2-dimethylaminoethyl); dimethylaminopropyl (1-dimethylaminopropyl, 2-dimethylaminopropyl, 3-dimethylaminopropyl); diethylaminomethyl; diethylaminoethyl (1-diethylaminoethyl, 2-diethylaminoethyl); diethylaminopropyl (1-diethylaminopropyl, 2- diethylamino-propyl, 3-diethylaminopropyl); diisopropylaminoethyl (1-diisopropylaminoethyl, 2-diisopropylaminoethyl); bis-2-methoxyethylamino; [2-(dimethylamino-ethyl)-ethyl-amino]-methyl; 3-[2-(dimethylamino-ethyl)-ethyl-amino]-propyl; hydroxymethyl; 2-hydroxyethyl; 3-hydroxypropyl; methoxy; ethoxy; propoxy; methoxymethyl; 2-methoxyethyl etc.

[0029] Halogen denotes fluorine, chlorine, bromine and/or iodine atoms.

[0030] Haloalkyl is derived from alkyl as hereinbefore defined in its broadest sense, when one or more hydrogen atoms of the hydrocarbon chain are replaced independently of one another by halogen atoms, which may be identical or different. It is immediately apparent from the indirect definition/derivation from alkyl that haloalkyl is made up of the sub-groups saturated halohydrocarbon chains, haloalkenyl and haloalkynyl, and further subdivision may be made into straight-chain (unbranched) and branched. If a haloalkyl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon atoms, independently of one another.

[0031] Typical examples include $-CF_3$; $-CHF_2$; $-CH_2F$; $-CF_2CF_3$; $-CHFCF_3$; $-CH_2CF_3$; $-CF_2CH_3$; $-CHFCH_3$; $-CF_2CF_2CF_3$; $-CF_2CH_2CH_3$; $-CF=CF_2$; $-CCl=CH_2$; $-CBr=CH_2$; $-CI=CH_2$; $-C\equiv C-CF_3$;$-CHFCH_2CH_3$; and $-CHFCH_2CF_3$.

[0032] Cycloalkyl is made up of the sub-groups monocyclic hydrocarbon rings, bicyclic hydrocarbon rings and spirohydrocarbon rings, while each sub-group may be further subdivided into saturated and unsaturated (cycloalkenyl). The term unsaturated means that in the ring system in question there is at least one double bond, but no aromatic system is formed. In bicyclic hydrocarbon rings two rings are linked such that they have at least two carbon atoms in common. In spirohydrocarbon rings one carbon atom (spiroatom) is shared by two rings. If a cycloalkyl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon atoms, independently of one another. Cycloalkyl itself may be linked to the molecule as substituent via any suitable position of the ring system.

[0033] Typical examples of individual sub-groups are listed below.

monocyclic saturated hydrocarbon rings:

[0034] cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; cycloheptyl etc.

monocyclic unsaturated hydrocarbon rings:

[0035] cycloprop-1-enyl; cycloprop-2-enyl; cyclobut-1-enyl; cyclobut-2-enyl; cyclopent-1-enyl; cyclopent-2-enyl; cyclopent-3-enyl; cyclohex-1-enyl; cyclohex-2-enyl; cyclohex-3-enyl; cyclohept-1-enyl; cyclohept-2-enyl; cyclohept-3-enyl; cyclohept-4-enyl; cyclobuta-1,3-dienyl; cyclopenta-1,4-dienyl; cyclopenta-1,3-dienyl; cyclopenta-2,4-dienyl; cyclohexa-1,3-dienyl; cyclohexa-1,5-dienyl; cyclohexa-2,4-dienyl; cyclohexa-1,4-dienyl; cyclohexa-2,5-dienyl etc.

saturated and unsaturated bicyclic hydrocarbon rings:

[0036] bicyclo[2.2.0]hexyl; bicyclo[3.2.0]heptyl; bicyclo[3.2.1]octyl; bicyclo[2.2.2]octyl; bicyclo[4.3.0]nonyl (octahydroindenyl); bicyclo[4.4.0]decyl (decahydronaphthalene); bicyclo[2,2,1]heptyl (norbornyl); (bicyclo[2.2.1]hepta-2,5-dienyl (norborna-2,5-dienyl); bicyclo[2,2,1]hept-2-enyl (norbornenyl); bicyclo[4.1.0]heptyl (norcaranyl); bicyclo-[3.1.1]heptyl (pinanyl) etc.

saturated and unsaturated spirohydrocarbon rings:

[0037] spiro[2.5]octyl, spiro[3.3]heptyl, spiro[4.5]dec-2-ene etc.

[0038] Cycloalkylalkyl denotes the combination of the above-defined groups alkyl and cycloalkyl, in each case in their broadest sense. The alkyl group as substituent is directly linked to the molecule and is in turn substituted by a cycloalkyl group. The alkyl and cycloalkyl may be linked in both groups via any carbon atoms suitable for this purpose. The respective sub-groups of alkyl and cycloalkyl are also included in the combination of the two groups.

[0039] Aryl denotes mono-, bi- or tricyclic carbon rings with at least one aromatic ring. If an aryl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon atoms, independently of one another. Aryl itself may be linked to the molecule as substituent via any suitable position of the ring system.

[0040] Typical examples include phenyl, naphthyl, indanyl (2,3-dihydroindenyl), 1,2,3,4-tetrahydronaphthyl and fluorenyl.

[0041] Carbo-bicyclic ring systems include for example indanyl, 1,2,3,4-tetrahydronaphthyl and 6,7,8,9-tetrahydrobenzocycloheptyl.

[0042] Arylalkyl denotes the combination of the groups alkyl and aryl as hereinbefore defined, in each case in their broadest sense. The alkyl group as substituent is directly linked to the molecule and is in turn substituted by an aryl group. The alkyl and aryl may be linked in both groups via any carbon atoms suitable for this purpose. The respective sub-groups of alkyl and aryl are also included in the combination of the two groups.

[0043] Typical examples include benzyl; 1-phenylethyl; 2-phenylethyl; phenylvinyl; phenylallyl etc.

[0044] Heteroaryl denotes monocyclic aromatic rings or polycyclic rings with at least one aromatic ring, which, compared with corresponding aryl or cycloalkyl, contain instead of one or more carbon atoms one or more identical or different heteroatoms, selected independently of one another from among nitrogen, sulphur and oxygen, while the resulting group must be chemically stable. If a heteroaryl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon and/or nitrogen atoms, independently of one another. Heteroaryl itself as substituent may be linked to the molecule via any suitable position of the ring system, both carbon and nitrogen.

[0045] Typical examples are listed below.

monocyclic heteroaryls:

[0046] furyl; thienyl; pyrrolyl; oxazolyl; thiazolyl; isoxazolyl; isothiazolyl; pyrazolyl; imidazolyl; triazolyl; tetrazolyl; oxadiazolyl; thiadiazolyl; pyridyl; pyrimidyl; pyridazinyl; pyrazinyl; triazinyl; pyridyl-*N*-oxide; pyrrolyl-*N*-oxide; pyrimidinyl-*N*-oxide; pyridazinyl-*N*-oxide; pyrazinyl-*N*-oxide; imidazolyl-*N*-oxide; isoxazolyl-*N*-oxide; oxazolyl-*N*-oxide; thiazolyl-*N*-oxide; oxadiazolyl-*N*-oxide; thiadiazolyl-*N*-oxide; triazolyl-*N*-oxide; tetrazolyl-*N*-oxide etc.

polycyclic heteroaryls:

[0047] indolyl; isoindolyl; benzofuryl; benzothienyl; benzoxazolyl; benzothiazolyl; benzisoxazolyl; benzisothiazolyl; benzimidazolyl; indazolyl; isoquinolinyl; quinolinyl; quinoxalinyl; cinnolinyl; phthalazinyl; quinazolinyl; benzotriazinyl; indolizinyl; oxazolopyridyl; imidazopyridyl; naphthyridinyl; indolinyl; isochromanyl; chromanyl; tetrahydroisoquinolinyl; isoindolinyl; isobenzotetrahydrofuryl; isobenzotetrahydrothienyl; isobenzothienyl; benzoxazolyl; pyridopyridyl; benzotetrahydrofuryl; benzotetrahydrothienyl; purinyl; benzodioxolyl; phenoxazinyl; phenothiazinyl; pteridinyl; benzothiazolyl; imidazopyridyl; imidazothiazolyl; dihydrobenzisoxazinyl; benzisoxazinyl; benzoxazinyl; dihydrobenzisothiazinyl; benzopyranyl; benzothiopyranyl; cumarinyl; isocumarinyl; chromonyl; chromanonyl; tetrahydroquinolinyl; dihydroquinolinyl; dihydroquinolinonyl; dihydroisoquinolinonyl; dihydrocumarinyl; dihydroisocumarinyl; isoindolinonyl; benzodioxanyl; ben-

zoxazolinonyl; quinolinyl-*N*-oxide; indolyl-*N*-oxide; indolinyl-*N*-oxide; isoquinolyl-*N*-oxide; quinazolinyl-*N*-oxide; quinoxalinyl-*N*-oxide; phthalazinyl-*N*-oxide; indolizinyl-*N*-oxide; indazolyl-*N*-oxide; benzothiazolyl-*N*-oxide; benzimidazolyl-*N*-oxide; benzo-thiopyranyl-S-oxide and benzothiopyranyl-*S,S*-dioxide etc.

[0048] Hetero-bicyclic ring systems include for example dihydrobenzofuryl, dihydroisobenzofuryl, dihydroindolyl dihydroisoindolyl, dihydrobenzthiophenyl, dihydroisobenzthiophenyl, dihydroindazolyl, 1,2-benzisoxazolyl, 1*H*-1,2-benzisoxazolyl, 1,2 benzthiazolyl, 2,3-tetrahydro-1*H*-isoquinolinyl, 3,4-tetrahydro-2*H*-isoquinolinyl, tetrahydroquinolinyl, chromanyl, isochromanyl, isochromenyl, thiochromanyl, thiochromenyl, dihydro-2*H*-phthalazinyl, tetrahydrocinnolinyl, tetrahydroquinazolinyl, tetrahydrobenzodiazepinyl and tetrahydrobenzoxazepinyl.

[0049] Heteroarylalkyl denotes the combination of the alkyl and heteroaryl groups defined hereinbefore, in each case in their broadest sense. The alkyl group as substituent is directly linked to the molecule and is in turn substituted by a heteroaryl group. The linking of the alkyl and heteroaryl may be achieved on the alkyl side via any carbon atoms suitable for this purpose and on the heteroaryl side by any carbon or nitrogen atoms suitable for this purpose. The respective sub-groups of alkyl and heteroaryl are also included in the combination of the two groups.

[0050] By the term heterocycloalkyl are meant groups which are derived from the cycloalkyl as hereinbefore defined if in the hydrocarbon rings one or more of the groups $-CH_2-$ are replaced independently of one another by the groups -O-, -S- or -NH- or one or more of the groups =CH- are replaced by the group =N-, while not more than five heteroatoms may be present in total, there must be at least one carbon atom between two oxygen atoms and between two sulphur atoms or between one oxygen and one sulphur atom and the group as a whole must be chemically stable. Heteroatoms may simultaneously be present in all the possible oxidation stages (sulphur → sulphoxide -SO-, sulphone $-SO_2-$; nitrogen → N-oxide). It is immediately apparent from the indirect definition/derivation from cycloalkyl that heterocycloalkyl is made up of the sub-groups monocyclic hetero-rings, bicyclic hetero-rings and spirohetero-rings, while each sub-group can also be further subdivided into saturated and unsaturated (heterocycloalkenyl). The term unsaturated means that in the ring system in question there is at least one double bond, but no aromatic system is formed. In bicyclic hetero-rings two rings are linked such that they have at least two atoms in common. In spirohetero-rings one carbon atom (spiroatom) is shared by two rings. If a heterocycloalkyl is substituted, the substitution may be mono- or polysubstitution in each case, at all the hydrogen-carrying carbon and/or nitrogen atoms, independently of one another. Heterocycloalkyl itself as substituent may be linked to the molecule via any suitable position of the ring system.

[0051] Typical examples of individual sub-groups are listed below.

monocyclic heterorings (saturated and unsaturated):

[0052] tetrahydrofuryl; pyrrolidinyl; pyrrolinyl; imidazolidinyl; thiazolidinyl; imidazolinyl; pyrazolidinyl; pyrazolinyl; piperidinyl; piperazinyl; oxiranyl; aziridinyl; azetidinyl; 1,4-dioxanyl; azepanyl; diazepanyl; morpholinyl; thiomorpholinyl; homomorpholinyl; homopiperidinyl; homopiperazinyl; homothiomorpholinyl; thiomorpholinyl-*S*-oxide; thiomorpholinyl-*S*,*S*-dioxide; 1,3-dioxolanyl; tetrahydropyranyl; tetrahydrothiopyranyl; [1,4]-oxazepanyl; tetrahydrothienyl; homothiomorpholinyl-S,S-dioxide; oxazolidinonyl; dihydropyrazolyl; dihydropyrrolyl; dihydropyrazinyl; dihydropyridyl; dihydro-pyrimidinyl; dihydrofuryl; dihydropyranyl; tetrahydrothienyl-*S*-oxide; tetrahydrothienyl-*S*,*S*-dioxide; homothiomorpholinyl-S-oxide; 2,3-dihydroazet; 2*H*-pyrrolyl; 4*H*-pyranyl; 1,4-dihydropyridinyl etc.

bicyclic heterorings (saturated and unsaturated):

[0053] 8-azabicyclo[3.2.1]octyl; 8-azabicyclo[5.1.0]octyl; 2-oxa-5-azabicyclo[2.2.1]heptyl; 8-oxa-3-aza-bicyclo[3.2.1]octyl; 3,8-diaza-bicyclo[3.2.1]octyl; 2,5-diaza-bicyclo-[2.2.1]heptyl; 1-aza-bicyclo[2.2.2]octyl; 3,8-diaza-bicyclo[3.2.1]octyl; 3,9-diaza-bicyclo[4.2.1]nonyl; 2,6-diaza-bicyclo[3.2.2]nonyl; hexahydro-furo[3,2-b]furyl; etc.

spiro-heterorings (saturated and unsaturated):

[0054] 1,4-dioxa-spiro[4.5]decyl; 1-oxa-3,8-diaza-spiro[4.5]decyl; and 2,6-diaza-spiro[3.3]heptyl; 2,7-diaza-spiro[4.4]nonyl; 2,6-diaza-spiro[3.4]octyl; 3,9-diaza-spiro[5.5]undecyl; 2,8-diaza-spiro[4.5]decyl etc.

[0055] Heterocycloalkylalkyl denotes the combination of the alkyl and heterocycloalkyl groups defined hereinbefore, in each case in their broadest sense. The alkyl group as substituent is directly linked to the molecule and is in turn substituted by a heterocycloalkyl group. The linking of the alkyl and heterocycloalkyl may be achieved on the alkyl side via any carbon atoms suitable for this purpose and on the heterocycloalkyl side by any carbon or nitrogen atoms suitable for this purpose. The respective sub-groups of alkyl and heterocycloalkyl are also included in the combination of the two groups.

[0056] By the term "suitable substituent" is meant a substituent that on the one hand is fitting on account of its valency and on the other hand leads to a system with chemical stability.

[0057] By "prodrug" is meant an active substance in the form of its precursor metabolite. (Prodrugs do not from part

of the invention) A distinction may be made between partly multi-part carrier-prodrug systems and biotransformation systems. The latter contain the active substance in a form that requires chemical or biological metabolisation. The skilled man will be familiar with prodrug systems of this kind (Sloan, Kenneth B.; Wasdo, Scott C. The role of prodrugs in penetration enhancement. Percutaneous Penetration Enhancers (2nd Edition) (2006).51-64; Lloyd, Andrew W. Prodrugs. Smith and Williams' Introduction to the Principles of Drug Design and Action (4th Edition) (2006), 211-232; Neervannan, Seshadri. Strategies to impact solubility and dissolution rate during drug lead optimization: salt selection and prodrug design approaches. American Pharmaceutical Review (2004), 7(5), 108.110-113). A suitable prodrug contains for example a substance of the general formulae which is linked via an enzymatically cleavable linker (e.g. carbamate, phosphate, N-glycoside or a disulphide group to a dissolution-improving substance (e.g. tetraethyleneglycol, saccharides, amino acids). Carrier-prodrug systems contain the active substance as such, bound to a masking group which can be cleaved by the simplest possible controllable mechanism. The function of masking groups according to the invention in the compounds according to the invention is to neutralise the charge for improving cell uptake. If the compounds according to the invention are used with a masking group, these may also additionally influence other pharmacological parameters, such as for example oral bioavailability, tissue distribution, pharmacokinetics and stability against non-specific phosphatases. The delayed release of the active substance may also involve a sustained-release effect. In addition, modified metabolisation may occur, thus resulting in a higher efficiency of the active substance or organic specificity. In the case of a prodrug formulation, the masking group or a linker that binds the masking group to the active substance is selected such that the prodrug is sufficiently hydrophilic to be dissolved in the blood serum, has sufficient chemical and enzymatic stability to reach the activity site and is also sufficiently hydrophilic to ensure that it is suitable for diffusion-controlled membrane transport. Furthermore, it should allow chemically or enzymatically induced release of the active substance within a reasonable period and, it goes without saying, the auxiliary components released should be non-toxic. Within the scope of the invention, however, the compound without a mask or linker, and a mask, may be regarded as a prodrug which first of all has to be prepared in the cell from the ingested compound by enzymatic and biochemical processes.

List of abbreviations

[0058]

abs.	absolute, anhydrous
Ac	acetyl
Bn	benzyl
Boc	*tert*.-butyloxycarbonyl
Bu	butyl
c	concentration
cHex	cyclohexane
d	day(s)
TLC	thin layer chromatography
DCM	dichloromethane
DEA	diethylamine
DIPEA	*N*-ethyl-*N*,*N*-diisopropylamine (Hünig base)
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulphoxide
ESI	electron spray ionization
Et	ethyl
EtOH	ethanol
h	hour(s) *O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyl-uronium
HATU	tetrafluorophosphate
hex	hexyl
HPLC	high performance liquid chromatography
i	iso
IR	infra red spectroscopy
conc.	concentrated
LC	liquid chromatography
Me	methyl
MeOH	methanol
min	minute(s)
MPLC	medium pressure liquid chromatography
MS	mass spectrometry

NMP	*N*-methylpyrrolidone
NP	normal phase
Pd_2dba_3	tris (dibenzylideneacetone)dipalladium(0)
Ph	phenyl
Pr	propyl
Py	pyridine
rac	racemic
R_f (Rf)	retention factor
RP	reversed phase
RT	ambient temperature
TBTU	*O*-(benzotriazol-1-yl)-*N*,*N*,*N'*,*N'*-tetramethyl-uronium tetrafluoroborate
Temp.	temperature
tert.	tertiary
TFA	trifluoroacetic acid
THF	tetrahydrofuran
$t_{Ret.}$	retention time (HPLC)
UV	ultraviolet
X-Phos	2-dicyclohexylphosphiono-2',4', 6' triisopropyl-1,1'-biphenyl

[0059] Features and advantages of the present invention will become apparent from the following detailed Examples which illustrate the fundamentals of the invention by way of example, without restricting its scope (Only examples covered by the scope of the claims form part of the invention). :

Preparation of the compounds according to the invention

General

[0060] All the reactions are carried out - unless stated otherwise - in commercially obtainable apparatus using methods conventionally used in chemical laboratories.

[0061] Air- and/or moisture-sensitive starting materials are stored under protective gas and corresponding reactions and manipulations using them are carried out under protective gas (nitrogen or argon).

[0062] **Microwave reactions** are carried out in an Initiator made by Biotage or an Explorer made by CEM in sealed containers (preferably 2, 5 or 20 mL), preferably with stirring.

Chromatography

[0063] For the preparative medium pressure chromatography (MPLC, normal phase) silica gel is used which is made by Millipore (named: Granula Silica Si-60A 35-70 μm) or C-18 RP-silica gel (RP-phase) made by Macherey Nagel (named: Polygoprep 100-50 C18).

[0064] The thin layer chromatography is carried out on ready-made silica gel 60 TLC plates on glass (with fluorescence indicator F-254) made by Merck.

[0065] The preparative high pressure chromatography (HPLC) is carried out using columns made by Waters (named: XTerra Prep. MS C18, 5 μM, 30 x 100 mm or XTerra Prep. MS C18, 5 μm, 50 x 100 mm OBD or Symmetrie C18, 5 μm, 19 x 100 mm or Sunfire C18 OBD, 19 x 100 mm, 5 μm or Sunfire Prep C10 μm OBD 50 x 150 mm or X-Bridge Prep C18 5 μm OBD 19 x 50 mm), Agilent (named: Zorbax SB-C8 5 μm PrepHT 21.2 x 50 mm) and Phenomenex (named: Gemini C18 5 μm AXIA 21.2 x 50 mm or Gemini C18 10 μm 50 x 150 mm), the analytical HPLC (reaction control) is carried out with columns made by Agilent (named: Zorbax SB-C8, 5 μm, 21.2 x 50 mm or Zorbax SB-C8 3.5 μm 2.1 x 50 mm) and Phenomenex (named: Gemini C18 3 μm 2 x 30 mm).

HPLC mass spectroscopy/UV spectrometry

[0066] The retention times/MS-ESI$^+$ for characterising the examples are obtained using an HPLC-MS apparatus (high performance liquid chromatography with mass detector) made by Agilent. Compounds that elute with the injection peak are given the retention time $t_{Ret.}$ = 0.00.

Method A:

[0067]

Column:	Waters, Xterra MS C18, 2.5 μm, 2.1 x 30 mm, Part.No. 186000592	
Eluant:	A: H_2O with 0.1% HCOOH; B: acetonitrile (HPLC grade)	
Detection:	MS: Positive and negative mode	
Mass range:	120 - 900 m/z	
Fragmentor:	120	
Gain EMV:	1; Threshold: 150; Stepsize: 0.25; UV: 254 nm ; Bandwidth: 1	
Injection:	Inj. Vol. 5 μL	
Separation:	Flow 1.10 mL/min	
Column temp.:	40°C	
Gradient:	0.00 min: 5 %	solvent B
	0.00 - 2.50 min:	5 % → 95 % solvent B
	2.50 - 2.80 min:	95 % solvent B
	2.81 - 3.10 min:	95 % → 5 % solvent B

Method B:

[0068]

Column:	Waters, Xterra MS C18, 2.5 μm, 2.1 x 50 mm, Part.No. 186000594
Eluant:	A: H_2O with 0.1 % HCOOH; B: acetonitrile with 0.1 % HCOOH
Detection:	MS: Positive and negative mode
Mass range:	100 - 1200 m/z
Fragmentor:	70
Gain EMV:	Threshold: 1 mAU; Stepsize: 2 nm; UV: 254 nm as well as 230 nm
Injection:	Standard 1 μL
Flow:	0.6 mL/min
Column temp.:	35°C
Gradient:	0.00 min: 5 % solvent B
	0.00 - 2.50 min: 5 % → 95 % solvent B
	2.50 - 4.00 min: 95 % solvent B
	4.00 - 4.50 min: 95 % → 5 % solvent B
	4.50 - 6.00 min: 95 % solvent A

Method C:

[0069]

Column: Waters, X-Bridge C18, 3.5 μm, 2.1 x 50 mm,

Eluant:	A: H_2O with 10mM NH_3; B: acetonitrile with 10nM NH_3
Detection:	MS: Positive and negative mode
Mass range:	100 - 800 m/z
Fragmentor:	70
Gain EMV:	Threshold: 1 mAU; Stepsize: 2 nm; UV: 220-320 nm
Injection:	Standard 1 μL
Flow:	0.8 mL/min
Column temp.:	25°C
Gradient:	0.00 min: 2 % solvent B
	0.00 - 4.00 min: 2 % → 98 % solvent B
	4.00 - 6.00 min: 98 % solvent B

Method D:

[0070]

Column:	Waters, X-Bridge C18, 3.5 μm, 2.1 x 50 mm,
Eluant:	A: H_2O with 0.1 % HCOOH; B: acetonitrile with 0.1 % HCOOH
Detection:	MS: Positive and negative mode
Mass range:	100 - 800 m/z
Fragmentor:	70
Gain EMV:	Threshold: 1 mAU; Stepsize: 2 nm; UV: 220-320 nm
Injection:	Standard 1 μL
Flow:	0.8 mL/min
Column temp.:	35°C
Gradient:	0.00 min: 2 % solvent B
	0.00 - 4.00 min: 2 % → 98 % solvent B
	4.00 - 6.00 min: 98 % solvent B

Method E:

[0071]

Column:	Phenomenex Gemini C18, 3.0 μm, 2.0 x 50 mm,
Eluant:	A: H_2O with 10mM NH_3; B: acetonitrile with 10nM NH_3
Detection:	MS: Positive and negative mode
Mass range:	100 - 800 m/z
Fragmentor:	70
Gain EMV:	Threshold: 1 mAU; Stepsize: 2 nm; UV: 220-320 nm
Injection:	Standard 1 μL
Flow:	1.0 mL/min
Column temp.:	35°C
Gradient:	0.00 min: 2 % solvent B
	0.00 - 3.50 min: 2 % → 98 % solvent B
	3.50 - 6.00 min: 98 % solvent B

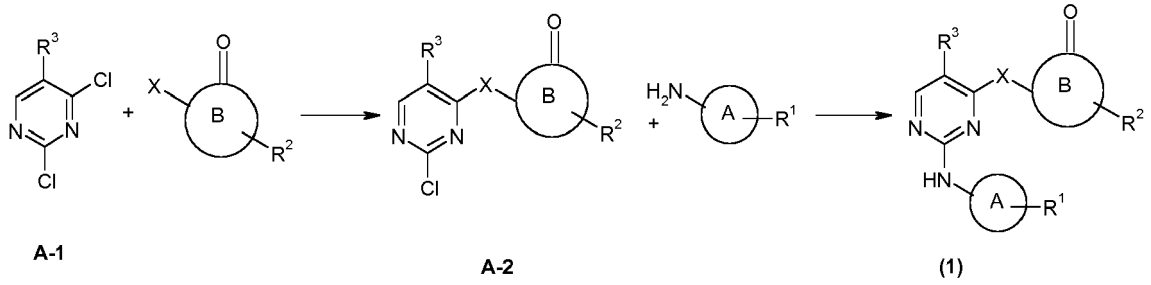
Method F:

[0072]

Column:	Phenomenex Gemini C18, 3.0 μm, 2.0 x 50 mm,
Eluant:	A: H_2O with 0.1 % HCOOH; B: acetonitrile with 0.1 % HCOOH
Detection:	MS: Positive and negative mode
Mass range:	100 - 800 m/z
Fragmentor:	70
Gain EMV:	Threshold: 1 mAU; Stepsize: 2 nm; UV: 220-320 nm
Injection:	Standard 1 μL
Flow:	1.0 mL/min
Column temp.:	35°C
Gradient:	0.00 min: 2 % solvent B
	0.00 - 3.50 min: 2 % → 98 % solvent B
	3.50 - 6.00 min: 95 % solvent B

[0073] The compounds according to the invention are prepared by the methods of synthesis described below, in which the substituents of the general formulae have the meanings specified hereinbefore. These methods are intended to illustrate the invention without restricting it to their content or limiting the scope of the compounds claimed to these Examples. Where the preparation of the starting compounds is not described, they are commercially obtainable or may be prepared analogously to known compounds or methods described herein. Substances described in the literature are prepared according to the published methods of synthesis.

Reaction scheme A



[0074] Example compounds of **type (1)** are prepared from 2,4-dichloro-pyrimidines **A-1 by** nucleophilic aromatic substitution of the chlorine in the 4 position of the pyrimidine with a phenol OR^2, a thiophenol SR^2 or by coupling benzylmetal halides $HalMetR^2$ and subsequently exchanging the second chlorine by means of an amine $A\text{-}NH_2$. Alternatively, starting from 2,4-dichloropyrimidines **A-1**, it is possible to carry out the exchange in position 2 of the pyrimidine with amines $A\text{-}NH_2$ and subsequent substitution of the chlorine in position 4 of the pyrimidine with a phenol OR^2, a thiophenol SR^2 or by coupling benzylmetal halides $HalMetR^2$. As an alternative to the conventional nucleophilic substitutions, the transition metal-catalysed reaction of $A\text{-}NH_2$ with the corresponding 2-chloropyrimidines **A-2** is possible. R^1 and R^2 are each suitable groups for arriving at example compounds.

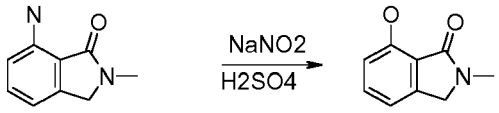
[0075] The nucleophilic aromatic substitutions at **A-1**, **A-2** and **A-3** are carried out using methods known from the literature (e.g.: WO2008/040951) in common solvents, such as for example THF, DCM, NMP, DMSO, toluene or DMF using a base such as for example DIPEA, pyridine, LiOH, Cs_2CO_3 or KO*t*Bu, an acid such as for example HCl or a Lewis acid such as for example $ZnCl_2$. The alcohols OR^2, the sulphides SR^2, the organometallic compounds $HalMetR^2$ and the amines $A\text{-}NH_2$ used are commercially obtainable or are synthesised by methods known from the literature. The 2-amino-4-oxopyrimidines, 2-amino-4-thiopyrimidines or 2-amino-4-carbapyrimidines **of type (1)** which may be obtained directly by these reaction methods may be further modified in $\mathbf{R^1}$ and $\mathbf{R^2}$ at a suitable point in the manner known from the literature or analogously to the literature to form further derivatives of **type (1).** Thus, for example, the groups $\mathbf{R^1}$ and $\mathbf{R^2}$ of directly accessible 2-amino-4-oxo-pyrimidines, 2-amino-4-thiopyrimidines or 2-amino-4-carbapyrimidines of **type (1),** which consist of a carboxylic acid, sulphonic acid, halogen-or amino-substituted aryl or heteroaryl, may be converted by reactions of substitution (at the heteroaryl itself), alkylation, acylation, amination or addition.

Starting materials

[0076] Where their preparation is not described, the starting materials are commercially obtainable, known from the literature or easily obtainable by the skilled man using general methods, for example
4-amino-2-chloro-5-methoxy-benzoic acid, 4-amino-2-fluoro-5-methoxy-benzoic acid, (WO2008/040951)
4-(4-chloro-5-trifluoromethyl-pyrimidin-2-ylamino)-benzoic acid (WO 2007003596)
4-(4-chloro-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methoxy-benzoic acid,
4-(4-chloro-5-trifluoromethyl-pyrimidin-2-ylamino)-2-chloro-5-methoxy-benzoic acid,
4-(4-chloro-5-trifluoromethyl-pyrimidin-2-ylamino)-2-fluoro-5-methoxy-benzoic acid, (analogously to WO 2007003596)
7-amino-2-methyl-2,3-dihydro-isoindol-1-one (WO2005/016894)
***tert*-butyl 4-benzylamino-3-fluoro-piperidine-1-carboxylate,** (J. Med. Chem. (1999), 42(12), 2087-2104).
8-amino-2-methyl-3,4-dihydro-isoquinolin-1-one (WO2005/016894)
benzyl (3S,4S)-4-*tert*-butoxycarbonylamino-3-hydroxy-piperidine-1-carboxylate and
benzyl (3R,4R)-4-*tert*-butoxycarbonylamino-3-hydroxy-piperidine-1-carboxylate (WO 2004/058144)

7-hydroxy-2-methyl-2,3-dihydro-isoindol-1-one

[0077]

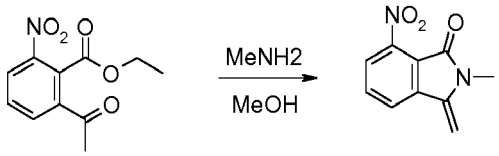


[0078] 7-amino-2-methyl-2,3-dihydro-isoindol-1-one (5 g) is suspended in a mixture of ice (12.6 g) and conc. H_2SO_4 (8.62 g). Aqueous sodium nitrite solution (2.5 molar, 16 mL) is added dropwise, so that the temperature does not rise above 0°C and the solution is stirred for 15 min at this temperature. Then H_20 (60 mL) is added and the solution is heated to 80°C for 30 min. For working up it is combined with 10 % NaCl solution (100 mL) and extracted twice with 100 mL of CH_2Cl_2. The combined organic phases are dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The final purification is carried out by preparative HPLC.

(R)-7-hydroxy-2,3-dimethyl-2,3-dihydro-isoindol-1-one and (S)-7-hydroxy-2,3-dimethyl-2,3-dihydro-isoindol-1-one

a) 2-methyl-3-methylene-7-nitro-2,3-dihydro-isoindol-1-one

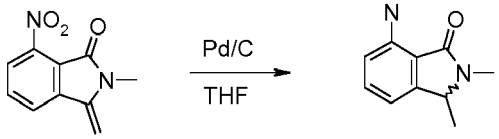
[0079]



[0080] Ethyl-2-acetyl-6-nitrobenzoate (11.12 g) is suspended in a mixture of MeOH (70 mL) and $MgSO_4$. Methylamine (2 molar in THF, 28.13 mL) is added dropwise and the solution is stirred for 15 min at this temperature. Then it is preheated to 70°C for 18 h. The solvent is eliminated in vacuo, the residue is taken up in dichloromethane (100 mL), washed with sodium chloride solution (10 %) dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. For purification it is recrystallised from toluene (250 mL).

b) 7-amino-2,3-dimethyl-2,3-dihydro-isoindol-1-one

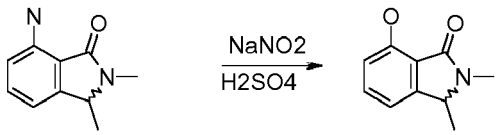
[0081]



[0082] 2-methyl-3-methylene-7-nitro-2,3-dihydro-isoindol-1-one (13.96 g) is suspended in THF and mixed with a spatula tip of Pd/C (5%) and hydrogenated under H_2 pressure (3 bar). For working up the catalyst is filtered off and the solvent is eliminated in vacuo.

c) 7-hydroxy-2,3-dimethyl-2,3-dihydro-isoindol-1-one

[0083]

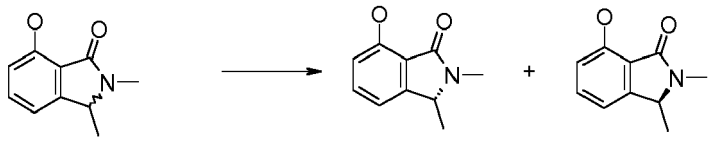


[0084] 7-amino-2,3-dimethyl-2,3-dihydro-isoindol-1-one (11.45 g) is suspended in a mixture of ice (27 g) and H_2SO_4 conc. (9.70 mL) and cooled to -10°C. Aqueous sodium nitrite solution (2.5 molar, 31.18 mL) is added dropwise, so that the temperature does not rise above 0°C and the solution is stirred for 15 min at this temperature. Then H_20 (135 mL)

is added and the solution is heated to 80°C for 15 min. For working up it is combined with 10 % NaCl solution (100 mL) and extracted twice with 100 mL of CH_2Cl_2. The organic phase is extracted with NaOH solution (0.2 molar) and then the aqueous phase is acidified (HCl aq. conc.) and re-extracted with CH_2Cl_2. The organic phase is dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo.

d) (R)-7-hydroxy-2,3-dimethyl-2,3-dihydro-isoindol-1-one and (S)-7-hydroxy-2,3-dimethyl-2,3-dihydro-isoindol-1-one

[0085]

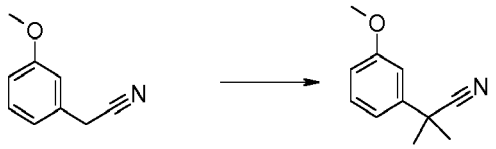


[0086] The two enantiomers are separated by chromatography of the racemate through a chirally modified column (CHIRALCEL® OD-I, n-heptane/CH2Cl2 50/50).

7-hydroxy-2,3,3-trimethyl-2,3-dihydro-isoindol-1-one

a) 2-(3-methoxy-phenyl)-2-methyl-propionitrile

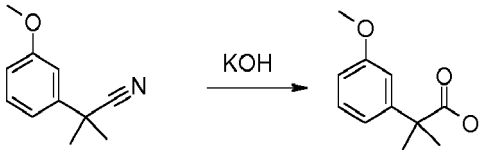
[0087]



[0088] NaH (14.13 g, 60 %) is suspended in THF (400 mL) and cooled to 0°C. (3-methoxyphenyl)-acetonitrile (20 g) is dissolved in THF (20 mL) and added dropwise. After 30 min at this temperature methyl iodide (19.46 mL) in THF (20 mL) is added. After 16 h at 0°C the reaction mixture is combined with H_20 and extracted 3 times with CH_2Cl_2. The combined organic phases are dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

b) 2-(3-methoxy-phenyl)-2-methyl-propionic acid

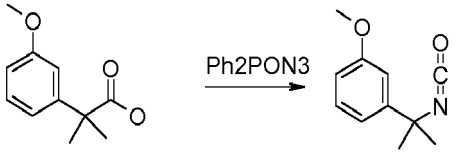
[0089]



2-(3-methoxy-phenyl)-2-methyl-propionitrile (28.55 g, 80 %) is dissolved in ethyleneglycol, combined with KOH (14.48 g) and heated to 150°C. After 18 h the reaction mixture is taken up in aqueous NaCl solution (10 %) and extracted 3 times with CH_2Cl_2 and EtOAc. The aqueous phase is then acidified with HCl (1 molar, aqueous) and extracted with EtOAc. The resulting organic phase is extracted another 3 times with HCl (1 molar, aqueous), dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

c) 1-(1-isocyanato-1-methylethyl)-3-methoxybenzene

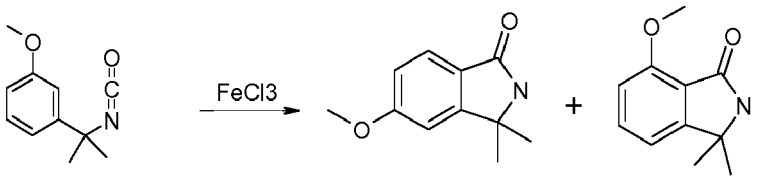
[0090]



[0091] 2-(3-methoxy-phenyl)-2-methyl-propionic acid (24.40 g) is dissolved in toluene (120 mL) and cooled to 0°C. Triethylamine (16.61 mL) and diphenylphosphorylazide (24.37 g) are added. After 0.5 h the mixture is heated to 110°C. After 3 h the reaction mixture is diluted with EtOAc, cooled to 0°C, extracted with $NaHCO_3$ solution and NaCl solution (H_2O, 10%), dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

d) 7-methoxy-3,3-dimethyl-2,3-dihydro-isoindol-1-one and 7-methoxy-3,3-dimethyl-2,3-dihydro-isoindol-1-one

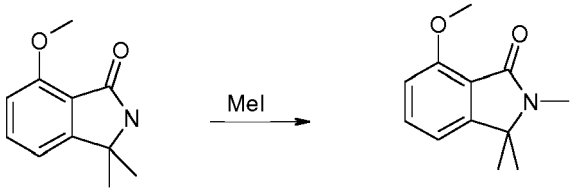
[0092]



[0093] $FeCl_3$ (40.00 g) is suspended in dichloroethane (10 mL) and cooled to 0°C. 1-(1-isocyanato-1-methylethyl)-3-methoxybenzene (21.40 g, dissolved in 10 mL dichloroethane) is added dropwise. After 1.5 h H_2O is added and the mixture is stirred for 15 min. After the addition of CH_2Cl_2 the aqueous phase is separated off and discarded. The organic phase is extracted with aqueous tartaric acid solution, dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The two regioisomers are separated using a silica gel column (cHex/EtOAc 20:80 to 0:100).

e) 7-methoxy-2,3,3-trimethyl-2,3-dihydro-isoindol-1-one

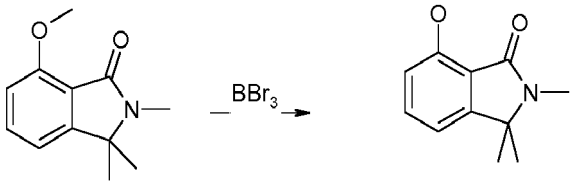
[0094]



[0095] 7-methoxy-3,3-dimethyl-2,3-dihydro-isoindol-1-one (3.16 g) is dissolved in THF (50 mL) and NaH (7.88 g) is added batchwise. After 5 min methyl iodide (7.18 mL) is added. After 18 h at 0°C the reaction mixture is combined with H_20/AcCN as well as Isolute and purified by RP HPLC.

f) 7-hydroxy-2,3,3-trimethyl-2,3-dihydro-isoindol-1-one

[0096]



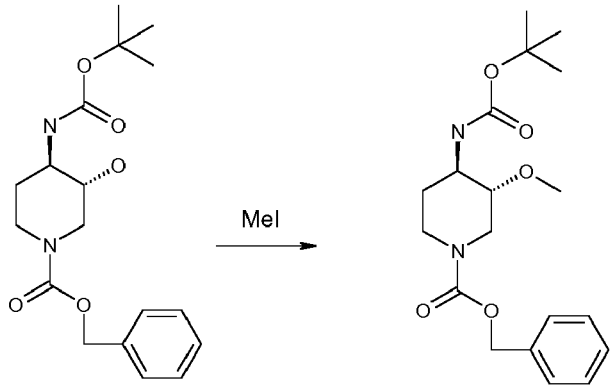
[0097] 7-methoxy-2,3,3-trimethyl-2,3-dihydro-isoindol-1-one (0.18 g) is dissolved in CH_2Cl_2 (4.5 mL) and cooled to

-78°C. After the addition of BBr_3 (1 molar in CH_2Cl_2, 2.92 mL) the reaction mixture is allowed to warm up to -10°C within 3 h. For working up it is diluted with CH_2Cl_2 and extracted with NaCl solution (H_2O, 10 %). The organic phase is dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

(3R,4R)-3-methoxy-1-methyl-piperidin-4-ylamine

a) benzyl (3R,4R)-4-*tert*-butoxycarbonylamino-3-methoxy-piperidine-1-carboxylate

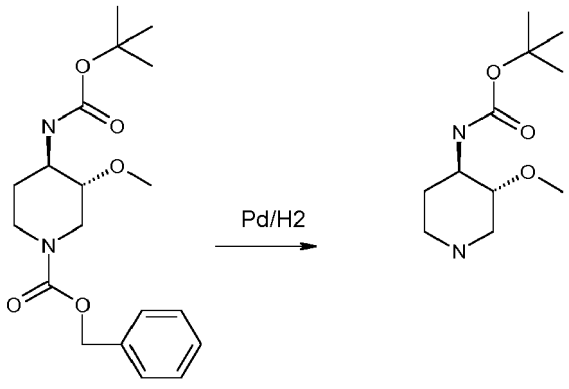
[0098]



benzyl (3S,4S)-4-*tert*-butoxycarbonylamino-3-hydroxy-piperidine-1-carboxylate (5.00 g) is dissolved in THF (6 mL) and combined with 30 mL aqueous, semiconcentrated NaOH solution, benzyltriethylammonium chloride as well as dimethylsulphate (2.26 mL). After 22 h H_2O (200 mL) is added and the mixture is extracted with EtOAc (150 mL). The organic phase is dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. Purification is carried out using a silica gel column (cHex/EtOAc 65/35).

b) tert-butyl ((3R,4R)-3-methoxy-piperidin-4-yl)-carbamate

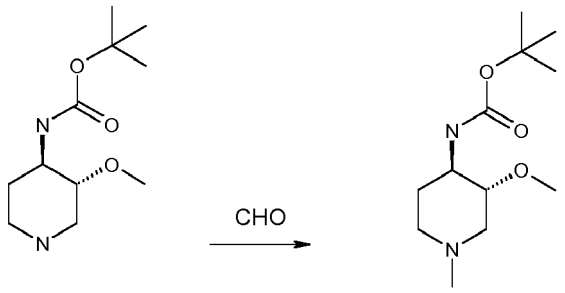
[0099]



[0100] Benzyl (3R,4R)-4-*tert*-butoxycarbonylamino-3-methoxy-piperidine-1-carboxylate (2.88 g) is dissolved in ethanol and combined with a spatula tip of Pd/C and hydrogenated under H_2 pressure (4 bar). After 18 h the catalyst is filtered off and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

c) tert-butyl ((3R,4R)-3-methoxy-1-methyl-piperidin-4-yl)-carbamate

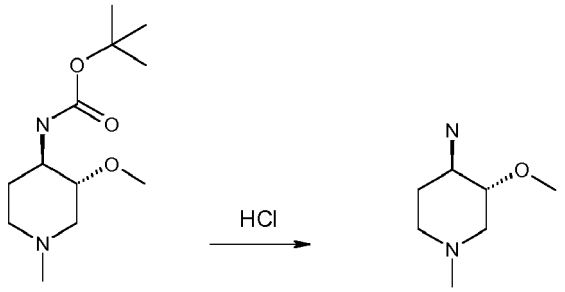
[0101]



[0102] Tert-butyl ((3R,4R)-3-methoxy-piperidin-4-yl)-carbamate (2.88 g) is dissolved with formaldehyde (1.79 mL, 37 % solution in H_2O) and acetic acid (100 μL) in DMF. Then $Na(OAc)_3BH$ (12.59 g) is added. After 20 h the reaction mixture is combined with aqueous $NaHCO_3$ solution (saturated with NaCl) and extracted 5 times with EtOAc. The combined organic phase is dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo. The residue is used in the next reaction step without any further purification.

d) (3R,4R)-3-methoxy-1-methyl-piperidin-4-ylamine

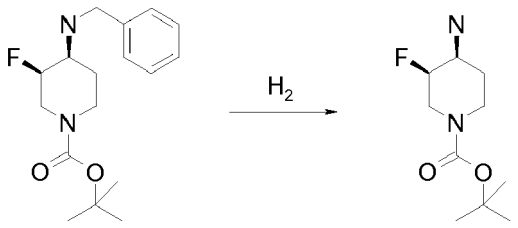
[0103]



[0104] Tert-butyl ((3R,4R)-3-methoxy-1-methyl-piperidin-4-yl)-carbamate (3.01 g) is combined with HCl (4 molar in dioxane, 25 mL). After 1 h the reaction mixture is freed from the solvent in vacuo and used in the next step without any further purification.

tert-butyl(3R,4S)-4-amino-3-fluoro-piperidine-1-carboxylate

[0105]

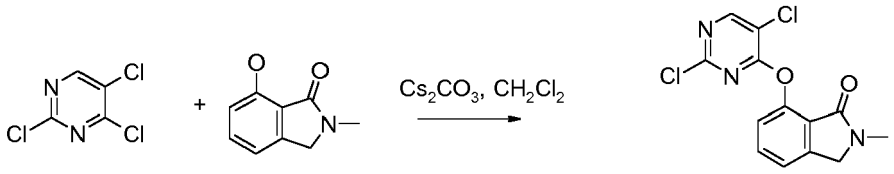


[0106] Tert-butyl (3R,4S)-4-benzylamino-3-fluoro-piperidine-1-carboxylate (2.13 g) is suspended in THF and mixed with a spatula tip of $Pd(OH)_2$ and hydrogenated under H_2 pressure (7 bar). For working up the catalyst is filtered off and the solvent is eliminated in vacuo and the residue is used in the next step without any further purification.

Example 1: Benzyl 2-chloro-4-[5-chloro-4-(2-methy|-3-oxo-2,3-dihydro-1*H*-isoindo|-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-benzoate

a) 7-(2,5-dichloro-pyrimidin-4-yloxy)-2-methyl-2,3-dihydro-isoindol-1-one

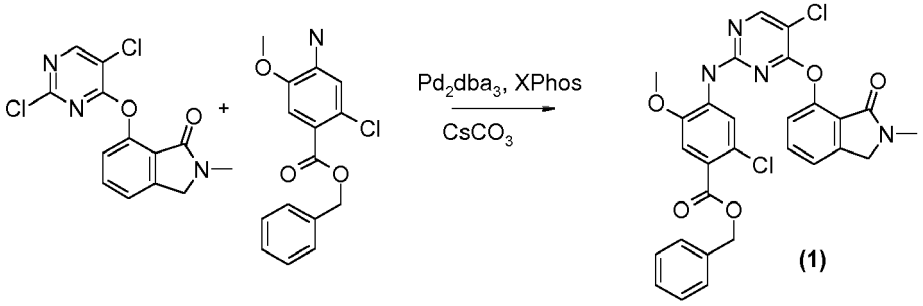
[0107]



[0108] 2,4,5-trichloropyrimidine (0.20 g) and 7-hydroxy-2-methyl-2,3-dihydro-isoindol-1-one are dissolved in DCM (10 mL), cooled to 0°C and combined with caesium carbonate (0.75 g). The cooling bath is removed and the mixture is stirred for 16 h. For working up the mixture is combined with 10 % NaCl solution (100 mL) and extracted three times with 75 mL ethyl acetate. The combined organic phases are dried on magnesium sulphate, filtered off from the desiccant and the solvent is eliminated in vacuo.

b) benzyl 2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*isoindol-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-benzoate

[0109]

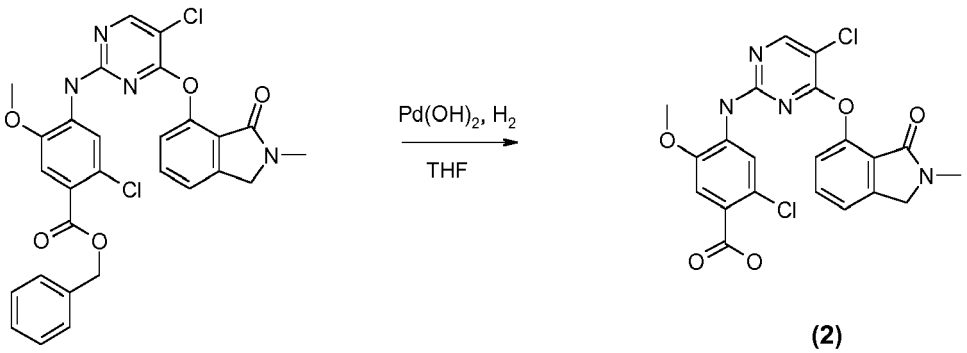


[0110] 7-(2,5-dichloro-pyrimidin-4-yloxy)-2-methyl-2,3-dihydro-isoindol-1-one (0.10 g), benzyl 4-amino-2-chloro-5-methoxy-benzoate (0.28 g), Pd_2dba_3 (18 mg), X-Phos (37 mg) and Cs_2CO_3 are weighed into a microwave vial and argon flushing is carried out. Then toluene (1 mL) and NMP (50 μL) are added, argon flushing is carried out again and the mixture is stirred for 5 min at 150°C in the microwave. For working up the mixture is diluted with ACN (20 mL) and combined with Isolute (Separtis GmbH). The solvent is eliminated in vacuo and then purified by preparative HPLC. (IC_{50} = 53 nmol)

Example 2: **2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*-isoindol-4-yloxy)-pyrimidin-2-ylamino]-5--methoxy-*N*-(1-methyl-piperidin-4-yl)-benzamide**

a) 2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*-isoindol-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-benzoic acid

[0111]

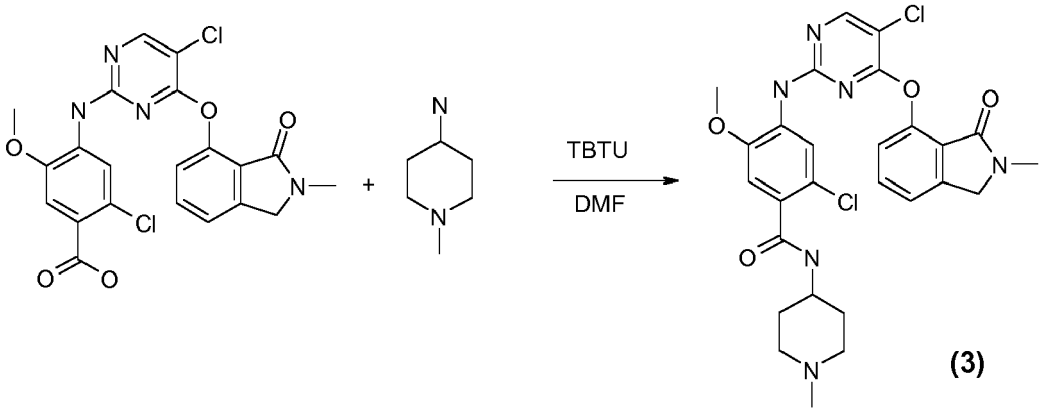


(2)

[0112] Benzyl 2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*-isoindol-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-benzoate (75 mg) is dissolved in THF (150 mL), $Pd(OH)_2$ (0.01 g) is added and the mixture is stirred for 2h under H_2 gas. For working up the mixture is diluted with ACN (20 mL) and Isolute is added. The solvent is filtered off from the catalyst and the solvent is eliminated in vacuo.

b) 2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*-isoindol-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-*N*-(1-methyl-piperidin-4-yl)-benzamide

[0113]

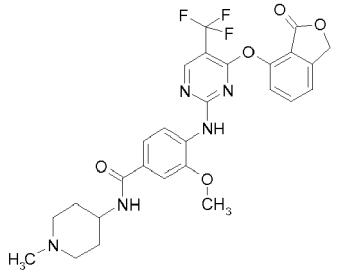


(3)

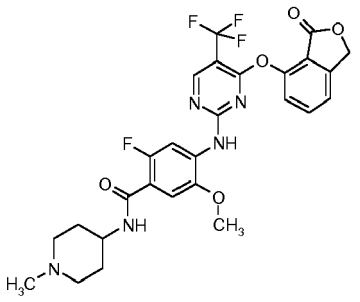
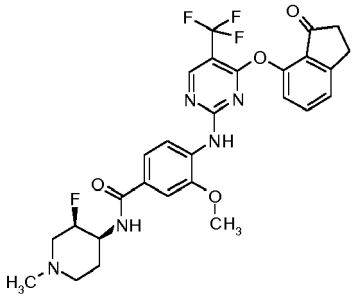
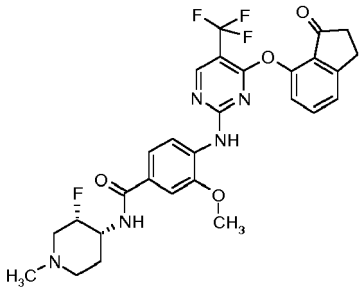
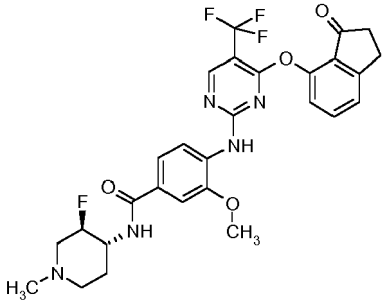
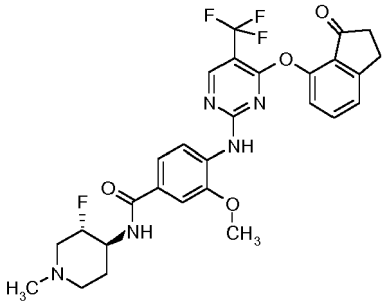
[0114] 2-chloro-4-[5-chloro-4-(2-methyl-3-oxo-2,3-dihydro-1*H*-isoindol-4-yloxy)-pyrimidin-2-ylamino]-5-methoxy-benzoic acid (65 mg), TBTU (60 mg) and DIPEA (0.1 mL) are suspended in DMF (0.50 mL) and stirred for 5 min. 1-methylpiperidin-4-amine (18 mg) is added and the reaction mixture is stirred for a further 20 min. The reaction mixture is purified by HPLC without working up. (IC_{50} = 1 nmol).

[0115] The following compounds **3** to **215** are synthesised analogously, with the corresponding 2-chloropyrimidines as educts:

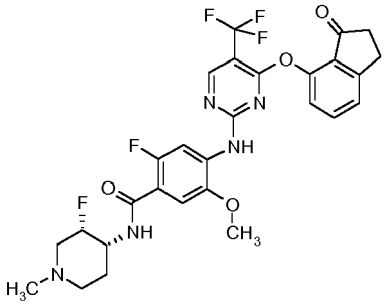
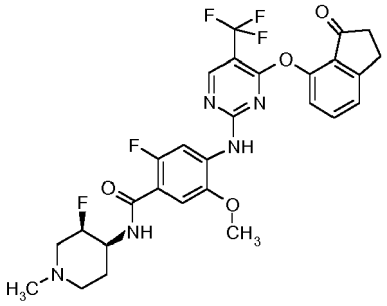
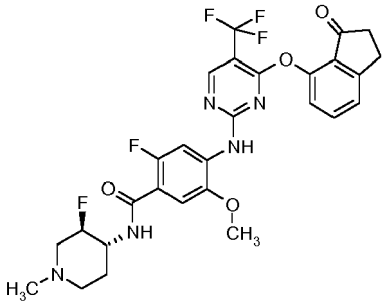
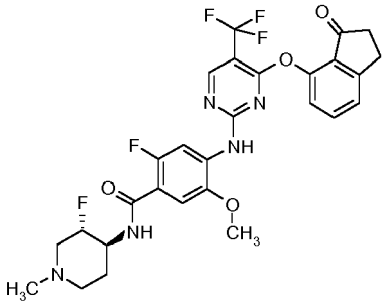
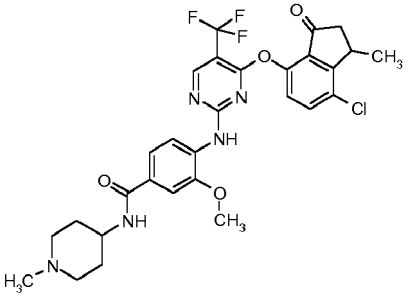
Table 1: Examples 3 - 215

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
3		1.90	558	3

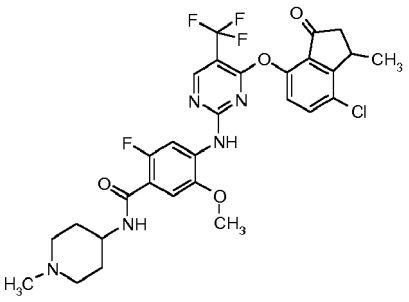
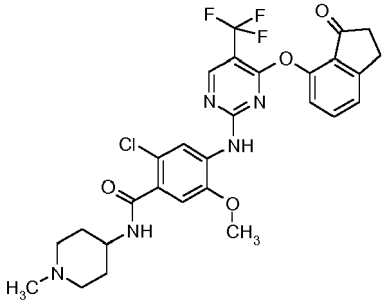
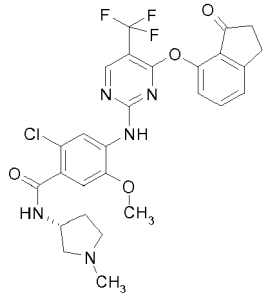
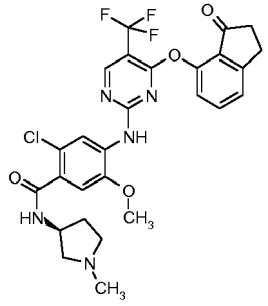
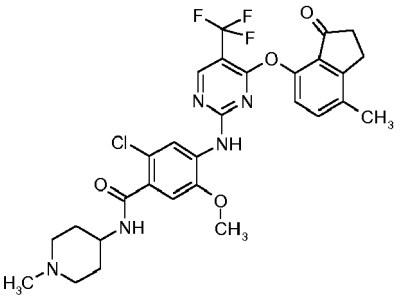
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
4		1.96	576	4
5		1.94	574	2
6		1.94	574	3
7		1.97	574	5
8		1.96	574	3

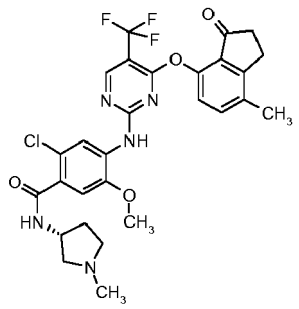
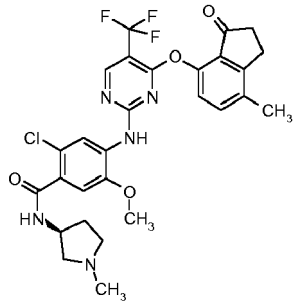
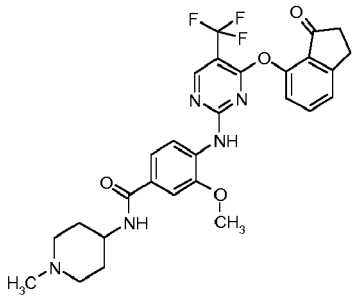
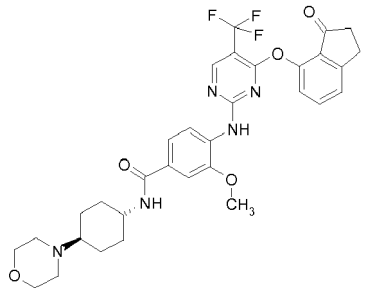
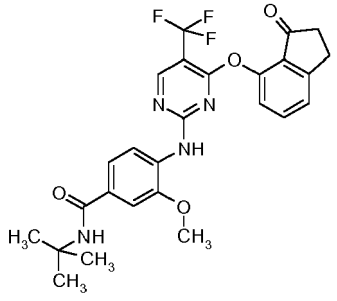
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
9		2.03	592	4
10		2.03	592	5
11		2.04	592	7
12		2.04	592	9
13		2.12	604	10

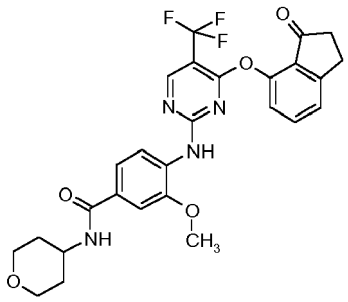
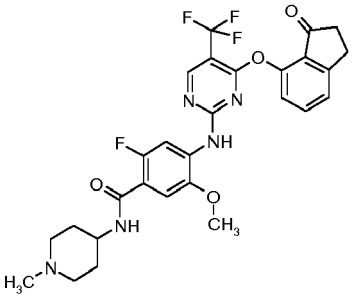
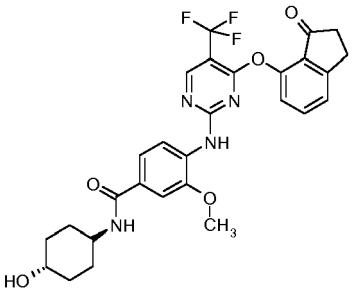
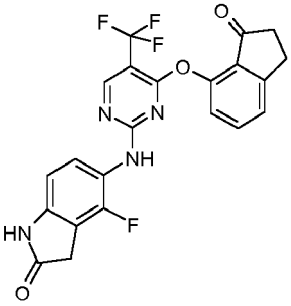
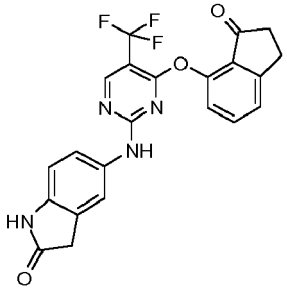
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
14		2.20	622	16
15		1.99	590	3
16		2.08	576	4
17		2.02	576	5
18		2.04	604	5

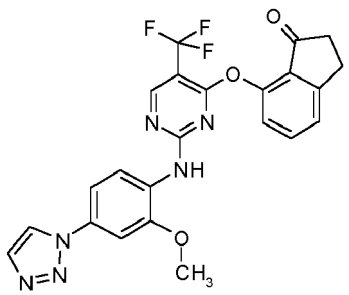
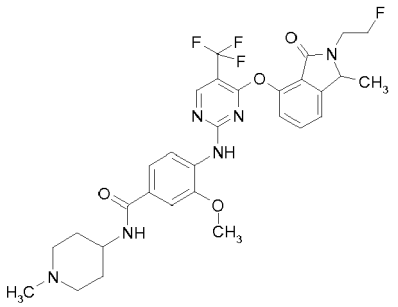
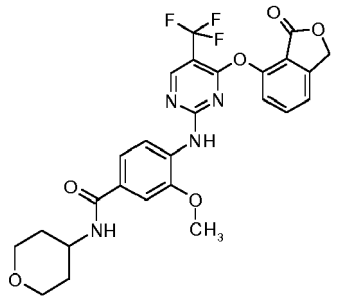
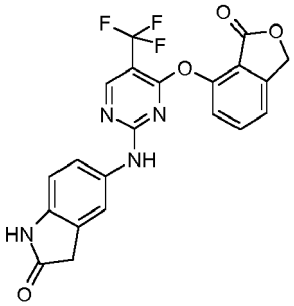
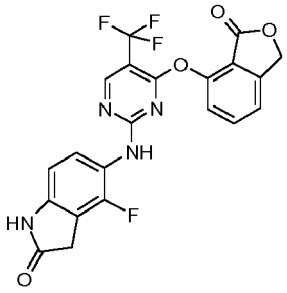
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
19		2.07	590	6
20		2.05	590	15
21		1.79	556	2
22		2.02	626	5
23		2.19	515	10

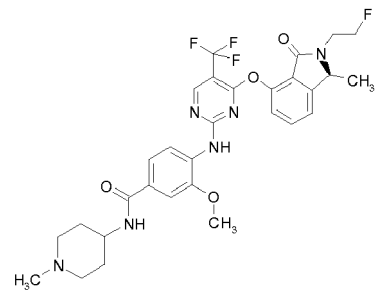
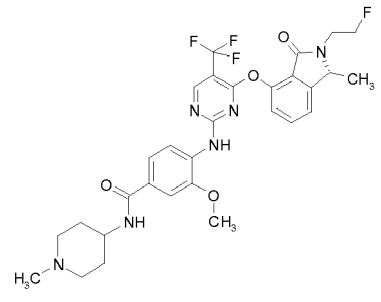
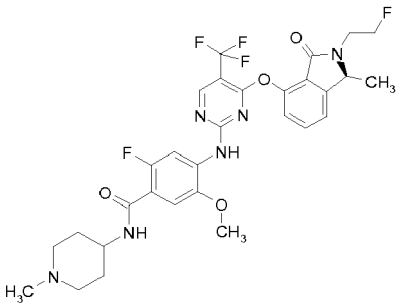
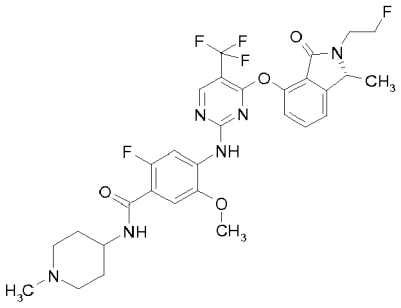
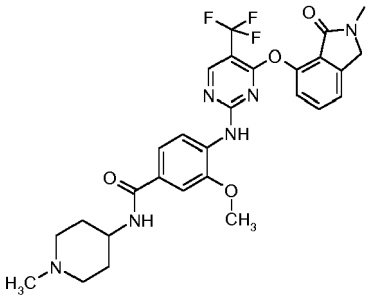
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
24		1.96	543	7
25		2.04	574	4
26		1.90	555	5
27		1.75	459	9
28		1.73	441	11

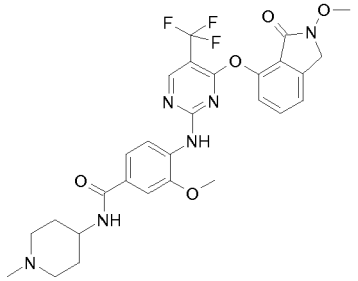
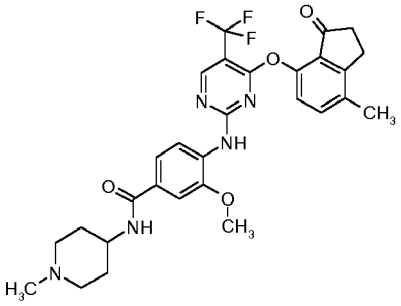
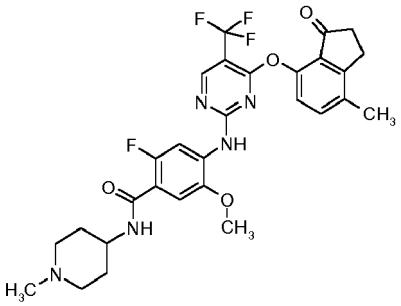
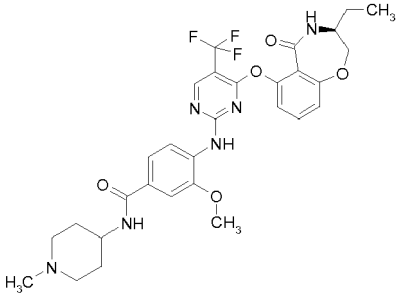
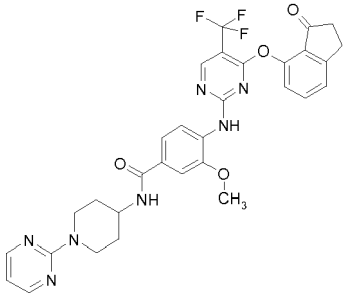
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
29		2.00	483	12
30		1.88	617	3
31		1.85	545	3
32		1.67	443	4
33		1.63	461	10

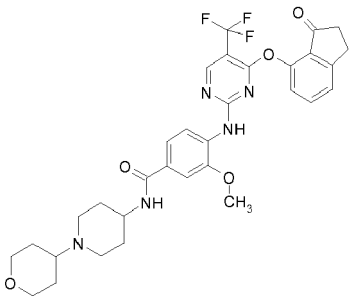
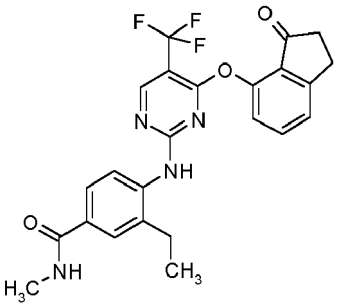
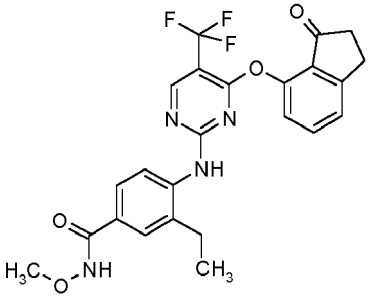
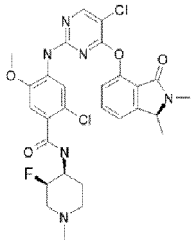
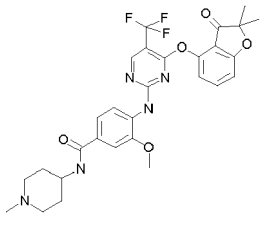
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
34		1.96	617	2
35		1.95	617	2
36		2.02	635	4
37		2.06	635	4
38		1.89	571	1

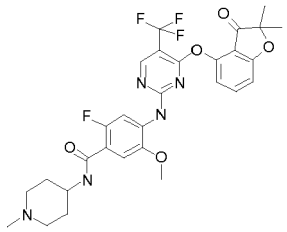
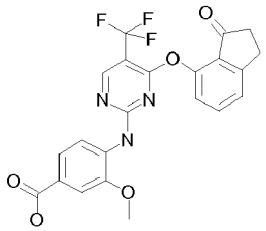
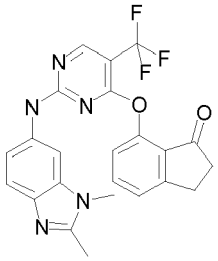
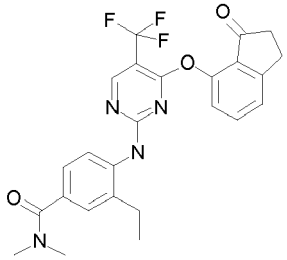
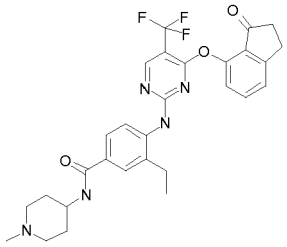
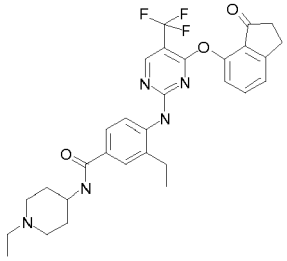
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
39		1.83	587	2
40		2.09	570	2
41		2.17	588	3
42		1.91	615	309
43		2.06	620	12

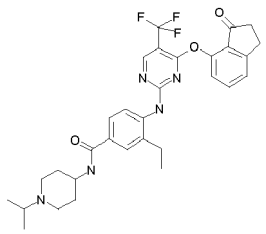
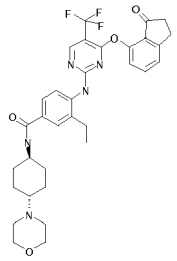
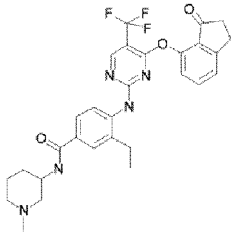
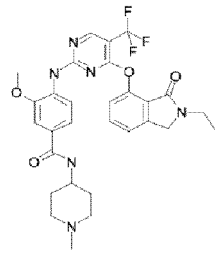
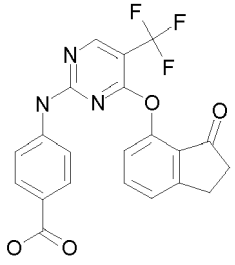
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
44		1.94	626	4
45		1.83	471	9
46		1.65	487	11
47		1.79	603	1
48		2.05	586	5

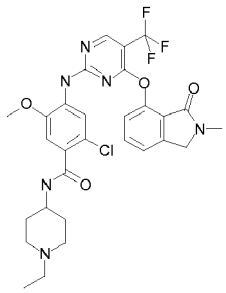
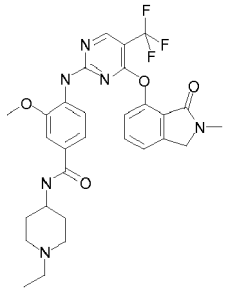
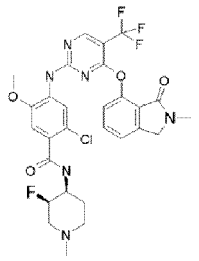
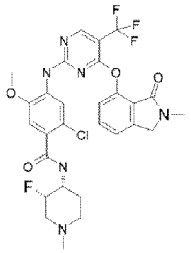
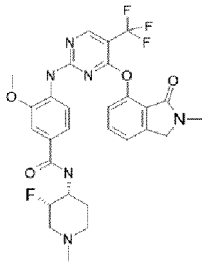
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
49		2.11	604	7
50		1.18	460	5
51		1.73	454	11
52		1.90	485	51
53		1.90	554	9
54		1.98	568	10

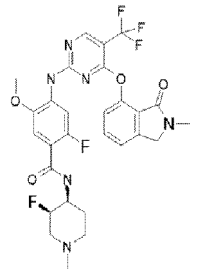
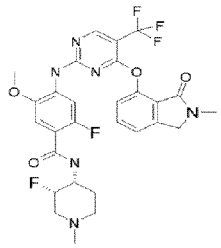
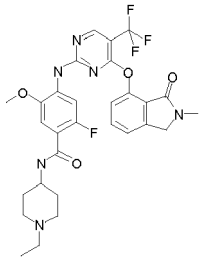
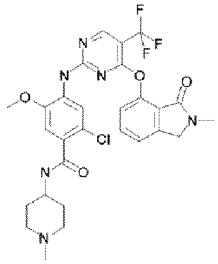
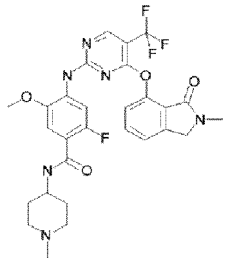
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
55		2.08	582	8
56		1.93	624	17
57		1.96	554	9
58		1.79	585	5
59		1.10	430	26

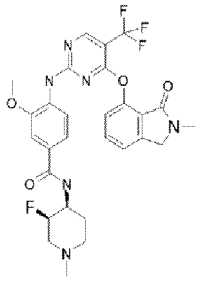
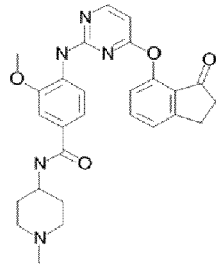
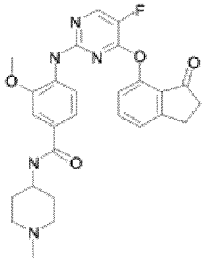
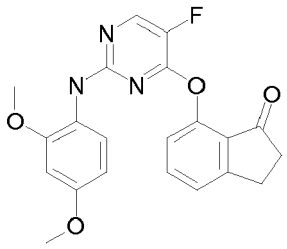
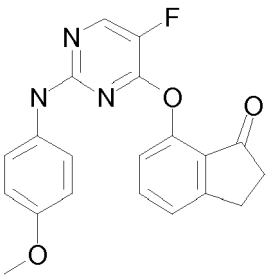
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
60		1.90	619	2
61		1.86	623	2
62		1.81	623	2
63		1.81	623	4
64		1.75	589	1

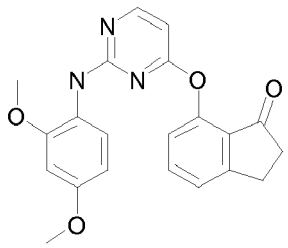
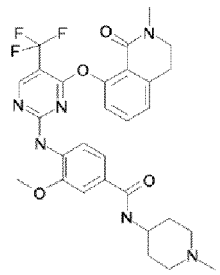
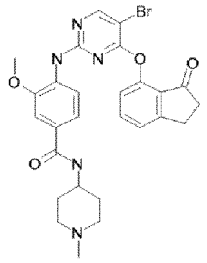
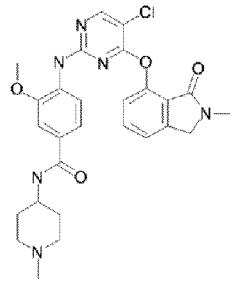
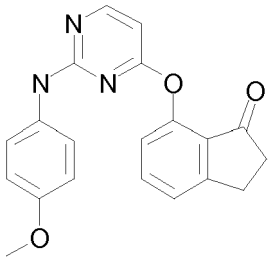
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
65		1.84	607	1
66		1.84	607	2
67		1.67	385	2
68		1.84	605	1
69		1.87	589	1

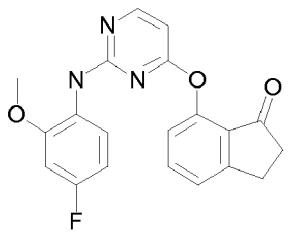
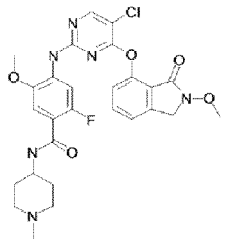
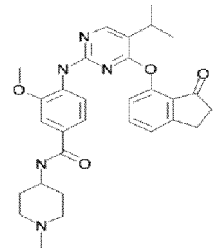
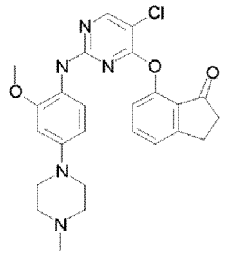
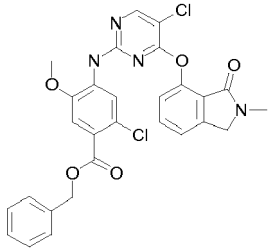
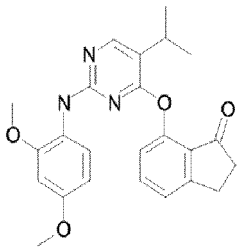
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
70		1.76	589	1
71		0.26	488	75
72		1.73	506	26
73		1.99	396	60
74		1.81	366	196

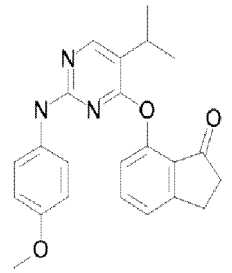
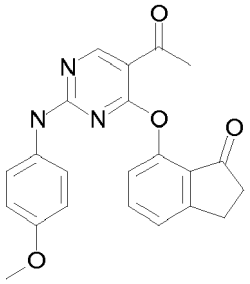
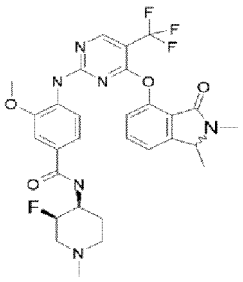
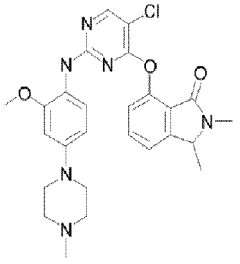
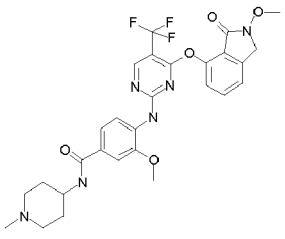
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
75		1.79	378	400
76		1.82	585	2
77		1.84	566	2
78		1.73	537	1
79		1.71	348	400

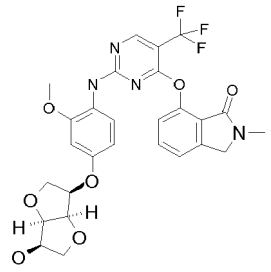
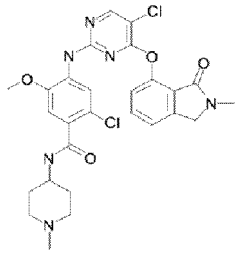
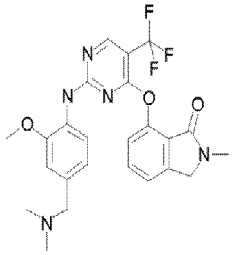
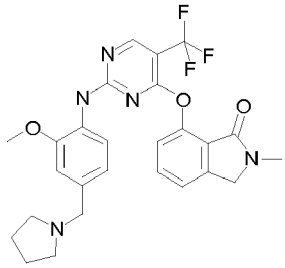
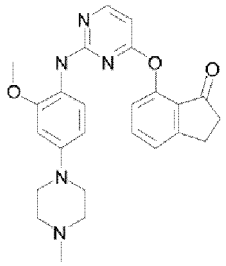
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
80		1.88	366	400
81		1.77	571	1
82		1.97	530	3
83		1.89	480	2
84		2.28	565	53
85		2.15	420	29

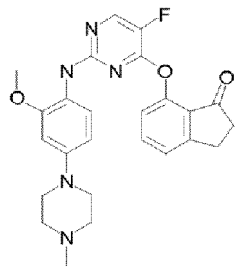
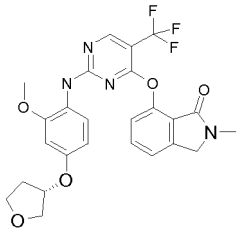
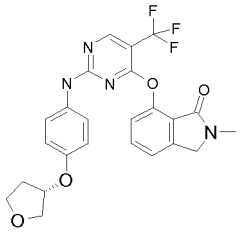
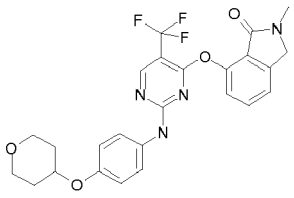
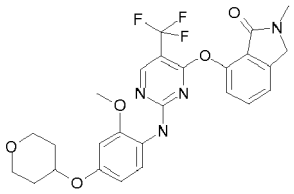
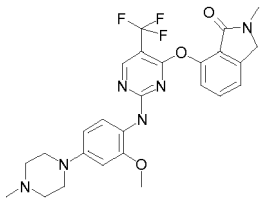
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
86		2.06	390	34
87		1.75	390	227
88		1.73	569	1
89		1.89	509	1
90		1.84	587	2

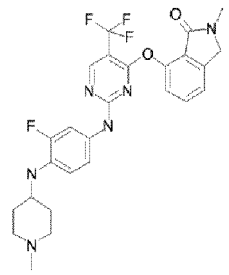
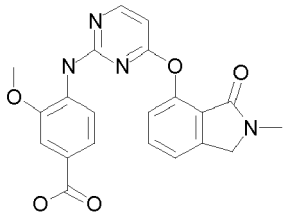
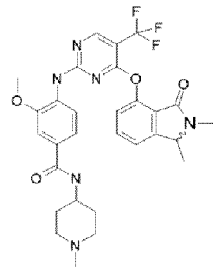
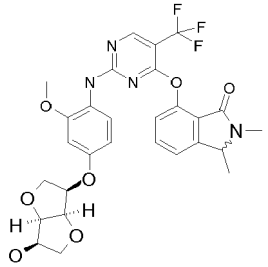
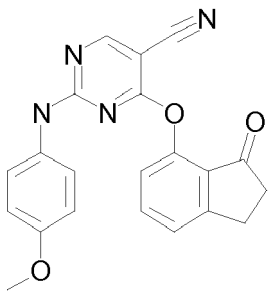
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
91		1.65	545	3
92		1.82	571	1
93		2.05	443	1
94		2.12	514	1
95		1.73	446	400

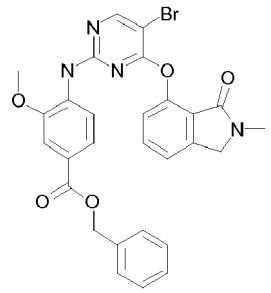
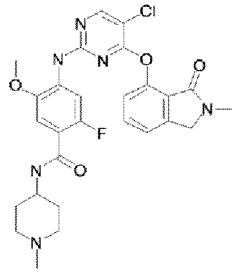
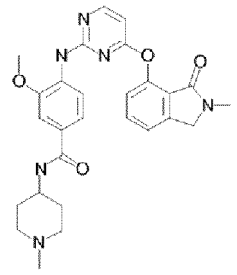
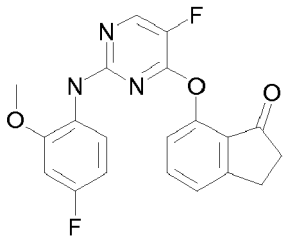
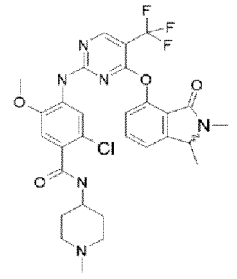
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
96		1.80	464	29
97		2.01	517	4
98		1.85	487	14
99		1.87	501	36
100		1.94	531	11
101		1.87	529	1

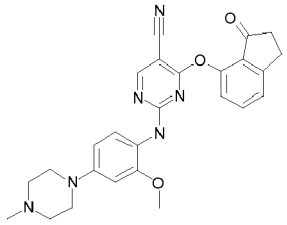
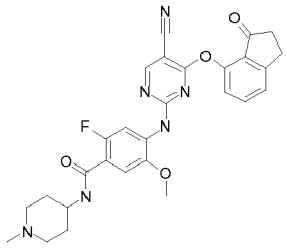
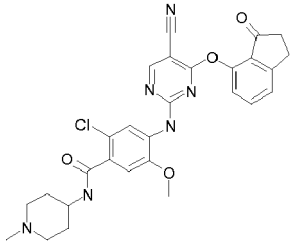
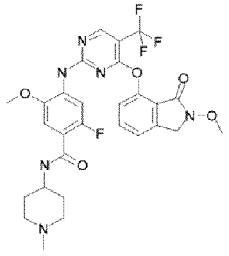
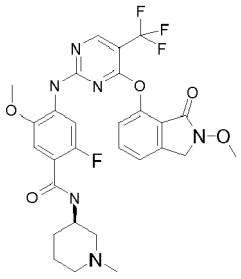
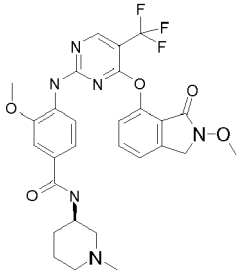
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
102		1.88	531	2
103		1.00	407	400
104		1.87	585	1
105		1.76	589	1
106		1.75	373	35

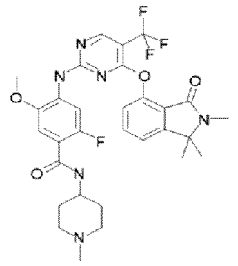
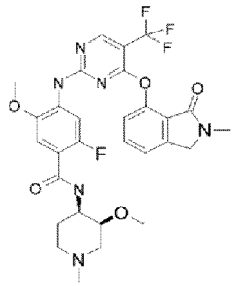
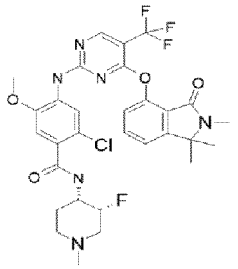
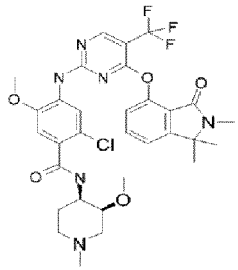
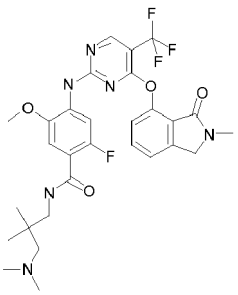
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
107		2.23	575	400
108		1.78	555	2
109		1.51	503	16
110		1.97	384	72
111		1.84	589	1

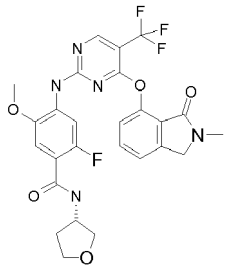
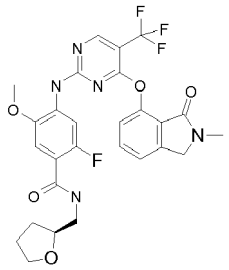
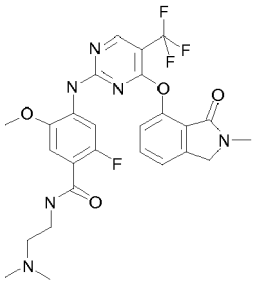
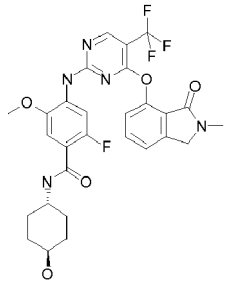
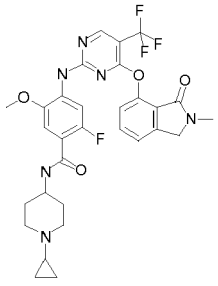
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
112		1.75	471	1
113		1.85	531	2
114		1.80	547	1
115		1.97	605	1
116		1.97	605	1
117		1.87	587	1

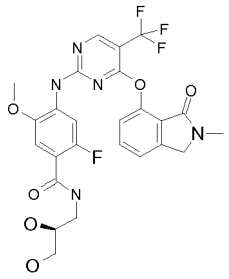
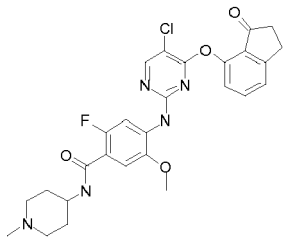
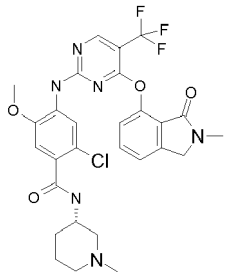
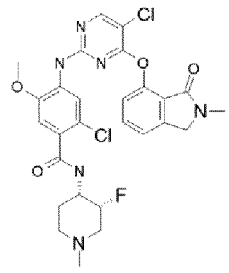
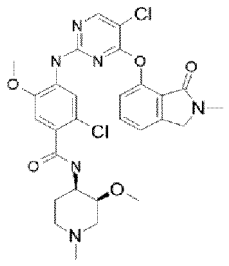
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
118		2.03	617	1
119		1.86	619	1
120		1.83	617	1
121		1.86	629	1
122		2.19	605	2

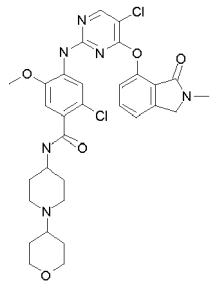
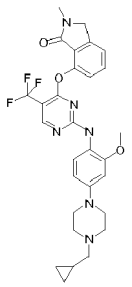
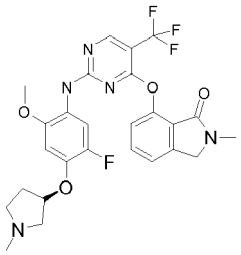
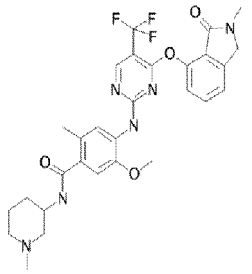
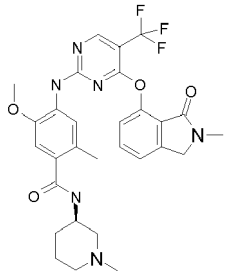
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
123		1.80	562	3
124		1.90	576	6
125		1.84	563	1
126		1.78	590	2
127		2.00	615	2

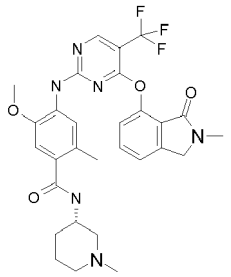
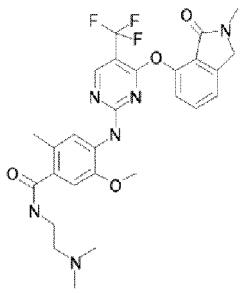
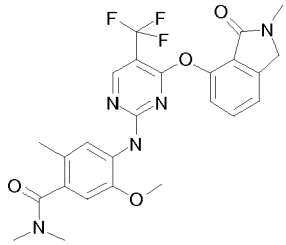
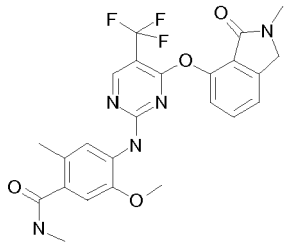
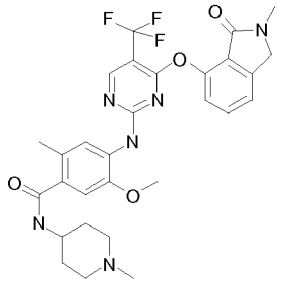
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
128		1.61	566	1
129		1.99	540	2
130		1.88	571	1
131		1.73	589	1
132		1.74	601	1

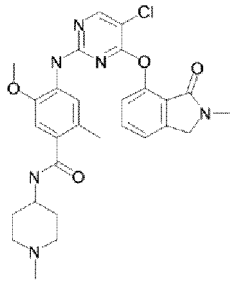
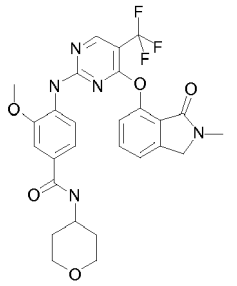
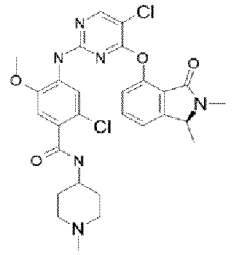
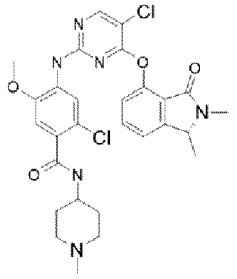
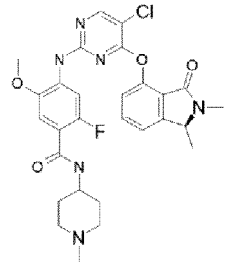
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
133		1.73	641	1
134		2.04	569	2
135		1.98	548	28
136		1.86	585	1
137		1.86	585	1

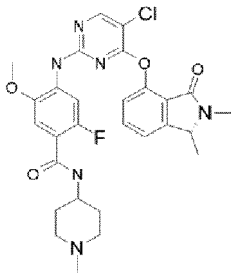
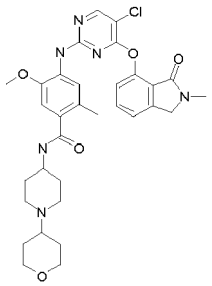
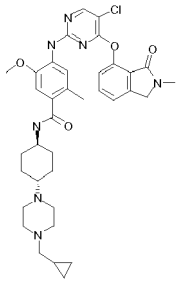
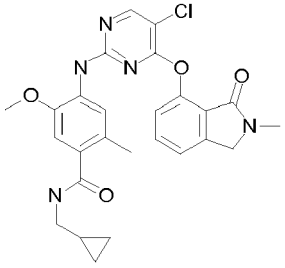
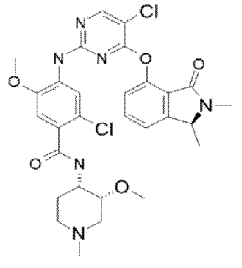
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
138		1.86	585	1
139		1.79	559	1
140		1.80	516	3
141		1.72	502	1
142		1.77	585	1

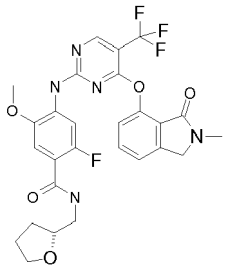
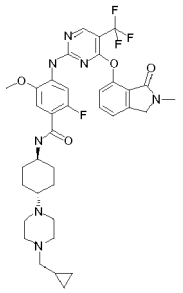
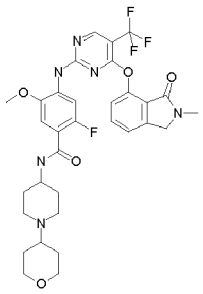
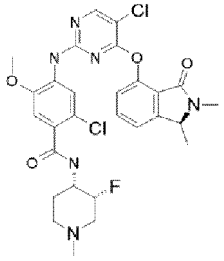
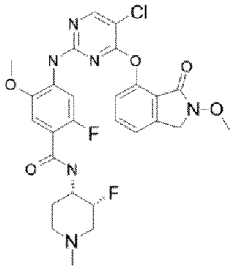
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
143		1.68	551	1
144		1.79	558	3
145		1.78	585	1
146		1.79	585	1
147		1.81	569	1

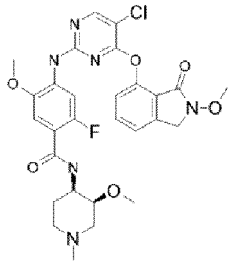
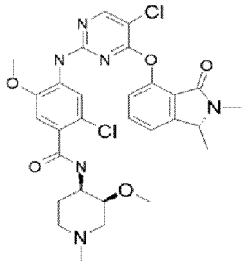
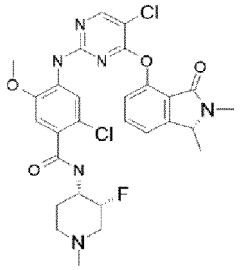
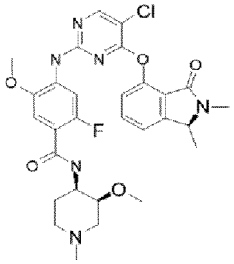
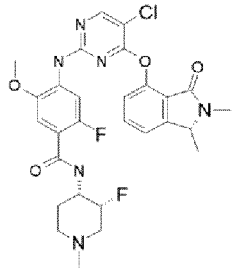
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
148		1.81	569	1
149		1.71	621	1
150		1.89	674	2
151		1.82	508	2
152		1.82	615	1

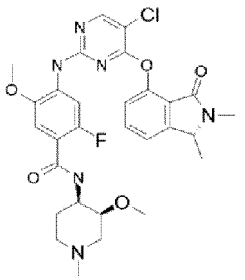
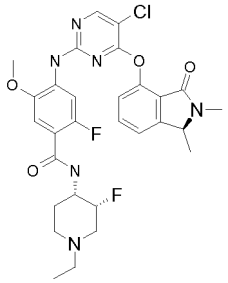
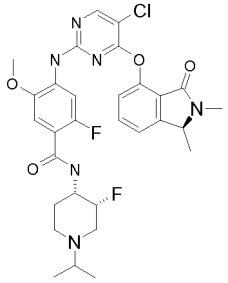
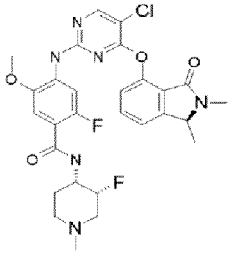
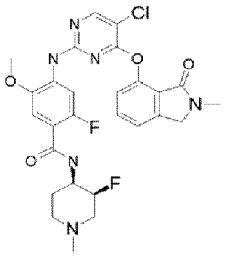
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
153		1.90	576	5
154		2.02	712	3
155		1.85	659	2
156		1.79	603	1
157		1.75	589	1

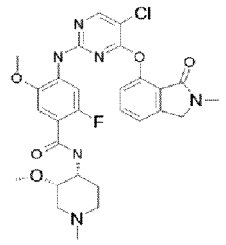
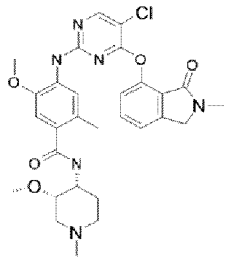
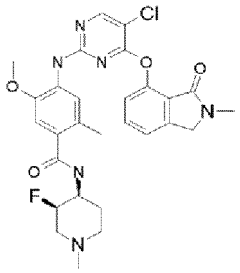
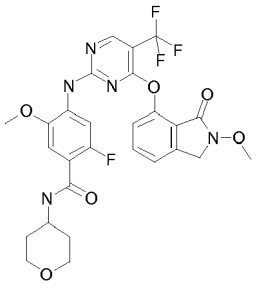
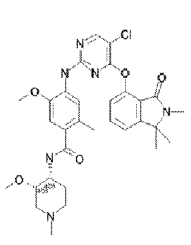
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
158		1.78	601	1
159		1.82	615	1
160		1.79	603	1
161		1.84	599	1
162		1.82	587	1

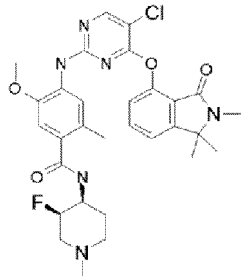
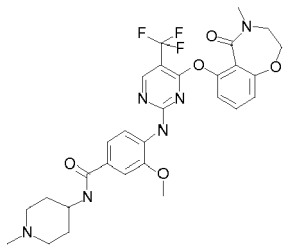
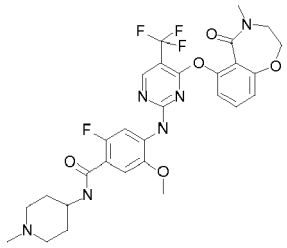
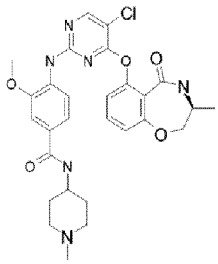
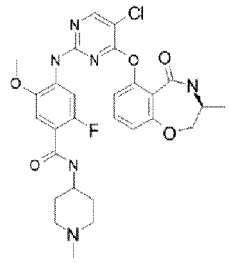
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
163		1.84	599	1
164		1.91	601	1
165		2.07	615	2
166		1.81	587	1
167		1.74	573	2

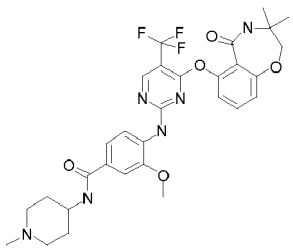
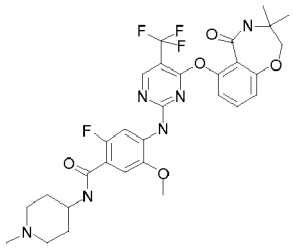
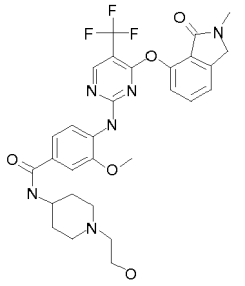
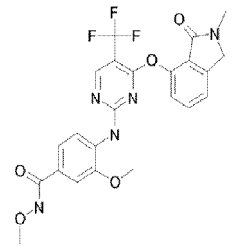
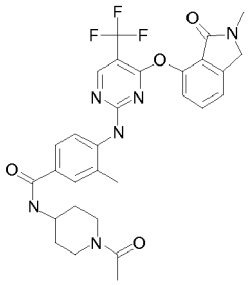
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
168		1.77	585	1
169		1.70	581	1
170		1.67	569	1
171		1.81	592	4
172	 Chiral	1.77	609	1

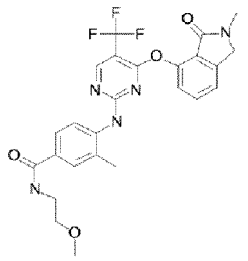
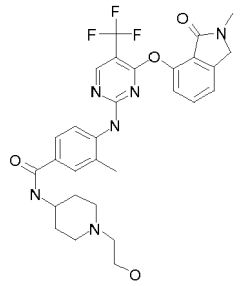
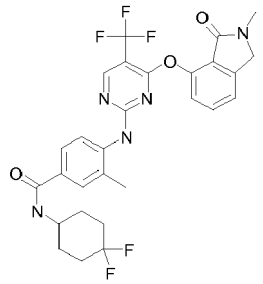
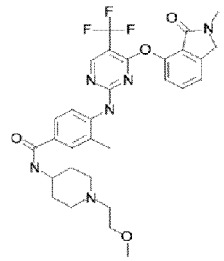
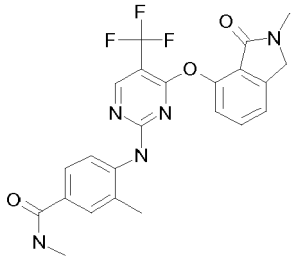
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
173		1.74	597	1
174		1.76	601	9
175		1.87	619	10
176		1.74	601	102
177		1.82	619	92

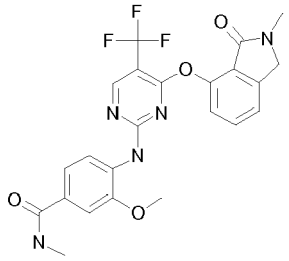
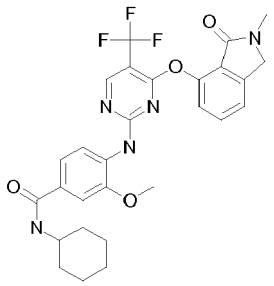
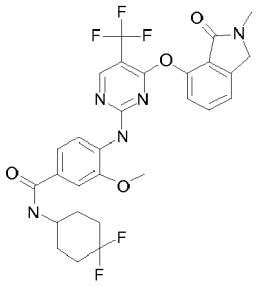
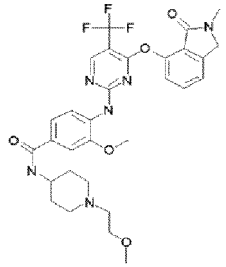
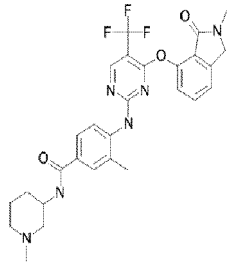
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
178		2.08	615	400
179		2.16	633	400
180		1.64	601	1
181		1.40	504	1
182		1.67	583	3

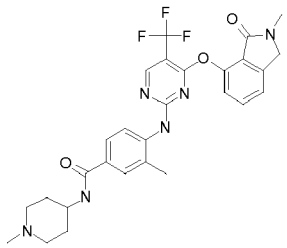
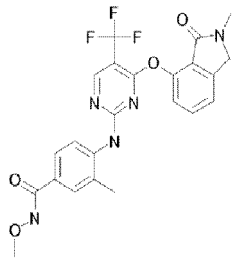
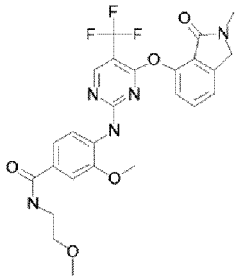
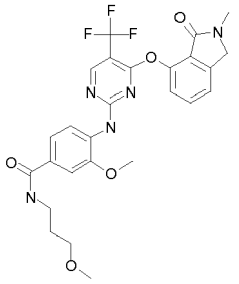
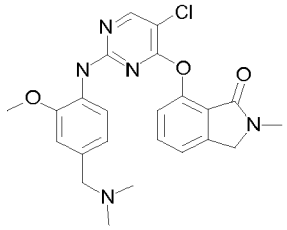
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
183		1.68	516	2
184		1.62	585	1
185		1.94	576	6
186		1.75	599	1
187		1.64	472	2

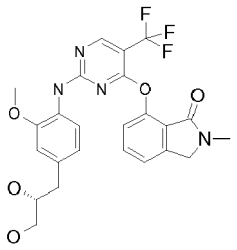
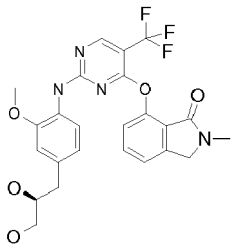
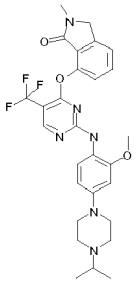
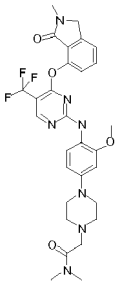
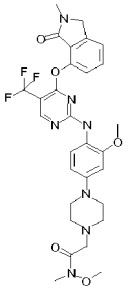
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
188		1.03	475	2
189		2.04	556	11
190		1.96	592	8
191		1.77	615	1
192		1.80	555	1

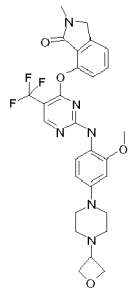
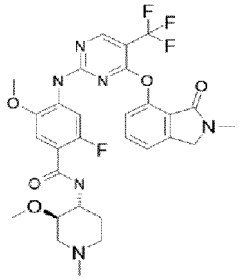
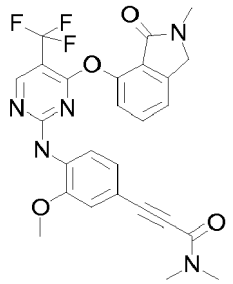
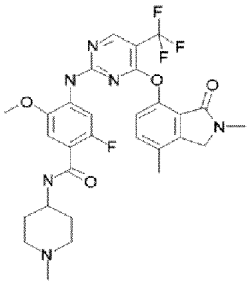
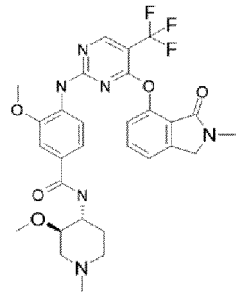
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
193		1.72	555	1
194		585	1.82	3
195		1.70	532	1
196		1.75	546	3
197		1,81	454	2

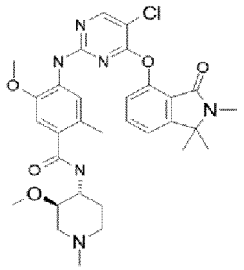
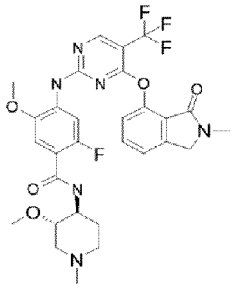
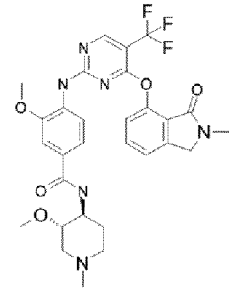
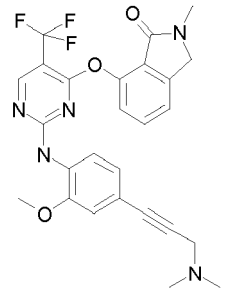
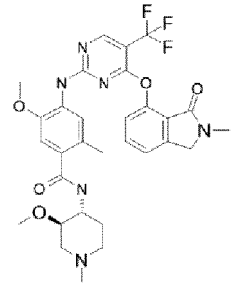
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
198		1.54	491	1
199		1.55	491	1
200		2.02	357	1
201		1.77	600	1
202		1.82	616	2

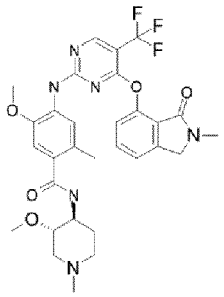
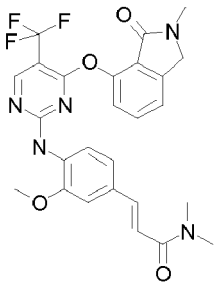
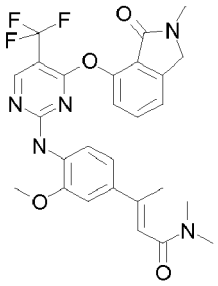
(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
203		1.76	571	2
204		1.95	619	2
205		1.91	526	4
206		1.88	603	2
207		1.70	601	1

(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
208		1.75	609	1
209		1.76	619	1
210		1.68	601	1
211		1.98	512	1
212		1.72	615	1

(continued)

No.	Structure	t_{Ret} (HPLC) [min]	MS $(M+H)^+$	PTK2 IC_{50} [nM]
213		1.74	615	1
214		1.82	528	4
215		1.86	542	3

[0116] The following Examples describe the biological activity of the compounds according to the invention without restricting the invention to these Examples.

PTK2 enzyme test

[0117] This test uses active PTK2 enzyme (Invitrogen Code PV3832) and poly-Glu-Tyr (4:1, Sigma P-0275) as the kinase substrate. The kinase activity is detected by means of the phosphorylation of the substrate in a DELFIA™ assay. The phosphorylated substrate is detected with the europium-labelled phosphotyrosine antibody PY20 (Perkin Elmer, No.: AD0038).

[0118] In order to determine concentration-activity curves with PTK2-inhibitors the compounds are serially diluted in 10 % DMSO/H_2O and 10 μL of each dilution are dispensed per well in a 96-well microtitre plate (clear U-shaped base plate, Greiner No. 650101) (the inhibitors are tested in duplicates) and mixed with 10 μL/well of PTK2 kinase (0.01 μg/well). PTK2 kinase is diluted accordingly beforehand with kinase dilution buffer (20 mM TRIS/HCl pH 7.5, 0.1 mM EDTA, 0.1 mM EGTA, 0.286 mM sodium orthovanadate, 10 % glycerol with the addition of freshly prepared BSA (fraction V 1 mg/mL) and DTT (1 mM)). The test compound and the PTK2 kinase are pre-incubated for 1 h at RT and shaken at 500 rpm. Then 20 μL ATP Mix (30 mM TRIS/HCl pH 7.5, 0.02 % Brij, 0.2 mM sodium orthovanadate, 10 mM magnesium acetate, 0.1 mM EGTA, 1 x Phosphatase Inhibitor Cocktail 1 (Sigma, No.: P2850), 50 μM ATP (Sigma, No.: A3377; 15 mM stock solution)) are added. The reaction is started by the addition of 10 μL/well of poly (Glu,Tyr) substrate (25 μg/well poly (Glu, Tyr), 0.05 μg/well biotinylated poly (Glu,Tyr) dissolved in 250 mM TRIS/HCl pH 7.5, 9 mM DTT) - the final concentration of DMSO is 2 %. After 1 h kinase reaction (the plates are shaken at 500 rpm), the reaction is stopped by the addition of 12 μL/well of 100 mM EDTA, pH 8. And shaken for a further 5 min at RT (500 U/min).

[0119] 55 μL of the reaction mixture are transferred into a streptavidin plate (Strepta Well High Bind (transparent, 96-well) made by Roche, No.: 11989685001) and incubated for 1 h at RT (shaking at 500 rpm). Then the microtitre plate

is washed three times with 200 μL/well D-PBS (Invitrogen, No.:14190). 100 μL of 1:2000 diluted DELFIA Eu-N1 Anti-Phosphotyrosine PY20 antibody (Perkin Elmer, No.: AD0038, 1:2000 diluted in DELFIA test buffer (Perkin Elmer, No.: 1244-111)) is then added and it is incubated for 1 h at RT (shaking at 500 rpm). Then the plate is washed three times with 200 μL/well DELFIA washing buffer (Perkin Elmer, No.: 1244-114), 200 μL/well strengthening solution (Perkin Elmer, No.: 1244-105) is added and the whole is incubated for 10 min at RT (shaking at 300 rpm).

[0120] The time-delayed europium fluorescence is then measured in a microtitre plate reader (Victor, Perkin Elmer). The positive control consists of wells that contain solvent (2 % DMSO in test buffer) and display uninhibited kinase activity. Wells that contain test buffer instead of enzyme act as a control for the background kinase activity.

[0121] The IC_{50} values are determined from concentration-activity analyses by iterative calculation using a sigmoidal curve analysis algorithm (FIFTY, based on GraphPAD Prism Version 3.03) with a variable Hill coefficient.

Soft-Agar Assay

[0122] This cellular test is used to determine the influence of PTK2-inhibitors on the growth of PC-3 prostate carcinoma cells in soft agar ('anchorage-independent growth'). After an incubation time of two weeks the cell vitality is demonstrated by Alamar Blue (resazurin) staining.

[0123] PC-3 cells (ATCC CRL-1435) are grown in cell culture flasks (175 cm^2) with F12 Kaighn's Medium (Gibco, No.: 21127) which has been supplemented with 10 % foetal calf serum (Invitrogen, No.: 16000-044). The cultures are incubated in the incubator at 37°C and 5 % CO_2 and are run twice a week. The test I carried out in microtitre plates (Greiner, No.: 655 185) and consists of a lower layer made up of 90 μL of medium with 1.2 % agarose (Invitrogen, 4 % agarose gel 1x liquid 40 mL, No.: 18300-012), followed by a cell layer in 60 μL medium and 0.3 % agarose and finally a top layer comprising 30 μL medium which contains the test compounds (without the addition of agarose). To prepare the lower layer, 4 % agarose are decocted with 10x D-PBS (Gibco, No.: 14200) and H_2O and thus prediluted on 3 % agarose in 1 x D-PBS. The latter is adjusted with culture medium (F12 Kaighn's /10 % FCS) and FCS to a final dilution of 1.2 % agarose in F12 Kaighn's Medium with 10 % FCS. Each well of a microtitre plate is supplied with 90 μL of the suspension for the lower layer and cooled to RT for 1 h. For the cell layer, PC-3 cells are detached using trypsin (Gibco, 0.05 %; No.: 25300), counted and seeded in 60 μL F12 Kaighn's (10 % FCS) with the addition of 0.3 % agarose (37°C). After cooling to RT for 1 h the test compounds (30 μL from serial dilutions) are added for quadruple measurements. The concentration of the test compounds usually covers a test range of between 10 μM and 0.3 nM. The compounds (stock solution: 10 mM in 100 % DMSO) are prediluted in F12 Kaighn's Medium + 6 % DMSO, to obtain a final concentration of 1 % DMSO. The cells are incubated at 37°C and 5 % CO_2 in a steam-saturated atmosphere for 14 days. The metabolic activity of living cells is then demonstrated with the dye Alamar Blue (AbD Serotec, No.: BUF012B). To do this, 18 μL/well of an Alamar Blue suspension are added and the whole is incubated for approx. 8 h in the incubator at 37°C. The positive control consists of empty wells that are filled with a mixture of 18 μL of Alamar Blue reduced by autoclaving and 180 μL of F12 Kaighn's Medium (10 % FCS). The fluorescence intensity is determined by means of a fluorescence spectrometer (SpectraMAX GeminiXS, Molecular Devices). The excitation wavelength is 530 nm, the emission wavelength is 590 nm.

[0124] The EC_{50} values are determined from concentrations-activity analyses by iterative calculation using a sigmoidal curve analysis algorithm (FIFTY, based on GraphPAD Prism Version 3.03) with a variable Hill coefficient.

Phospho-PTK2 (pY397) Assay

[0125] This cellular test is used to determine the influence of PTK2-inhibitors on the state of the PTK2-phosphorylation at tyrosine 397 (pY397).

[0126] PC-3 cells (prostate carcinoma, ATCC CRL-1435) are grown in cell culture flasks (175 cm^2) with F12 Kaighn's Medium (Gibco, No.: 21127) with the addition of 10 % foetal calf serum (Invitrogen, No.: 16000-044). The cultures are incubated in the incubator at 37°C and 5 % CO_2 and run twice a week.

[0127] For the test, 2 x 10^4 cells pro well/90μL medium are plated out in 96-well microtitre plates (Costar, No.: 3598) and incubated overnight in the incubator at 37°C and 5 % CO_2. The test compounds (10 μL from serial dilution) are added the next day. The concentration of the test compounds usually covers a range of 50 μM and 0.8 nM. The test compounds (stock solution: 10 mM in 100 % DMSO) are diluted in medium/medium 10 % DMSO such that the final concentration is 1 % DMSO. The cells are then incubated in the incubator at 37°C and 5 % CO_2 for 2 h. Then the culture supernatant is removed and the cells are fixed with 150 μL 4 % formaldehyde in D-PBS for 20 min at RT. The cell lawn is washed five times with 200 μL 0.1 % Triton X-100 in D-PBS for 5 min in each case and then incubated for 90 min with blocking buffer (5 % skimmed milk powder (Maresi Fixmilch) in TBST (25 mM Tris/HCl, pH 8.0, 150 mM NaCl, 0.05 % Tween 20). The blocking buffer is replaced by 50 μL of the first antibody anti-phospho PTK2 [pY397] rabbit monoclonal (Invitrogen/Biosource, No.: 44-625G), which is diluted 1:200 in blocking buffer. For control purposes, alternatively a PTK2 [total] antibody (clone 4.47 mouse monoclonal, Upstate, No.: 05-537), diluted 1:400 in blocking buffer is used. This incubation is carried out at 4°C overnight. Then the cell lawn is washed five times with 100 μL of 0.1 % Tween in

D-PBS for 5 min in each case and 50 μL/well of second antibody are added. In order to detect bound phospho-PTK2 [pY397] antibody a goat-anti-rabbit antibody is used which is coupled with horseradish peroxidase (Dako, No.: P0448; 1:500 dilution in blocking buffer). In order to detect bound PTK2 [total]-antibodies a rabbit-anti-mouse antibody is used, which is also coupled with horseradish peroxidase (Dako, No.: PO161; 1:1000 dilution in blocking buffer). This incubation is carried out for 1 h at RT with gentle shaking. The cell lawn is then again washed five times with 100 μL of 0.1 % Tween in D-PBS for 5 min in each case. Peroxidase staining is carried out by adding 100 μL staining solution (1:1 mixture of TMB peroxidase substrate (KPL, No.: 50-76-02) and peroxidase solution B (H_2O_2) (KPL, No.: 50-65-02). The development of the stain takes place for 10 - 30 min in the dark. The reaction is stopped by the addition of 100 μL/well of a 1 M phosphoric acid solution. The absorption is determined photometrically at 450 nm with an absorption measuring device (VICTOR^3 PerkinElmer). The inhibition of the anti-phospho PTK2 [pY397] immune staining is used to determine EC_{50} values. The staining with anti-PTK2 [total]-antibodies is for control purposes and should remain constant under the influence of inhibitor. The EC_{50} values are determined from concentration-activity analyses by iterative calculation with the aid of a sigmoidal curve analysis algorithm (FIFTY, based on GraphPAD Prism Version 3.03) with a variable Hill coefficient.

[0128] The substances of the present invention are PTK2-kinase inhibitors. In view of their biological properties the new compounds of general formulae (1a)-1(d) and the physiologically acceptable salts thereof are suitable for the treatment of diseases characterised by excessive or abnormal cell proliferation.

[0129] Such diseases include for example: viral infections (e.g. HIV and Kaposi's sarcoma); inflammatory and autoimmune diseases (e.g. colitis, arthritis, Alzheimer's disease, glomerulonephritis and wound healing); bacterial, fungal and/or parasitic infections; leukaemias, lymphomas and solid tumours (e.g. carcinomas and sarcomas), skin diseases (e.g. psoriasis); diseases based on hyperplasia which are characterised by an increase in the number of cells (e.g. fibroblasts, hepatocytes, bones and bone marrow cells, cartilage or smooth muscle cells or epithelial cells (e.g. endometrial hyperplasia)); bone diseases and cardiovascular diseases (e.g. restenosis and hypertrophy).

[0130] For example, the following cancers may be treated with compounds according to the invention, without being restricted thereto:

brain tumours such as for example acoustic neurinoma, astrocytomas such as fibrillary, protoplasmic, gemistocytary, anaplastic, pilocytic astrocytomas, glioblastoma, gliosarcoma, pleomorphic xanthoastrocytoma, subependymal large-cell giant cell astrocytoma and desmoplastic infantile astrocytoma; brain lymphomas, brain metastases, hypophyseal tumour such as prolactinoma, hypophyseal incidentaloma, HGH (human growth hormone) producing adenoma and corticotrophic adenoma, craniopharyngiomas, medulloblastoma, meningeoma and oligodendroglioma; nerve tumours such as for example tumours of the vegetative nervous system such as neuroblastoma, ganglioneuroma, paraganglioma (pheochromocytoma, chromaffinoma) and glomus-caroticum tumour, tumours on the peripheral nervous system such as amputation neuroma, neurofibroma, neurinoma (neurilemmoma, Schwannoma) and malignant Schwannoma, as well as tumours of the central nervous system such as brain and bone marrow tumours; intestinal cancer such as for example carcinoma of the rectum, colon, anus and duodenum; eyelid tumours (basalioma or adenocarcinoma of the eyelid apparatus); retinoblastoma; carcinoma of the pancreas; carcinoma of the bladder; lung tumours (bronchial carcinoma - small-cell lung cancer (SCLC), non-small-cell lung cancer (NSCLC) such as for example spindle-cell plate epithelial carcinomas, adenocarcinomas (acinary, paillary, bronchiolo-alveolar) and large-cell bronchial carcinoma (giant cell carcinoma, clear-cell carcinoma)); breast cancer such as ductal, lobular, mucinous or tubular carcinoma, Paget's carcinoma; non-Hodgkin's lymphomas (B-lymphatic or T-lymphatic NHL) such as for example hair cell leukaemia, Burkitt's lymphoma or mucosis fungoides; Hodgkin's disease; uterine cancer (corpus carcinoma or endometrial carcinoma); CUP syndrome (Cancer of Unknown Primary); ovarian cancer (ovarian carcinoma - mucinous or serous cystoma, endometriodal tumours, clear cell tumour, Brenner's tumour); gall bladder cancer; bile duct cancer such as for example Klatskin tumour; testicular cancer (germinal or non-germinal germ cell tumours); laryngeal cancer such as for example supra-glottal, glottal and subglottal tumours of the vocal cords; bone cancer such as for example osteochondroma, chondroma, chondroblastoma, chondromyxoid fibroma, chondrosarcoma, osteoma, osteoid osteoma, osteoblastoma, osteosarcoma, non-ossifying bone fibroma, osteofibroma, desmoplastic bone fibroma, bone fibrosarcoma, malignant fibrous histiocyoma, osteoclastoma or giant cell tumour, Ewing's sarcoma, and plasmocytoma, head and neck tumours (HNO tumours) such as for example tumours of the lips, and oral cavity (carcinoma of the lips, tongue, oral cavity), nasopharyngeal carcinoma (tumours of the nose, lymphoepithelioma), pharyngeal carcinoma, oropharyngeal carcinomas, carcinomas of the tonsils (tonsil malignoma) and (base of the) tongue, hypopharyngeal carcinoma, laryngeal carcinoma (cancer of the larynx), tumours of the paranasal sinuses and nasal cavity, tumours of the salivary glands and ears; liver cell carcinoma (hepatocellular carcinoma (HCC); leukaemias, such as for example acute leukaemias such as acute lymphatic/lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML); chronic lymphatic leukaemia (CLL), chronic myeloid leukaemia (CML); stomach cancer (papillary, tubular or mucinous adenocarcinoma, adenosquamous, squamous or undifferentiated carcinoma; malignant melanomas such as for example superficially spreading (SSM), nodular (NMM),

lentigo-maligna (LMM), acral-lentiginous (ALM) or amelanotic melanoma (AMM); renal cancer such as for example kidney cell carcinoma (hypernephroma or Grawitz's tumour); oesophageal cancer; penile cancer; prostate cancer; vaginal cancer or vaginal carcinoma; thyroid carcinomas such as for example papillary, follicular, medullary or anaplastic thyroid carcinoma; thymus carcinoma (thymoma); cancer of the urethra (carcinoma of the urethra, urothelial carcinoma) and cancer of the vulva.

[0131] The new compounds may be used for the prevention, short-term or long-term treatment of the above-mentioned diseases, optionally also in combination with radiotherapy or other "state-of-the-art" compounds, such as e.g. cytostatic or cytotoxic substances, cell proliferation inhibitors, anti-angiogenic substances, steroids or antibodies.

[0132] The compounds of general formulae (1a)-1(d) may be used on their own or in combination with other active substances according to the invention, optionally also in combination with other pharmacologically active substances.

[0133] Chemotherapeutic agents which may be administered in combination with the compounds according to the invention include, without being restricted thereto, hormones, hormone analogues and antihormones (e.g. tamoxifen, toremifene, raloxifene, fulvestrant, megestrol acetate, flutamide, nilutamide, bicalutamide, aminoglutethimide, cyproterone acetate, finasteride, buserelin acetate, fludrocortisone, fluoxymesterone, medroxyprogesterone, octreotide), aromatase inhibitors (e.g. anastrozole, letrozole, liarozole, vorozole, exemestane, atamestane), LHRH agonists and antagonists (e.g. goserelin acetate, luprolide), inhibitors of growth factors (growth factors such as for example "platelet derived growth factor" and "hepatocyte growth factor", inhibitors are for example "growth factor" antibodies, "growth factor receptor" antibodies and tyrosinekinase inhibitors, such as for example gefitinib, lapatinib and trastuzumab); signal transduction inhibitors (e.g. imatinib and sorafenib); antimetabolites (e.g. antifolates such as methotrexate, premetrexed and raltitrexed, pyrimidine analogues such as 5-fluorouracil, capecitabin and gemcitabin, purine and adenosine analogues such as mercaptopurine, thioguanine, cladribine and pentostatin, cytarabine, fludarabine); antitumour antibiotics (e.g. anthracyclins such as doxorubicin, daunorubicin, epirubicin and idarubicin, mitomycin-C, bleomycin, dactinomycin, plicamycin, streptozocin); platinum derivatives (e.g. cisplatin, oxaliplatin, carboplatin); alkylation agents (e.g. estramustin, meclorethamine, melphalan, chlorambucil, busulphan, dacarbazin, cyclophosphamide, ifosfamide, temozolomide, nitrosoureas such as for example carmustin and lomustin, thiotepa); antimitotic agents (e.g. Vinca alkaloids such as for example vinblastine, vindesin, vinorelbin and vincristine; and taxanes such as paclitaxel, docetaxel); topoisomerase inhibitors (e.g. epipodophyllotoxins such as for example etoposide and etopophos, teniposide, amsacrin, topotecan, irinotecan, mitoxantron) and various chemotherapeutic agents such as amifostin, anagrelid, clodronat, filgrastin, interferon alpha, leucovorin, rituximab, procarbazine, levamisole, mesna, mitotane, pamidronate and porfimer.

[0134] Suitable preparations include for example tablets, capsules, suppositories, solutions, - particularly solutions for injection (s.c., i.v., i.m.) and infusion - elixirs, emulsions or dispersible powders. The content of the pharmaceutically active compound(s) should be in the range from 0.1 to 90 wt.-%, preferably 0.5 to 50 wt.-% of the composition as a whole, i.e. In amounts which are sufficient to achieve the dosage range specified below. The doses specified may, if necessary, be given several times a day.

[0135] Suitable tablets may be obtained, for example, by mixing the active substance(s) with known excipients, for example inert diluents such as calcium carbonate, calcium phosphate or lactose, disintegrants such as corn starch or alginic acid, binders such as starch or gelatine, lubricants such as magnesium stearate or talc and/or agents for delaying release, such as carboxymethyl cellulose, cellulose acetate phthalate, or polyvinyl acetate. The tablets may also comprise several layers.

[0136] Coated tablets may be prepared accordingly by coating cores produced analogously to the tablets with substances normally used for tablet coatings, for example collidone or shellac, gum arabic, talc, titanium dioxide or sugar. To achieve delayed release or prevent incompatibilities the core may also consist of a number of layers. Similarly the tablet coating may consist of a number of layers to achieve delayed release, possibly using the excipients mentioned above for the tablets.

[0137] Syrups or elixirs containing the active substances or combinations thereof according to the invention may additionally contain a sweetener such as saccharine, cyclamate, glycerol or sugar and a flavour enhancer, e.g. a flavouring such as vanillin or orange extract. They may also contain suspension adjuvants or thickeners such as sodium carboxymethyl cellulose, wetting agents such as, for example, condensation products of fatty alcohols with ethylene oxide, or preservatives such as p-hydroxybenzoates.

[0138] Solutions for injection and infusion are prepared in the usual way, e.g. with the addition of isotonic agents, preservatives such as p-hydroxybenzoates, or stabilisers such as alkali metal salts of ethylenediamine tetraacetic acid, optionally using emulsifiers and/or dispersants, whilst if water is used as the diluent, for example, organic solvents may optionally be used as solvating agents or dissolving aids, and transferred into injection vials or ampoules or infusion bottles.

[0139] Capsules containing one or more active substances or combinations of active substances may for example be prepared by mixing the active substances with inert carriers such as lactose or sorbitol and packing them into gelatine capsules.

[0140] Suitable suppositories may be made for example by mixing with carriers provided for this purpose, such as

neutral fats or polyethyleneglycol or the derivatives thereof.

[0141] Excipients which may be used include, for example, water, pharmaceutically acceptable organic solvents such as paraffins (e.g. petroleum fractions), vegetable oils (e.g. groundnut or sesame oil), mono- or polyfunctional alcohols (e.g. ethanol or glycerol), carriers such as e.g. natural mineral powders (e.g. kaolins, clays, talc, chalk), synthetic mineral powders (e.g. highly dispersed silicic acid and silicates), sugars (e.g. cane sugar, lactose and glucose) emulsifiers (e.g. lignin, spent sulphite liquors, methylcellulose, starch and polyvinylpyrrolidone) and lubricants (e.g. magnesium stearate, talc, stearic acid and sodium lauryl sulphate).

[0142] The preparations are administered by the usual methods, preferably by oral or transdermal route, most preferably by oral route. For oral administration the tablets may, of course contain, apart from the abovementioned carriers, additives such as sodium citrate, calcium carbonate and dicalcium phosphate together with various additives such as starch, preferably potato starch, gelatine and the like. Moreover, lubricants such as magnesium stearate, sodium lauryl sulphate and talc may be used at the same time for the tabletting process. In the case of aqueous suspensions the active substances may be combined with various flavour enhancers or colourings in addition to the excipients mentioned above.

[0143] For parenteral use, solutions of the active substances with suitable liquid carriers may be used.

[0144] The dosage for intravenous use is from 1 - 1000 mg per hour, preferably between 5 and 500 mg per hour.

[0145] However, it may sometimes be necessary to depart from the amounts specified, depending on the body weight, the route of administration, the individual response to the drug, the nature of its formulation and the time or interval over which the drug is administered. Thus, in some cases it may be sufficient to use less than the minimum dose given above, whereas in other cases the upper limit may have to be exceeded. When administering large amounts it may be advisable to divide them up into a number of smaller doses spread over the day.

[0146] The formulation examples that follow illustrate the present invention without restricting its scope:

Examples of pharmaceutical formulations

A)

Tablets	per tablet
active substance according to formula **(1)**	100 mg
lactose	140 mg
corn starch	240 mg
polyvinylpyrrolidone	15 mg
magnesium stearate	5 mg
	500 mg

[0147] The finely ground active substance, lactose and some of the corn starch are mixed together. The mixture is screened, then moistened with a solution of polyvinylpyrrolidone in water, kneaded, wet-granulated and dried. The granules, the remaining corn starch and the magnesium stearate are screened and mixed together. The mixture is compressed to produce tablets of suitable shape and size.

B)

Tablets	per tablet
active substance according to formula **(1)**	80 mg
lactose	55 mg
corn starch	190 mg
microcrystalline cellulose	35 mg
polyvinylpyrrolidone	15 mg
sodium-carboxymethyl starch	23 mg
magnesium stearate	2 mg
	400 mg

[0148] The finely ground active substance, some of the corn starch, lactose, microcrystalline cellulose and polyvinylpyrrolidone are mixed together, the mixture is screened and worked with the remaining corn starch and water to form a granulate which is dried and screened. The sodiumcarboxymethyl starch and the magnesium stearate are added and mixed in and the mixture is compressed to form tablets of a suitable size.

C) Ampoule solution

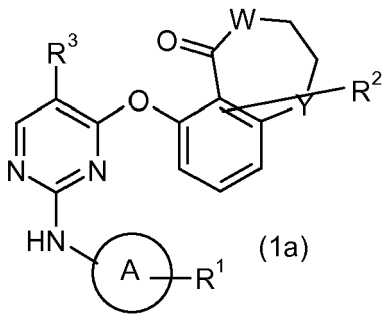
[0149]

active substance according to formula **(1)**	50 mg
sodium chloride	50 mg
water for inj.	5 ml

[0150] The active substance is dissolved in water at its own pH or optionally at pH 5.5 to 6.5 and sodium chloride is added to make it isotonic. The solution obtained is filtered free from pyrogens and the filtrate is transferred under aseptic conditions into ampoules which are then sterilised and sealed by fusion. The ampoules contain 5 mg, 25 mg and 50 mg of active substance.

Claims

1. A compound of general formula **(Ia),**



(1a)

wherein

A denotes a group, optionally substituted by one or more identical or different **R^1,** selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;

R^1 and **R^2** each independently of one another denote hydrogen or a group selected from among **R^a, R^b** and **R^a** substituted by one or more identical or different **R^c** and/or **R^b;**

R^3 denotes a group selected from among hydrogen, halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

W and **Y** each independently of one another represent CH_2, O, N-R^e or N-OR^e;

each **R^a** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^b** is a suitable group and is independently selected from among =O, $-OR^c$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$;

each **R^c** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^d** and/or **R^e** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^d** is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$,

-OS(O)R^e, -OS(O)$_2R^e$, -OS(O)$_2OR^e$, -OS(O)NR^eR^e, -OS(O)$_2NR^eR^e$, -C(O)R^e, -C(O)OR^e, -C(O)SR^e, -C(O)NR^eR^e, -C(O)N(R^g)NR^eR^e, -C(O)N(R^g)OR^e, -C(NR^g)NR^eR^e, -C(NOH)R^e, -C(NOH)NR^eR^e, -OC(O)R^e, -OC(O)OR^e, -OC(O)SR^e, -OC(O)NR^eR^e, -OC(NR^g)NR^eR^e, -SC(O)R^e, -SC(O)OR^e, -SC(O)NR^eR^e, -SC(NR^g)NR^eR^e, -N(R^g)C(O)R^e, -N[C(O)R^e]$_2$, -N(OR^g)C(O)R^e, -N(R^g)C(NR^g)R^e, -N(R^g)N(R^g)C(O)R^e, -N[C(O)R^e]NR^eR^e, -N(R^g)C(S)R^e, -N(R^g)S(O)R^e, -N(R^g)S(O)OR^e -N(R^g)S(O)$_2R^e$, -N[S(O)$_2R^e$]$_2$, -N(R^g)S(O)$_2OR^e$, -N(R^g)S(O)$_2NR^eR^e$, -N(R^g)[S(O)$_2$]$_2R^e$, -N(R^g)C(O)OR^e, -N(R^g)C(O)SR^e, -N(R^g)C(O)NR^eR^e, -N(R^g)C(O)$NR^gNR^eR^e$, -N(R^g)N(R^g)C(O)NR^eR^e, -N(R^g)C(S)NR^eR^e, -[N(R^g)C(O)]$_2R^e$, -N(R^g)[C(O)]$_2R^e$, -N{[C(O)]$_2R^e$}$_2$, -N(R^g)[C(O)]$_2OR^e$, -N(R^g)[C(O)]$_2NR^eR^e$, -N{[C(O)]$_2OR^e$}$_2$, -N{[C(O)]$_2NR^eR^e$}$_2$, -[N(R^g)C(O)]$_2OR^e$, -N(R^g)C(NR^g)OR^e, -N(R^g)C(NOH)R^e, -N(R^g)C(NR^g)SR^e and -N(R^g)C(NR^g)NR^eR^e;

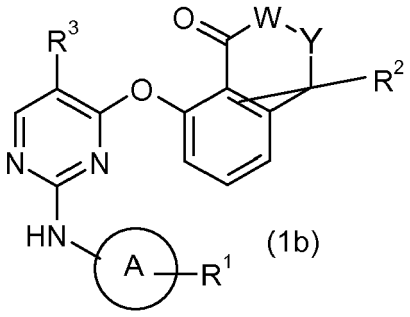
each **R^e** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^f** and/or **R^g** selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^f** is a suitable group and is independently selected from among halogen and -CF_3; and

each **R^g** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

2. A compound of general formula **(Ib),**



(1b)

wherein

A denotes a group, optionally substituted by one or more identical or different **R^1,** selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;

R^1 and **R^2** each independently of one another denote hydrogen or a group selected from among **R^a, R^b** and **R^a** substituted by one or more identical or different **R^c** and/or **R^b;**

R^3 denotes a group selected from among hydrogen, halogen, -OR^c, -OCF_3, -SR^c, -NR^cR^c, -CF_3, -CN, -OCN, -SCN, -NO, -NO_2, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

W and **Y** each independently of one another represent CH_2, O, N-R^e or N-OR^e;

each **R^a** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^b** is a suitable group and is independently selected from among =O, -OR^c, C_{1-3}haloalkyloxy, -OCF_3, =S, -SR^c, =NR^c, =NOR^c, =NNR^cR^c, =NN(R^g)C(O)NR^cR^c, -NR^cR^c, -ONR^cR^c, -N(OR^c)R^c, -N(R^g)NR^cR^c, halogen, -CF_3, -CN, -NC, -OCN, -SCN, -NO, -NO_2, =N_2, -N_3, -S(O)R^c, -S(O)OR^c, -S(O)$_2R^c$, -S(O)$_2OR^c$, -S(O)NR^cR^c, -S(O)$_2NR^cR^c$, -OS(O)R^c, -OS(O)$_2R^c$, -OS(O)$_2OR^c$, -OS(O)NR^cR^c, -OS(O)$_2NR^cR^c$, -C(O)R^c, -C(O)OR^c, -C(O)SR^c, -C(O)NR^cR^c, -C(O)N(R^g)NR^cR^c, -C(O)N(R^g)OR^c, -C(NR^g)NR^cR^c, -C(NOH)R^c, -C(NOH)NR^cR^c, -OC(O)R^c, -OC(O)OR^c, -OC(O)SR^c, -OC(O)NR^cR^c, -OC(NR^g)NR^cR^c, -SC(O)R^c, -SC(O)OR^c, -SC(O)NR^cR^c, -SC(NR^g)NR^cR^c, -N(R^g)C(O)R^c, -N[C(O)R^c]$_2$, -N(OR^g)C(O)R^c, -N(R^g)C(NR^g)R^c, -N(R^g)N(R^g)C(O)R^c, -N[C(O)R^c]NR^cR^c, -N(R^g)C(S)R^c, -N(R^g)S(O)R^c, -N(R^g)S(O)OR^c, -N(R^g)S(O)$_2R^c$, -N[S(O)$_2R^c$]$_2$, -N(R^g)S(O)$_2OR^c$, -N(R^g)S(O)$_2NR^cR^c$, -N(R^g)[S(O)$_2$]$_2R^c$, -N(R^g)C(O)OR^c, -N(R^g)C(O)SR^c, -N(R^g)C(O)NR^cR^c, -N(R^g)C(O)$NR^gNR^cR^c$, -N(R^g)N(R^g)C(O)NR^cR^c, -N(R^g)C(S)NR^cR^c, -[N(R^g)C(O)]$_2R^c$, -N(R^g)[C(O)]$_2R^c$, -N{[C(O)]$_2R^c$}$_2$, -N(R^g)[C(O)]$_2OR^c$, -N(R^g)[C(O)]$_2NR^cR^c$, -N{[C(O)]$_2OR^c$}$_2$, -N{[C(O)]$_2NR^cR^c$}$_2$, -[N(R^g)C(O)]$_2OR^c$, -N(R^g)C(NR^g)OR^c, -N(R^g)C(NOH)R^c, -N(R^g)C(NR^g)SR^c and -N(R^g)C(NR^g)NR^cR^c;

each **R^c** independently of one another denotes hydrogen or a group optionally substituted by one or more identical

or different **R^{d}** and/or **R^{e}** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^{d}** is a suitable group and is independently selected from among =O, -OR^{e}, C_{1-3}haloalkyloxy, -OCF$_3$, =S, -SR^{e}, =NR^{e}, =NOR^{e}, =NNR^{e}R^{e}, =NN(R^{g})C(O)NR^{e}R^{e}, -NR^{e}R^{e}, -ONR^{e}R^{e}, -N(R^{g})NR^{e}R^{e}, halogen, -CF$_3$, -CN, -NC, -OCN, -SCN, -NO, -NO$_2$, =N$_2$, -N$_3$, -S(O)R^{e}, -S(O)OR^{e}, -S(O)$_2$R^{e}, -S(O)$_2$OR^{e}, -S(O)NR^{e}R^{e}, -S(O)$_2$NR^{e}R^{e}, -OS(O)R^{e}, -OS(O)$_2$R^{e}, -OS(O)$_2$OR^{e}, -OS(O)NR^{e}R^{e}, -OS(O)$_2$NR^{e}R^{e}, -C(O)R^{e}, -C(O)OR^{e}, -C(O)SR^{e}, -C(O)NR^{e}R^{e}, -C(O)N(R^{g})NR^{e}R^{e}, -C(O)N(R^{g})OR^{e}, -C(NR^{g})NR^{e}R^{e}, -C(NOH)R^{e}, -C(NOH)NR^{e}R^{e}, -OC(O)R^{e}, -OC(O)OR^{e}, -OC(O)SR^{e}, -OC(O)NR^{e}R^{e}, -OC(NR^{g})NR^{e}R^{e}, -SC(O)R^{e}, -SC(O)OR^{e}, -SC(O)NR^{e}R^{e}, -SC(NR^{g})NR^{e}R^{e}, -N(R^{g})C(O)R^{e}, -N[C(O)R^{e}]$_2$, -N(OR^{g})C(O)R^{e}, -N(R^{g})C(NR^{g})R^{e}, -N(R^{g})N(R^{g})C(O)R^{e}, -N[C(O)R^{e}]NR^{e}R^{e}, -N(R^{g})C(S)R^{e}, -N(R^{g})S(O)R^{e}, -N(R^{g})S(O)OR^{e} -N(R^{g})S(O)$_2$R^{e}, -N[S(O)$_2$R^{e}]$_2$, -N(R^{g})S(O)$_2$OR^{e}, -N(R^{g})S(O)$_2$NR^{e}R^{e}, -N(R^{g})[S(O)$_2$]$_2$R^{e}, -N(R^{g})C(O)OR^{e}, -N(R^{g})C(O)SR^{e}, -N(R^{g})C(O)NR^{e}R^{e}, -N(R^{g})C(O)NR^{g}NR^{e}R^{e}, -N(R^{g})N(R^{g})C(O)NR^{e}R^{e}, -N(R^{g})C(S)NR^{e}R^{e}, -[N(R^{g})C(O)]$_2$R^{e}, -N(R^{g})[C(O)]$_2$R^{e}, -N{[C(O)]$_2$R^{e}}$_2$, -N(R^{g})[C(O)]$_2$OR^{e}, -N(R^{g})[C(O)]$_2$NR^{e}R^{e}, -N{[C(O)]$_2$OR^{e}}$_2$, -N{[C(O)]$_2$NR^{e}R^{e}}$_2$, -[N(R^{g})C(O)]$_2$OR^{e}, -N(R^{g})C(NR^{g})OR^{e}, -N(R^{g})C(NOH)R^{e}, -N(R^{g})C(NR^{g})SR^{e} and -N(R^{g})C(NR^{g})NR^{e}R^{e};

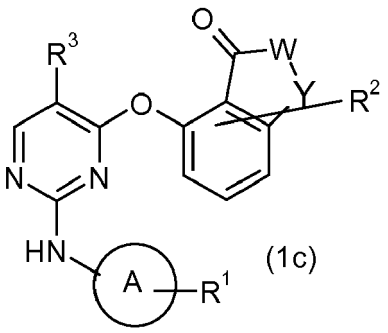
each **R^{e}** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f}** and/or **R^{g}** selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^{f}** is a suitable group and is independently selected from among halogen and -CF$_3$; and

each **R^{g}** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

3. A compound of general formula **(1c),**



(1c)

wherein

A denotes a group, optionally substituted by one or more identical or different **R^{1},** selected from among C_{3-10}cycloalkyl, 3-8 membered heterocycloalkyl, C_{6-15}aryl and 5-12 membered heteroaryl;

R^{1} and **R^{2}** each independently of one another denote hydrogen or a group selected from among **R^{a}, R^{b}** and **R^{a}** substituted by one or more identical or different **R^{c}** and/or **R^{b};**

R^{3} denotes a group selected from among hydrogen, halogen, -OR^{c}, -OCF$_3$, -SR^{c}, -NR^{c}R^{c}, -CF$_3$, -CN, -OCN, -SCN, -NO, -NO$_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

W and **Y** each independently of one another represent CH$_2$, O, N-R^{e} or N-OR^{e};

each **R^{a}** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^{b}** is a suitable group and is independently selected from among =O, -OR^{c}, C_{1-3}haloalkyloxy, -OCF$_3$, =S, -SR^{c}, =NR^{c}, =NOR^{c}, =NNR^{c}R^{c}, =NN(R^{g})C(O)NR^{c}R^{c}, -NR^{c}R^{c}, -ONR^{c}R^{c}, -N(OR^{c})R^{c}, -N(R^{g})NR^{c}R^{c}, halogen, -CF$_3$, -CN, -NC, -OCN, -SCN, -NO, -NO$_2$, =N$_2$, -N$_3$, -S(O)R^{c}, -S(O)OR^{c}, -S(O)$_2$R^{c}, -S(O)$_2$OR^{c}, -S(O)NR^{c}R^{c}, -S(O)$_2$NR^{c}R^{c}, -OS(O)R^{c}, -OS(O)$_2$R^{c}, -OS(O)$_2$OR^{c}, -OS(O)NR^{c}R^{c}, -OS(O)$_2$NR^{c}R^{c}, -C(O)R^{c}, -C(O)OR^{c}, -C(O)SR^{c}, -C(O)NR^{c}R^{c}, -C(O)N(R^{g})NR^{c}R^{c}, -C(O)N(R^{g})OR^{c}, -C(NR^{g})NR^{c}R^{c}, -C(NOH)R^{c}, -C(NOH)NR^{c}R^{c}, -OC(O)R^{c}, -OC(O)OR^{c}, -OC(O)SR^{c}, -OC(O)NR^{c}R^{c}, -OC(NR^{g})NR^{c}R^{c}, -SC(O)R^{c}, -SC(O)OR^{c}, -SC(O)NR^{c}R^{c}, -SC(NR^{g})NR^{c}R^{c}, -N(R^{g})C(O)R^{c}, -N[C(O)R^{c}]$_2$, -N(OR^{g})C(O)R^{c}, -N(R^{g})C(NR^{g})R^{c}, -N(R^{g})N(R^{g})C(O)R^{c}, -N[C(O)R^{c}]NR^{c}R^{c},

$-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$;

each **R^c** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^d** and/or **R^e** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^d** is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ and $-N(R^g)C(NR^g)NR^eR^e$;

each **R^e** independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different **R^f** and/or **R^g** selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

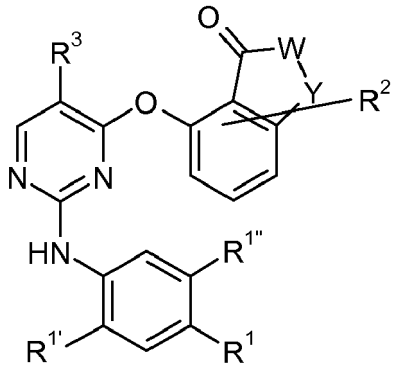
each **R^f** is a suitable group and is independently selected from among halogen and $-CF_3$; and

each **R^g** independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkyl, 5-12 membered heteroaryl or 6-18 membered heteroarylalkyl;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

4. A compound according to one of claims 1 to 3, wherein **A** is phenyl.

5. A compound of general formula **(1d)** according to claim 3,



(1d)

wherein

W and **Y** each independently of one another represent CH_2, O, N-R^e or N-OR^e, and

R^1 denotes hydrogen or a group selected from among **R^a, R^b** and **R^a** substituted by one or more identical or different **R^c** and/or **R^b,**

each **R^a** is selected independently of one another from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-16}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each **R^b** is a suitable group and is independently selected from among =O, $-OR^c$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, halogen, $-CF_3$,

-CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ and $-N(R^g)C(NR^g)NR^cR^c$,

each $\mathbf{R^c}$ independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^d}$ and/or $\mathbf{R^e}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each $\mathbf{R^d}$ is a suitable group and is independently selected from among =O, $-OR^e$, C_{1-3}haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ and $-N(R^g)C(NR^g)NR^eR^e$,

each $\mathbf{R^e}$ independently of one another denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^f}$ and/or $\mathbf{R^g}$ selected from among C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{4-11}cycloalkylalkyl, C_{6-10}aryl, C_{7-16}arylalkyl, 2-6 membered heteroalkyl, 3-8 membered heterocycloalkyl, 4-14 membered heterocycloalkylalkyl, 5-12 membered heteroaryl and 6-18 membered heteroarylalkyl;

each $\mathbf{R^f}$ is a suitable group and is independently selected from among halogen and $-CF_3$; and

each $\mathbf{R^g}$ independently of one another denotes hydrogen, C_{1-6}alkyl, C_{3-8}cycloalkyl, and

$\mathbf{R^{1'}}$ and $\mathbf{R^{1''}}$ each independently of one another denote a group selected from among hydrogen, halogen and $-OR^c$,

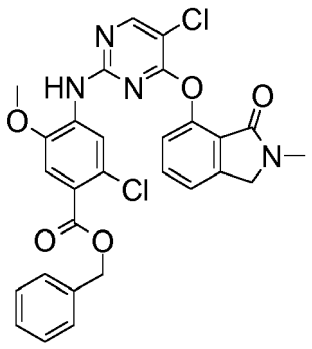
$\mathbf{R^2}$ denotes hydrogen or a group selected from among $\mathbf{R^a}$, $\mathbf{R^b}$ and $\mathbf{R^a}$ substituted by one or more identical or different $\mathbf{R^c}$ and/or $\mathbf{R^b}$, and

$\mathbf{R^3}$ denotes a group selected from among hydrogen, halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}alkyl, C_{1-3}haloalkyl and C_{1-3}haloalkyloxy;

optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

6. A compound according to one of claims 1 to 5, wherein $\mathbf{R^3}$ is Cl or CF_3.

7. A compound selected from among

1	

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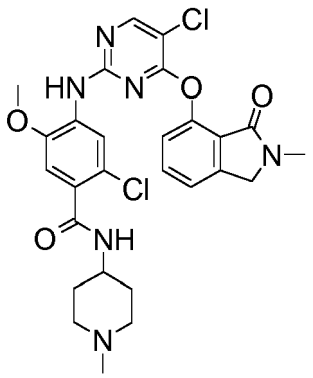
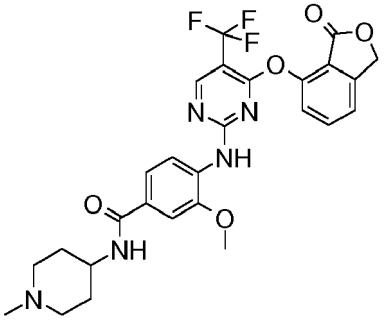
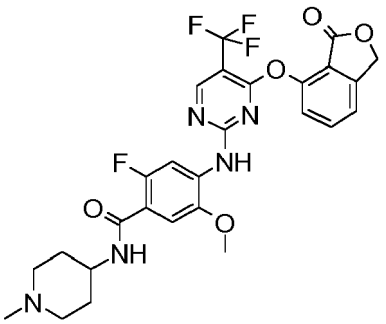
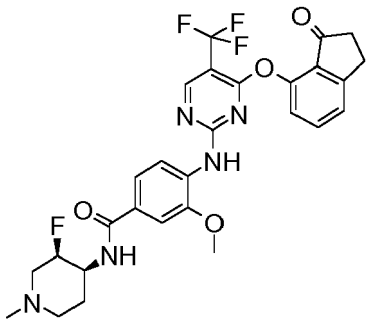
2	
3	
4	
5	

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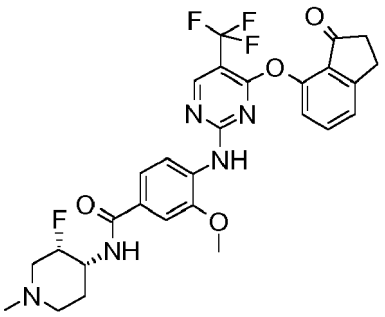
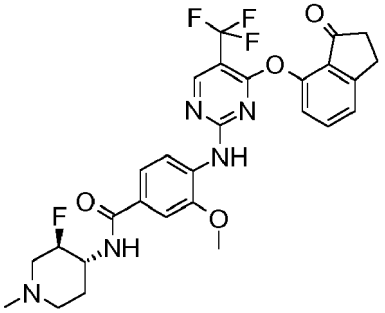
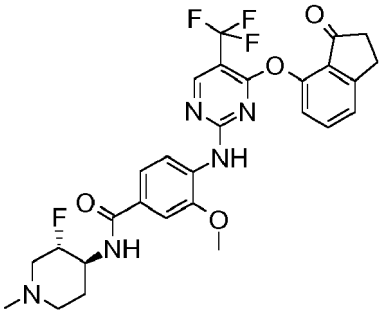
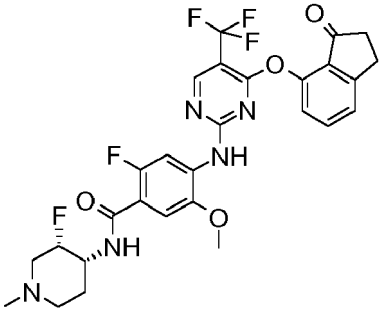
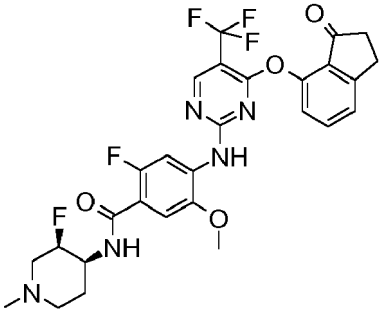
6	
7	
8	
9	
10	

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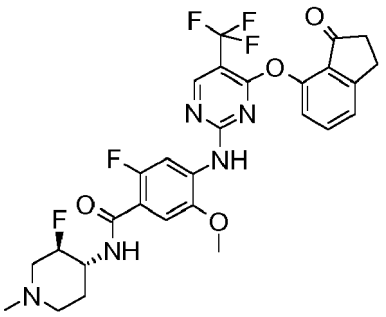
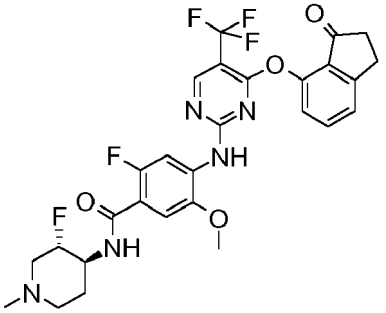
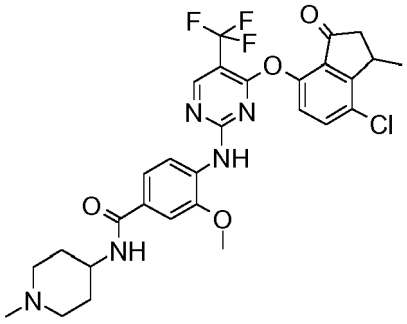
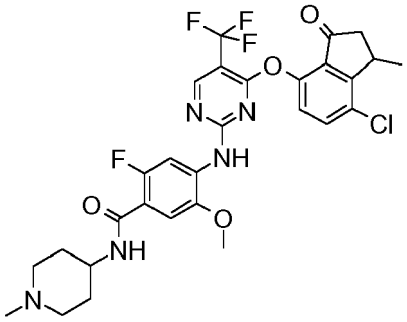
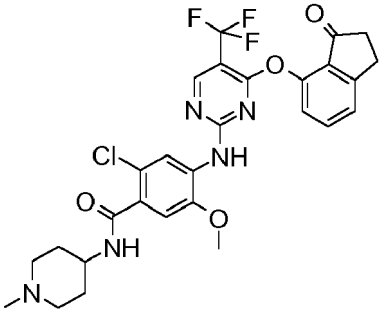
11	
12	
13	
14	
15	

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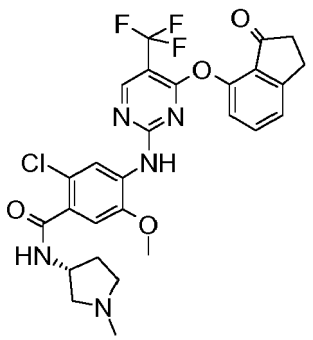
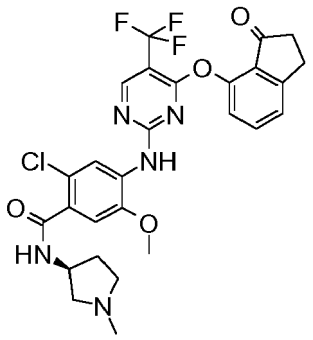
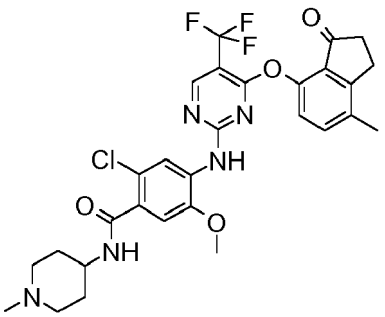
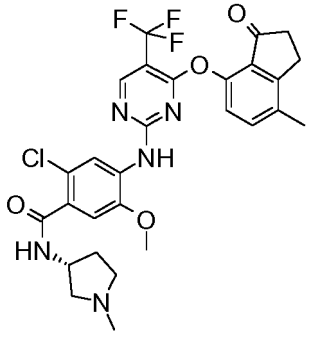
16	
17	
18	
19	

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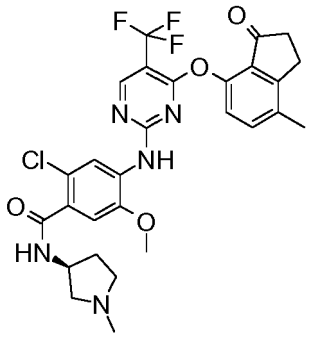
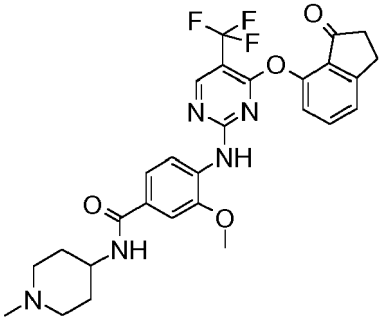
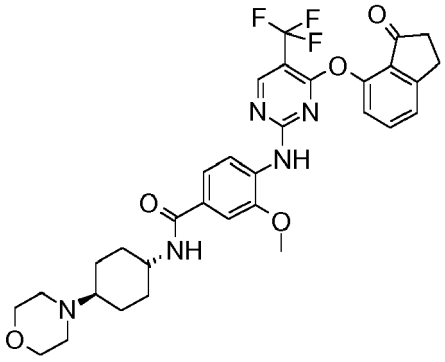
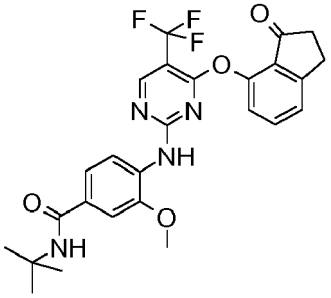
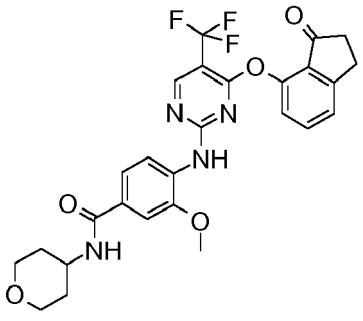
20	
21	
22	
23	
24	

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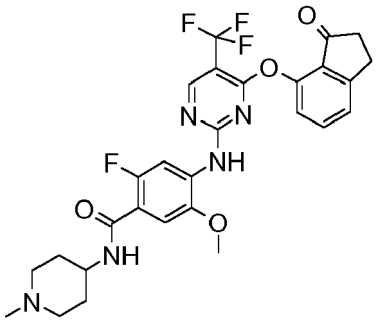
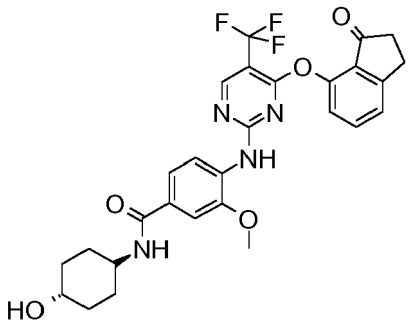
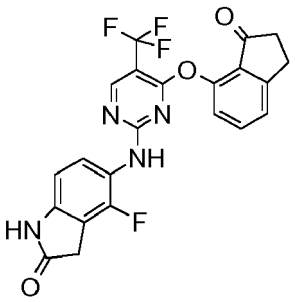
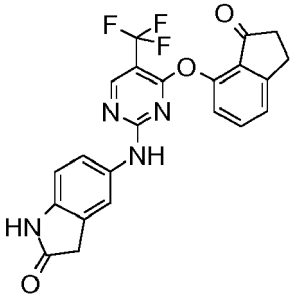
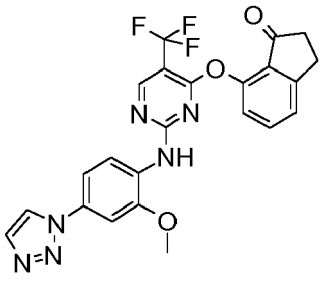
25	
26	
27	
28	
29	

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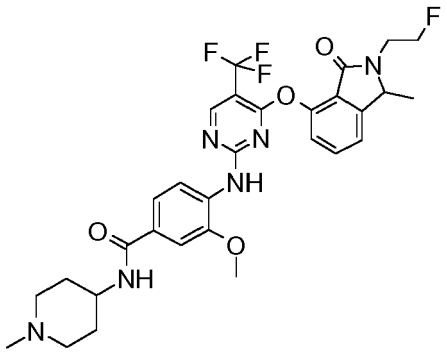
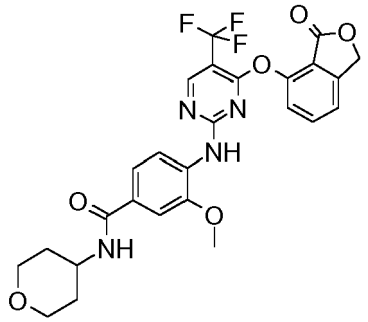
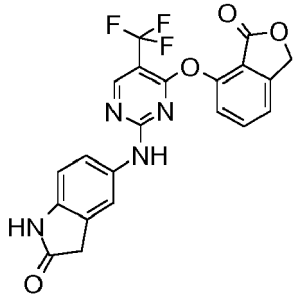
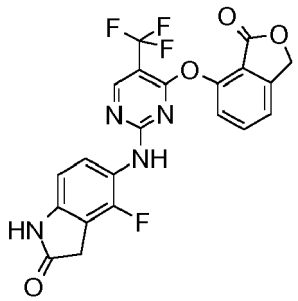
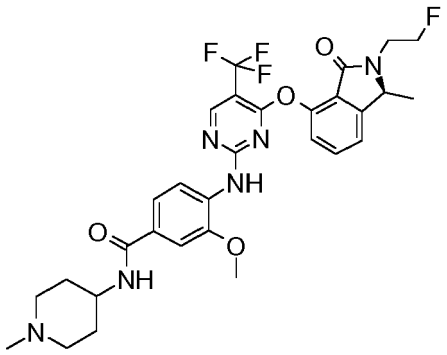
30	
31	
32	
33	
34	

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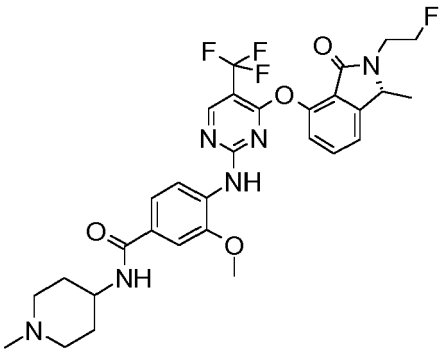
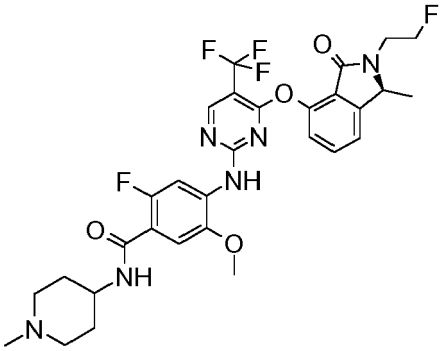
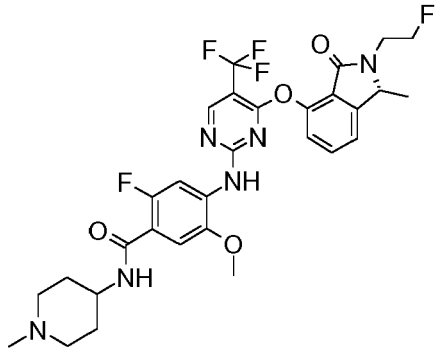
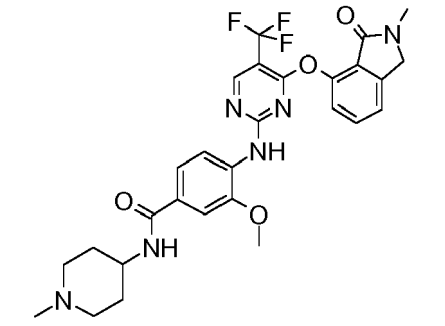
35	
36	
37	
38	

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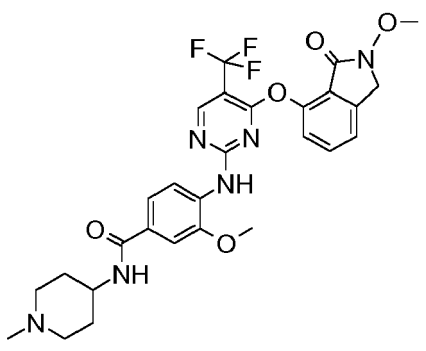
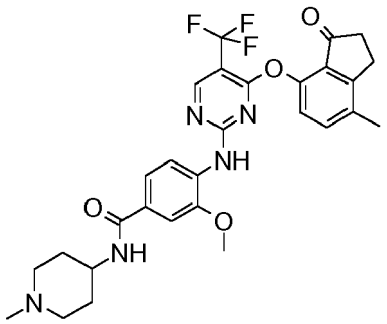
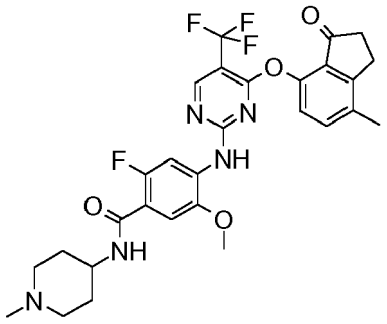
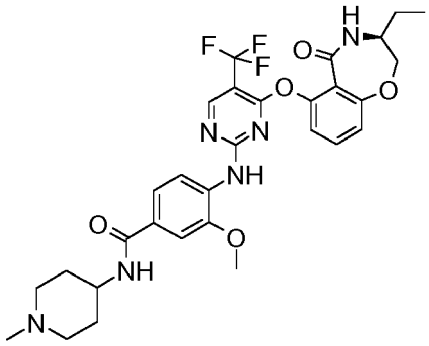
39	
40	
41	
42	

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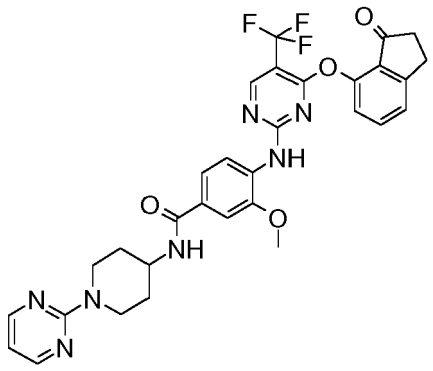
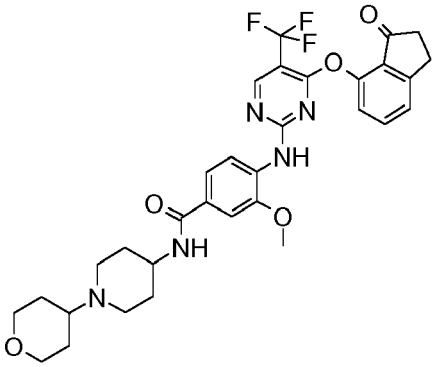
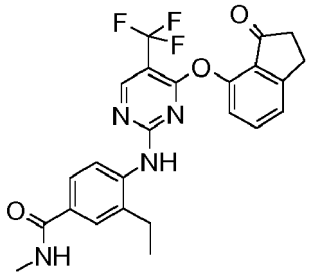
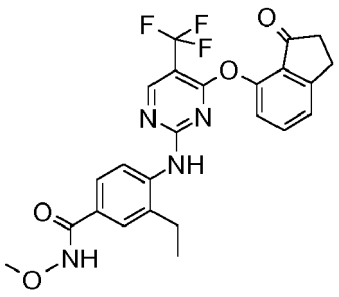
43	
44	
45	
46	

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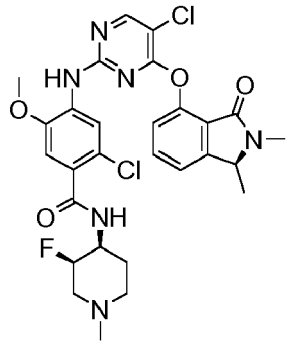
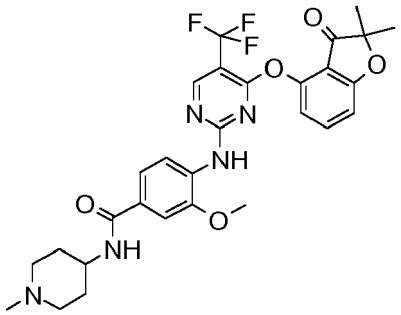
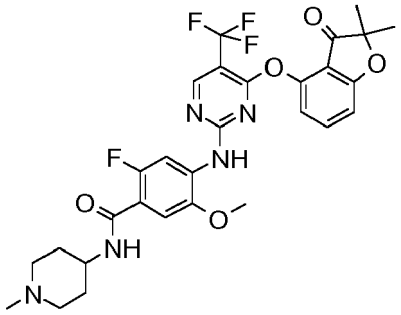
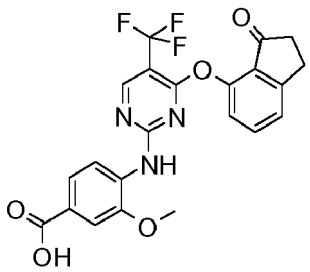
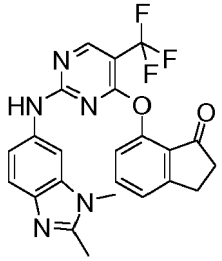
47	
48	
49	
50	
51	

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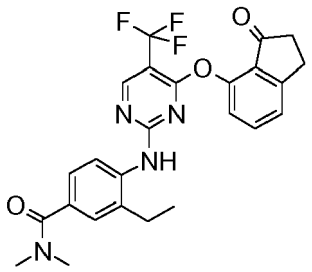
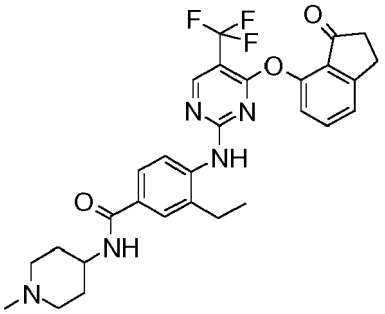
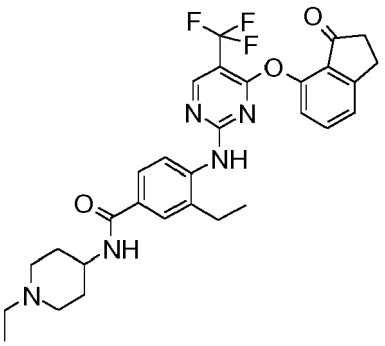
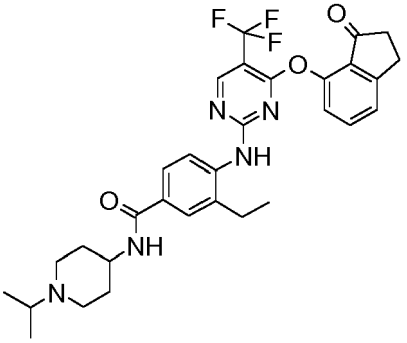
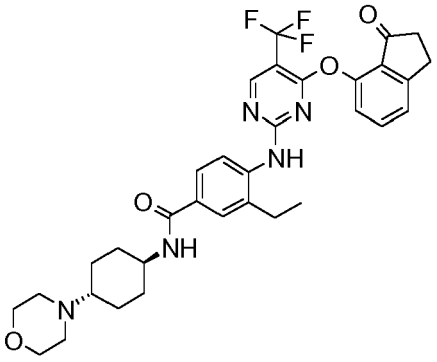
52	
53	
54	
55	
56	

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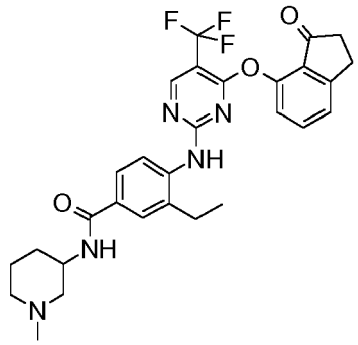
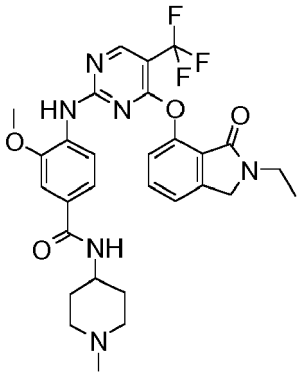
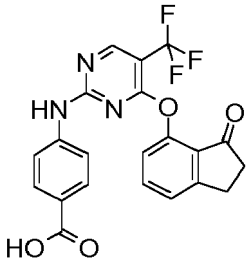
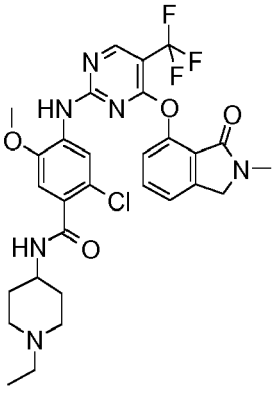
57	
58	
59	
60	

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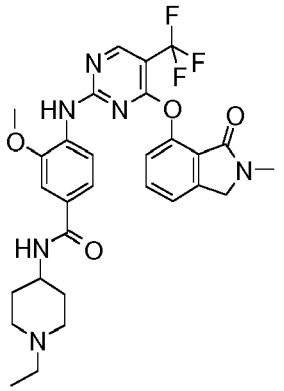
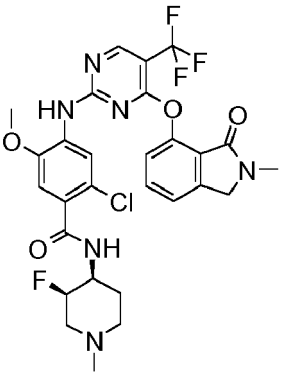
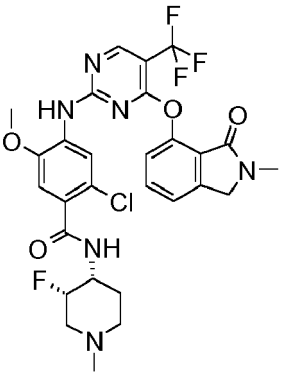
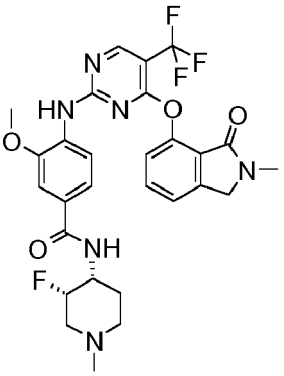
61	
62	
63	
64	

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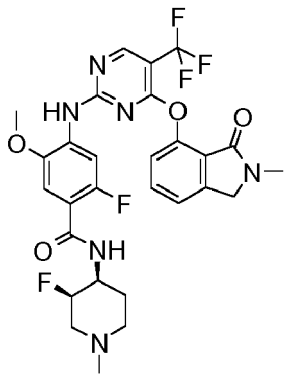
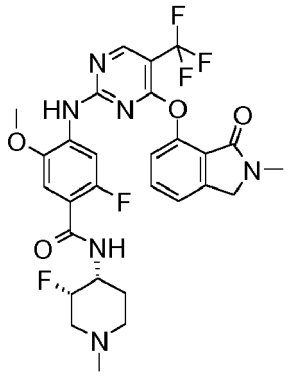
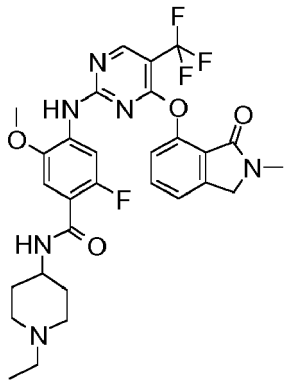
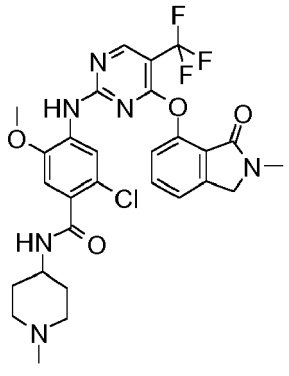
65	
66	
67	
68	

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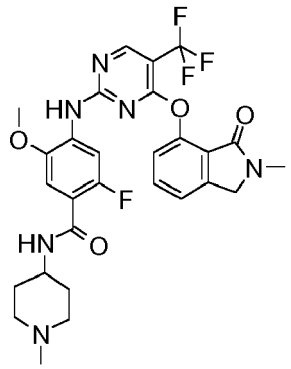
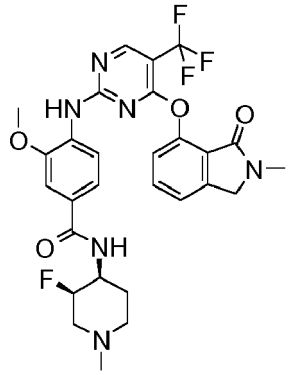
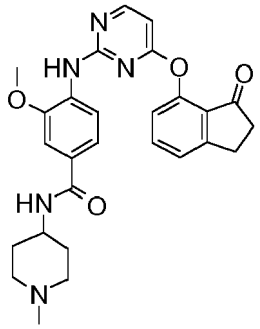
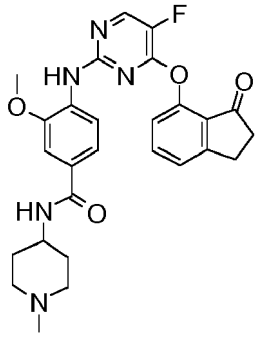
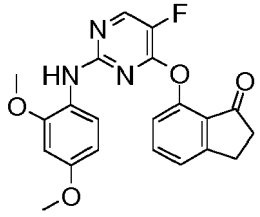
69	
70	
71	
72	
73	

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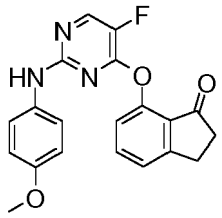
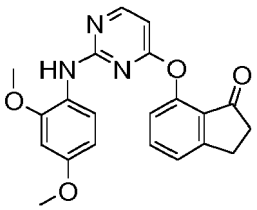
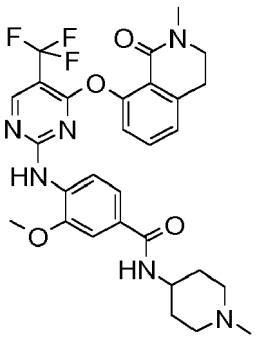
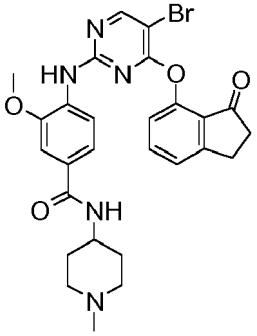
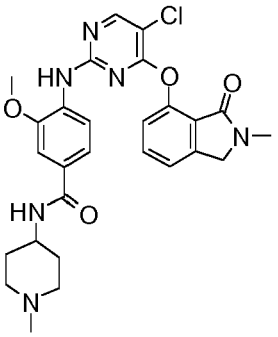
74	
75	
76	
77	
78	

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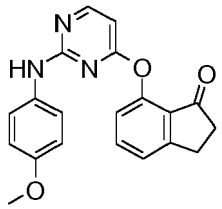
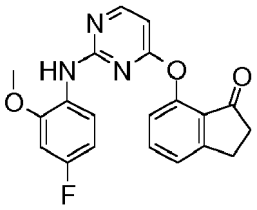
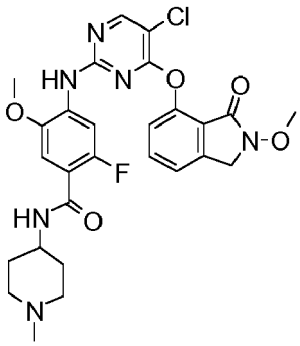
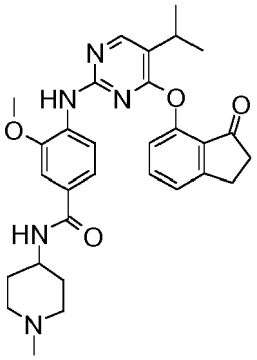
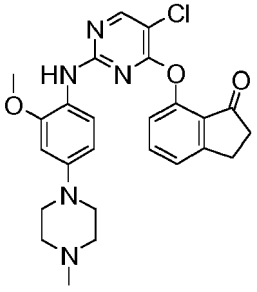
79	
80	
81	
82	
83	

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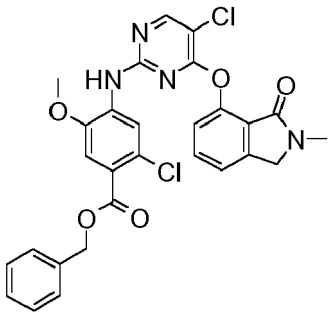
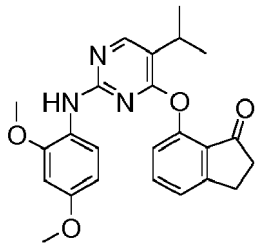
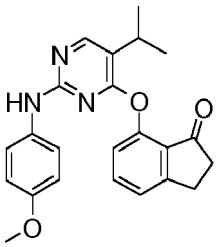
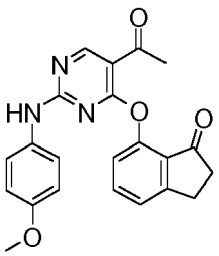
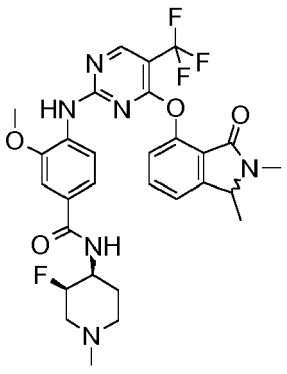
84	
85	
86	
87	
88	

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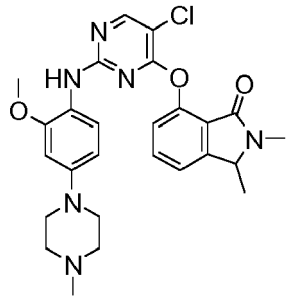
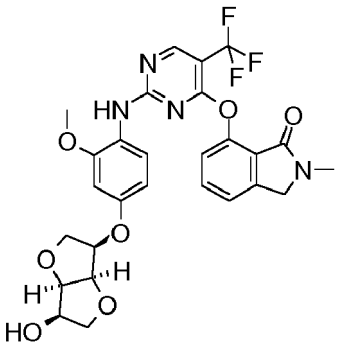
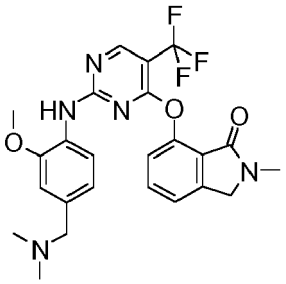
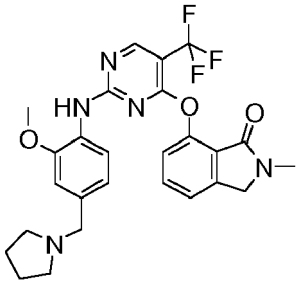
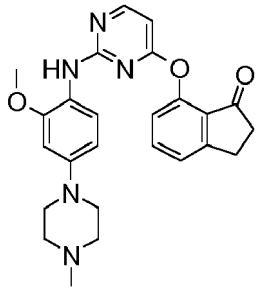
89	
91	
93	
94	
95	

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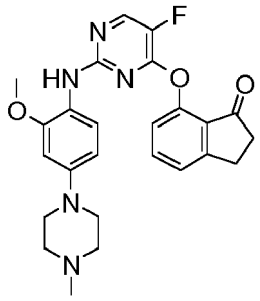
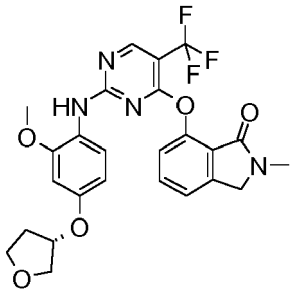
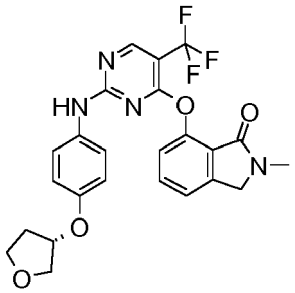
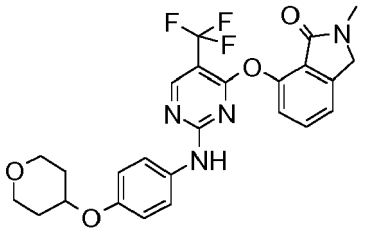
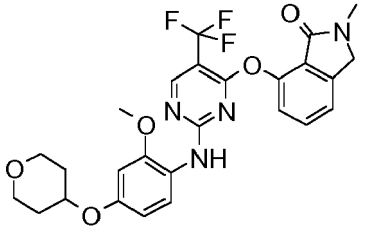
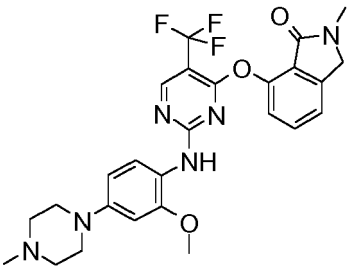
96	
97	
98	
99	
100	
101	

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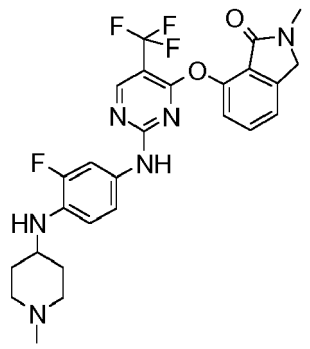
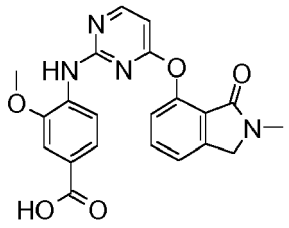
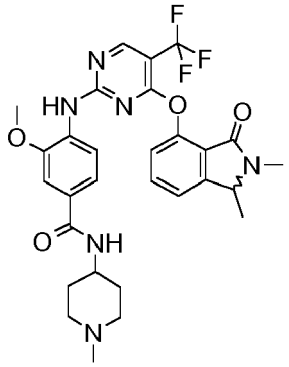
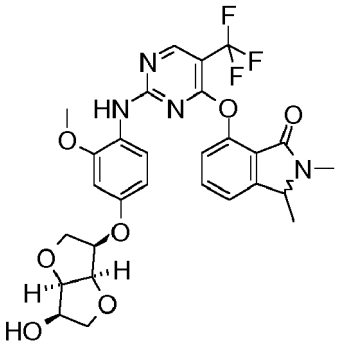
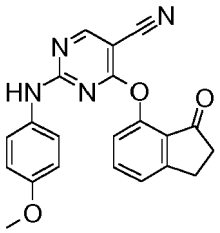
102	
103	
104	
105	
106	

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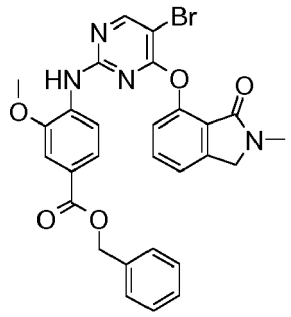
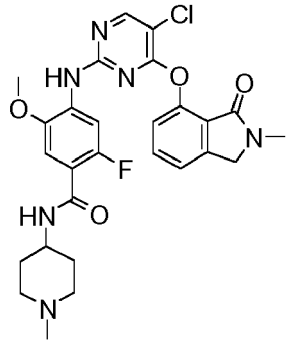
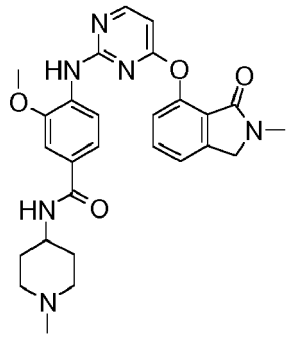
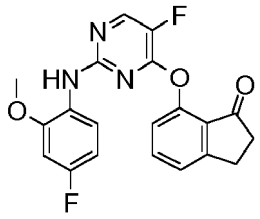
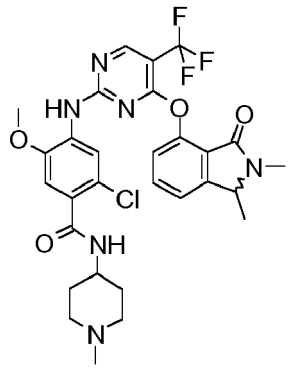
107	
108	
109	
110	
111	

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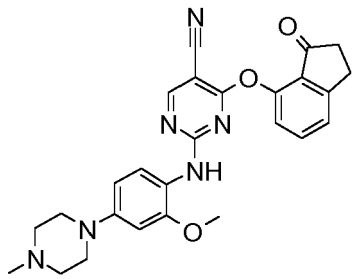
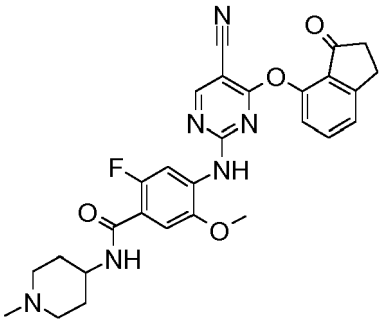
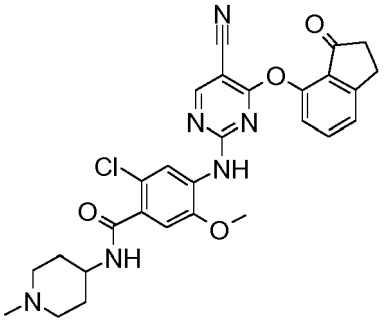
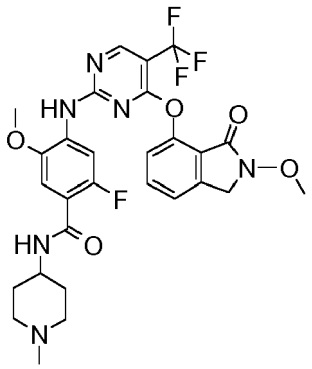
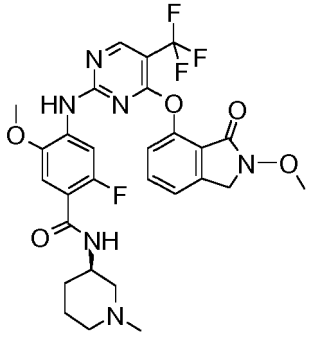
112	
113	
114	
115	
116	

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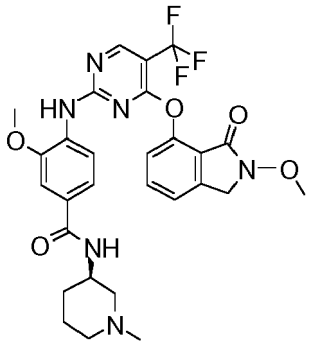
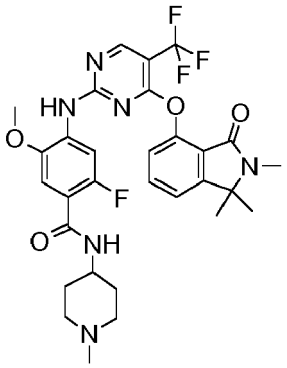
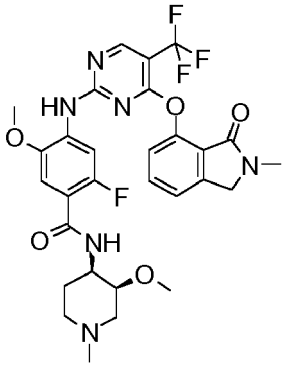
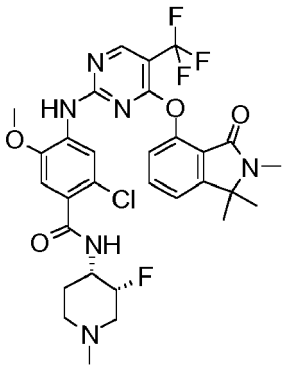
117	
118	
119	
120	

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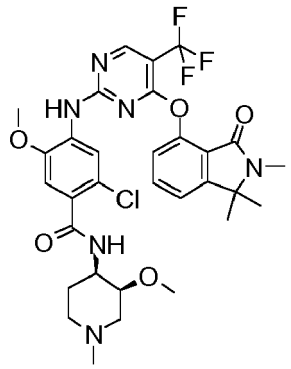
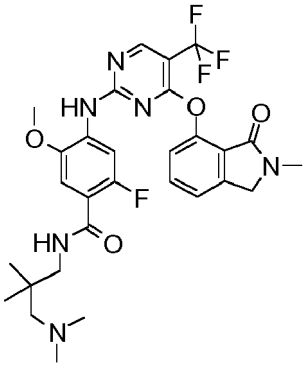
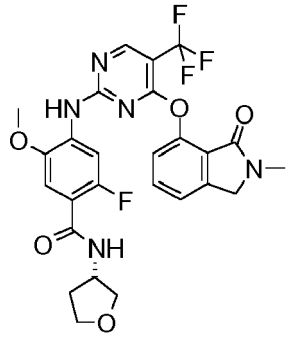
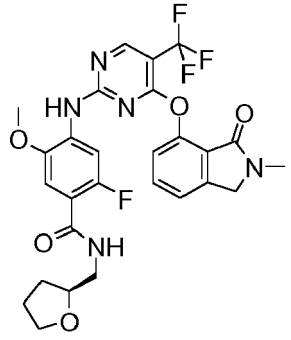
121	
122	
123	
124	

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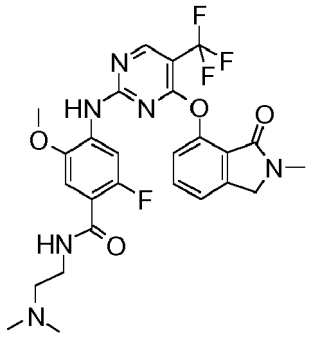
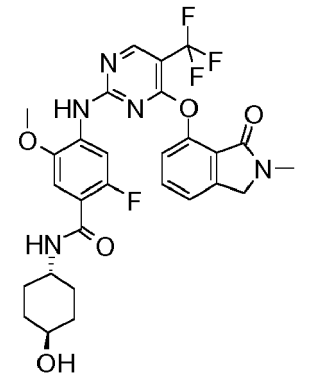
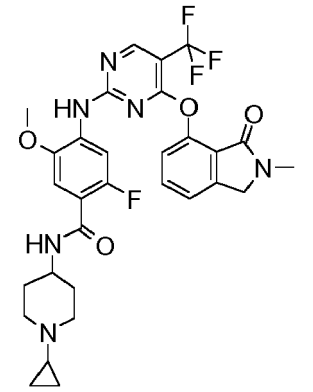
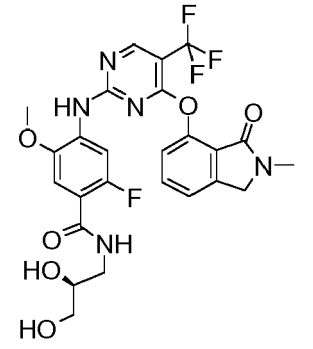
125	
126	
127	
128	

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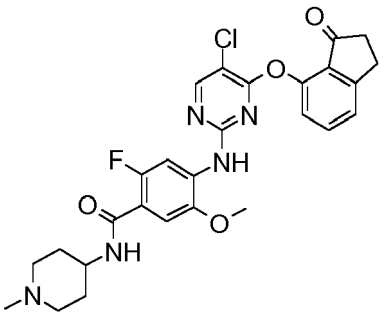
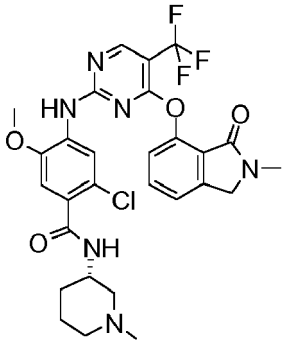
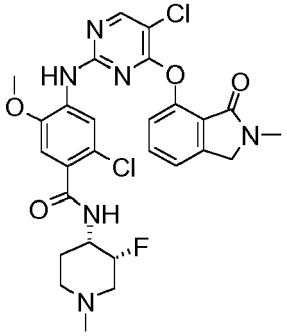
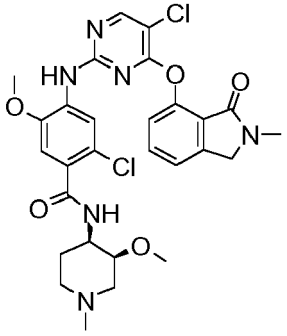
129	
130	
131	
132	

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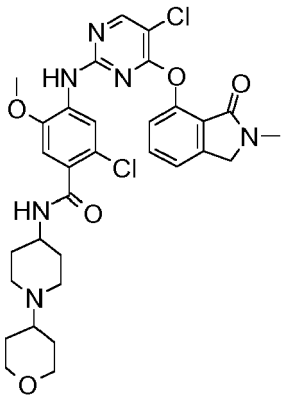
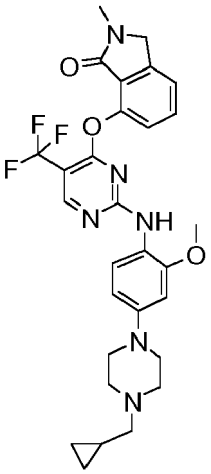
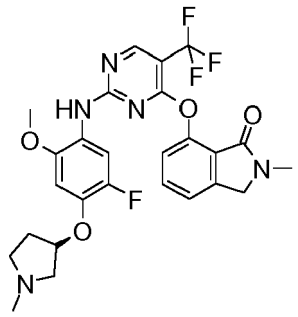
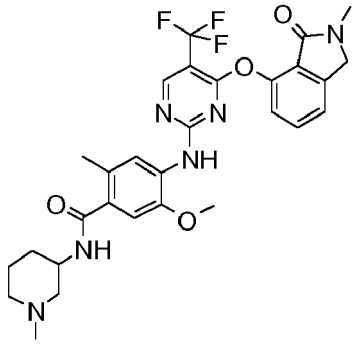
133	
134	
135	
136	

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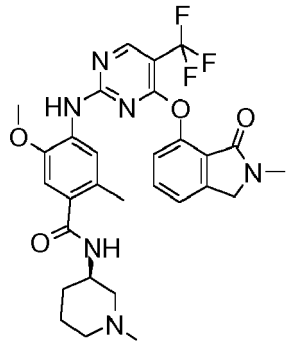
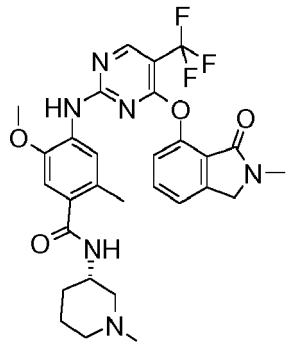
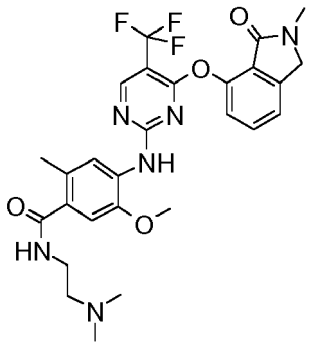
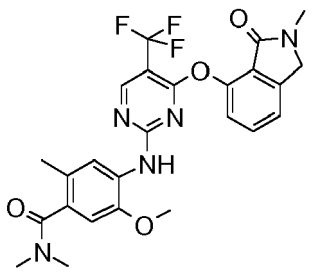
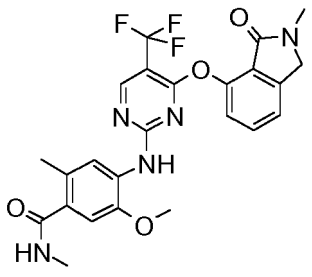
137	
138	
139	
140	
141	

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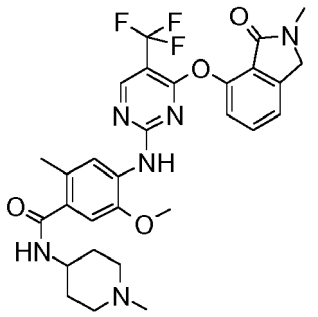
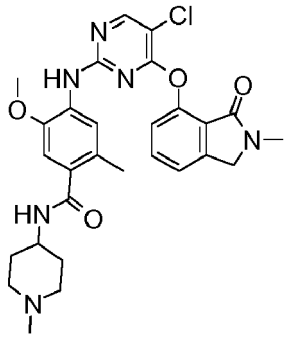
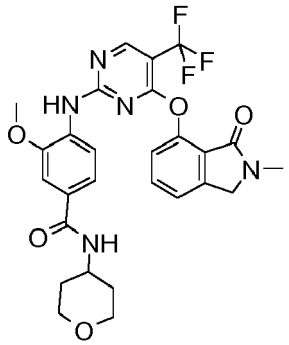
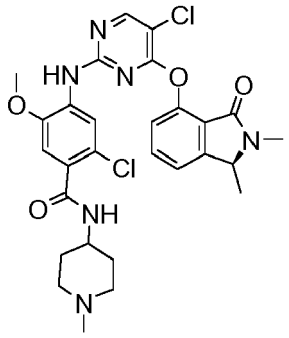
142	
143	
144	
145	

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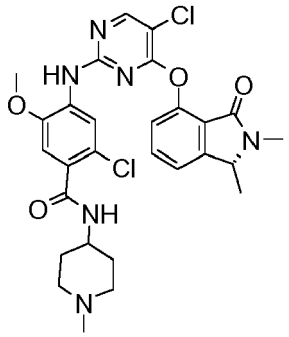
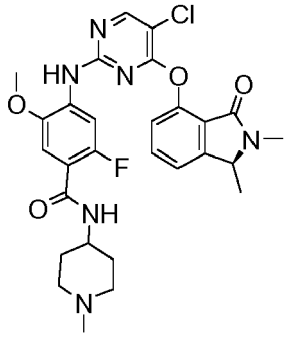
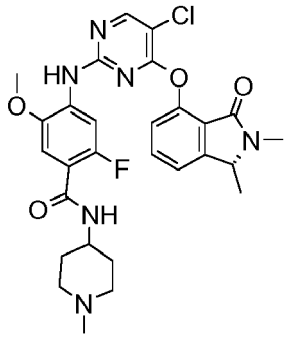
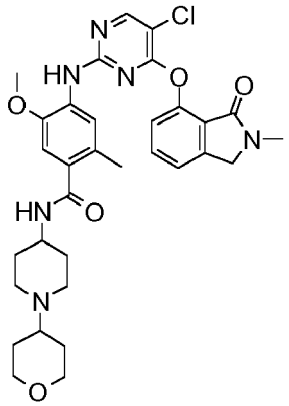
146	
147	
148	
149	

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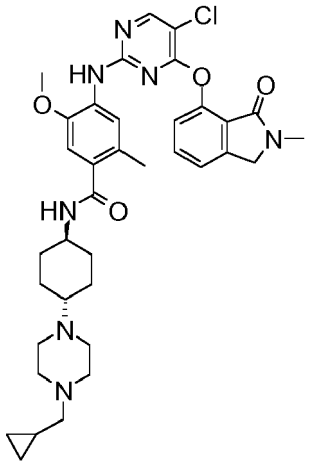
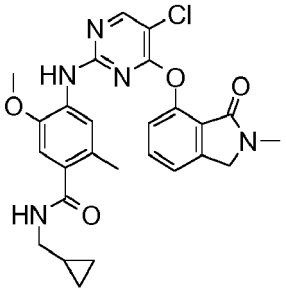
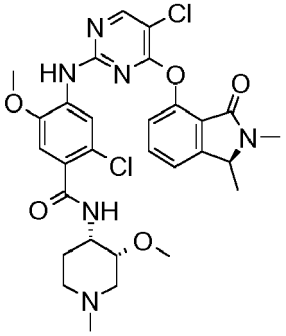
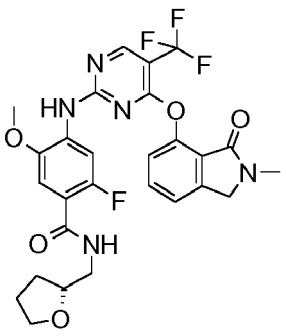
150	
151	
152	
153	

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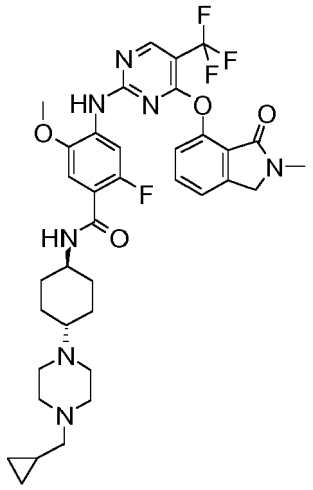
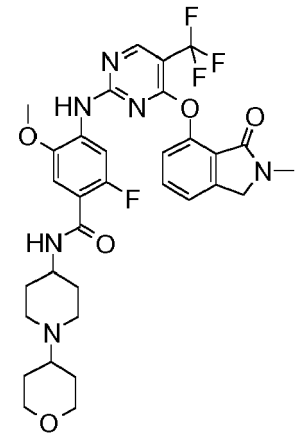
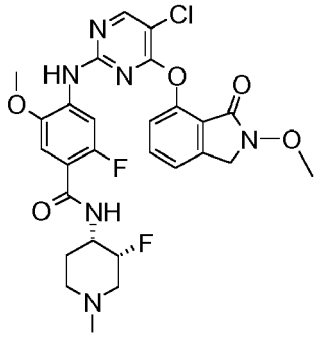
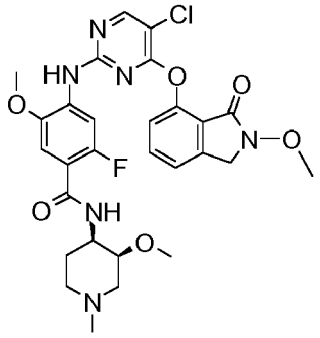
154	
155	
157	
158	

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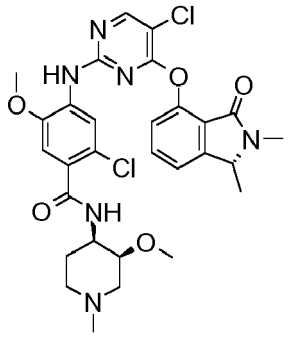
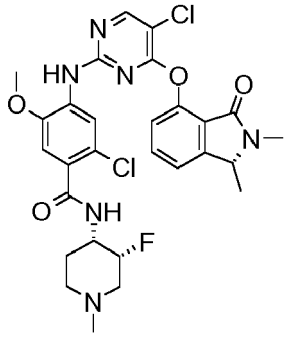
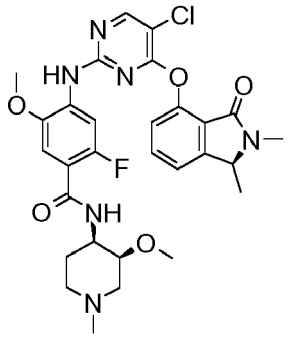
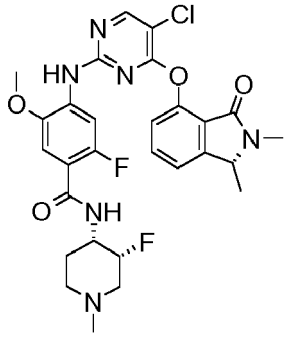
159	
160	
161	
162	

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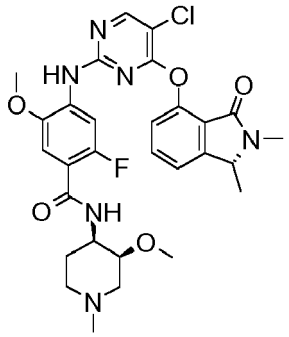
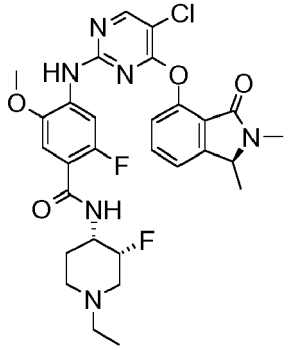
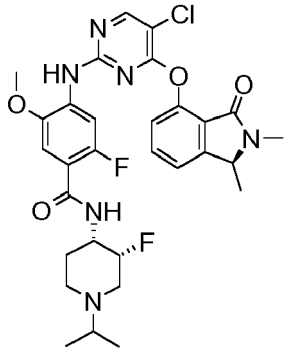
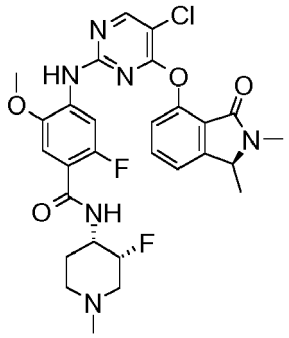
163	
164	
165	
166	

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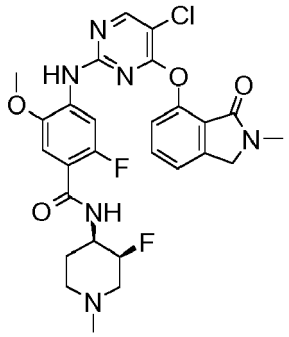
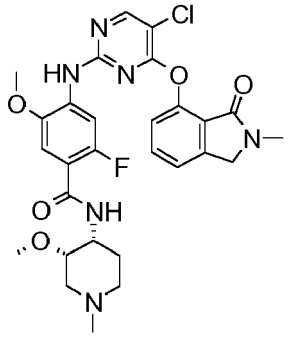
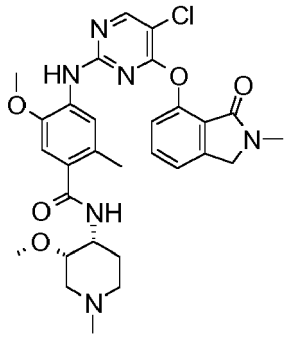
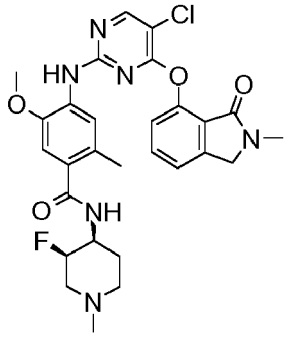
167	
168	
169	
170	

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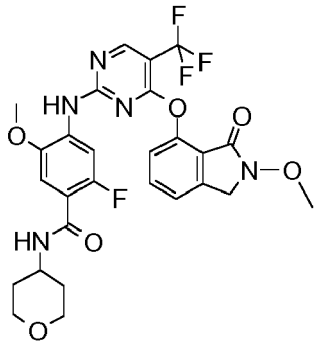
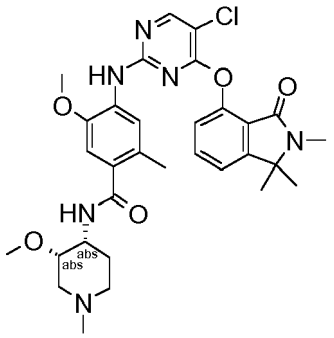
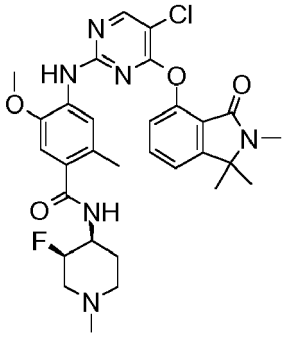
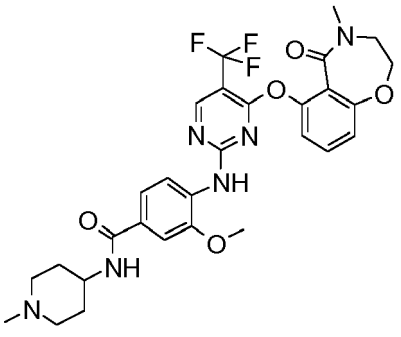
171	
172	 Chiral
173	
174	

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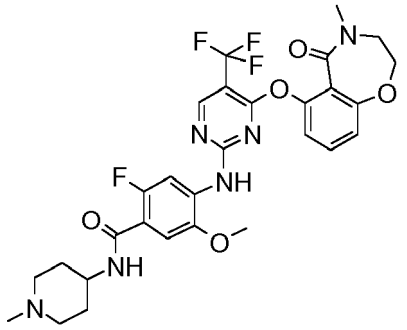
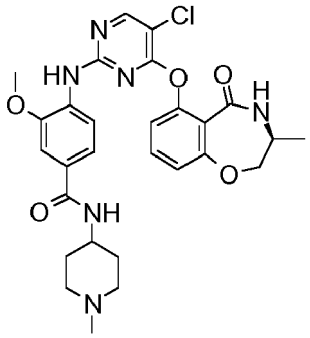
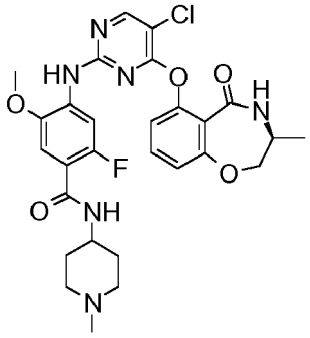
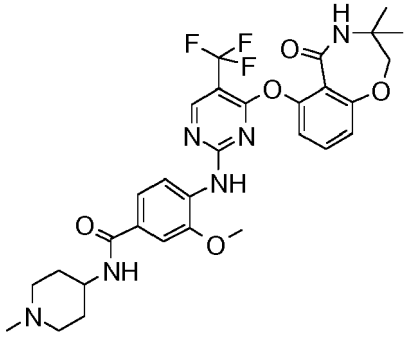
175	
176	
177	
178	

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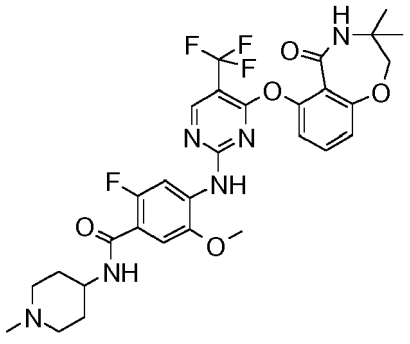
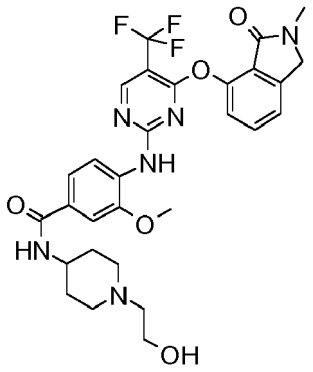
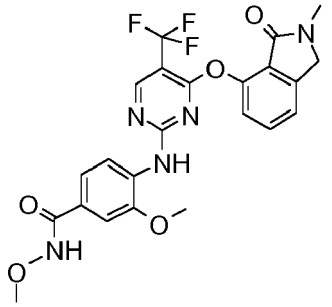
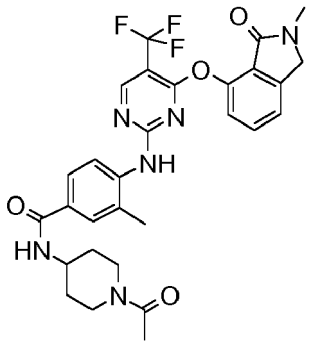
179	
180	
181	
182	

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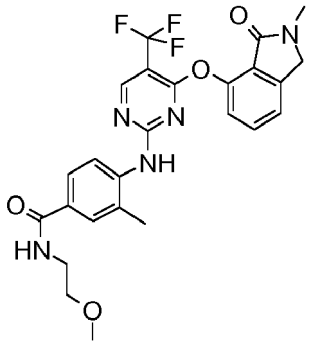
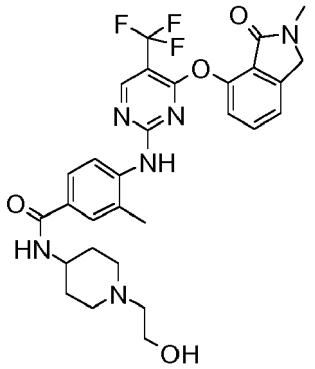
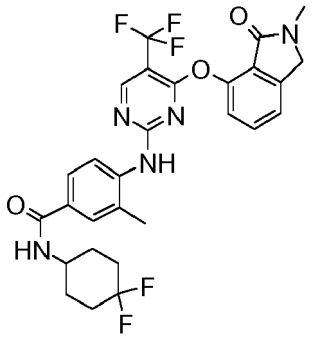
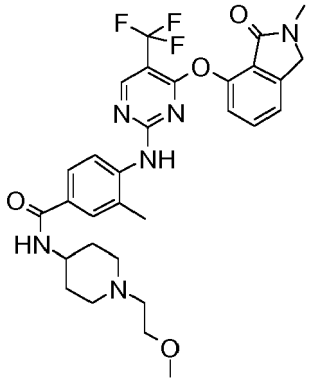
183	
184	
185	
186	

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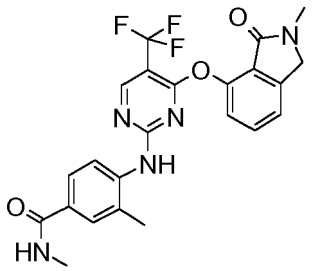
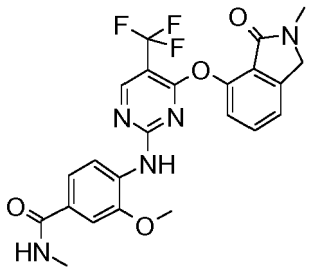
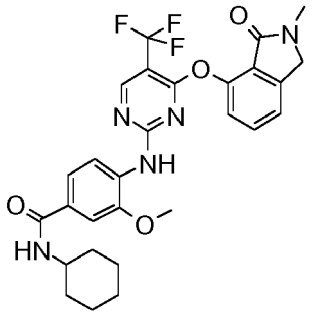
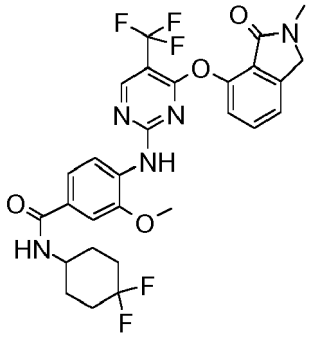
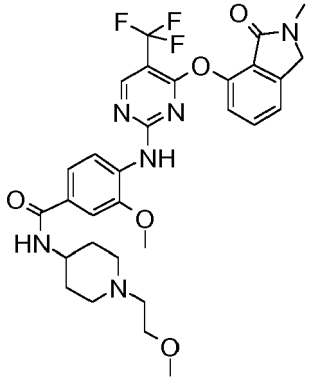
187	
188	
189	
190	
191	

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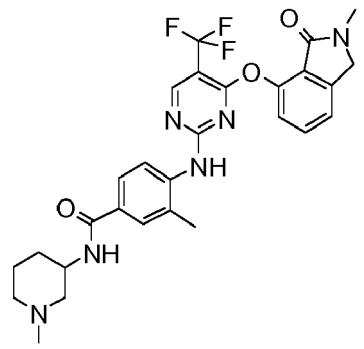
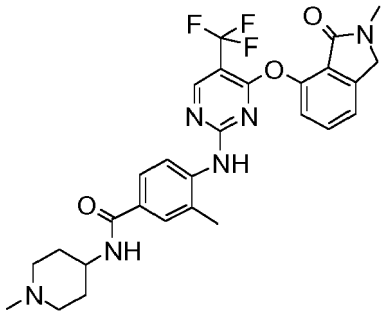
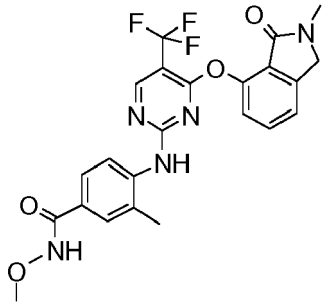
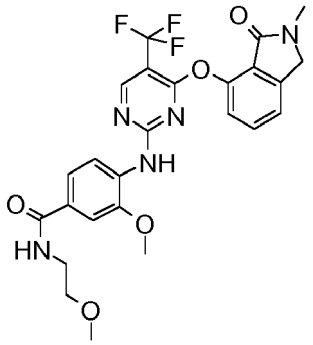
192	
193	
194	
195	

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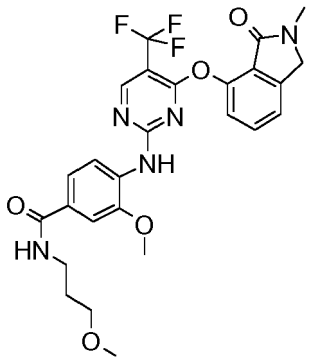
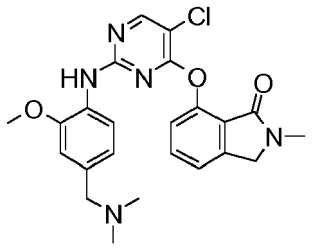
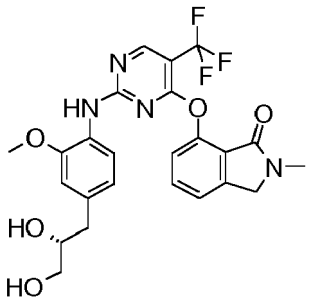
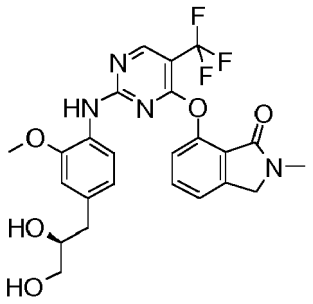
196	
197	
198	
199	

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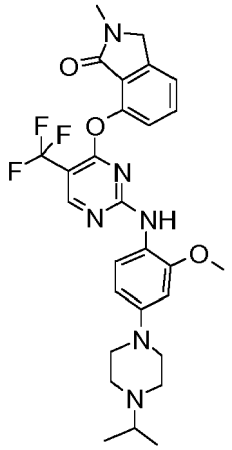
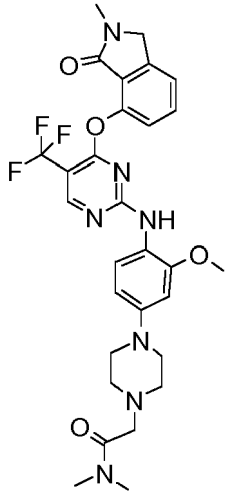
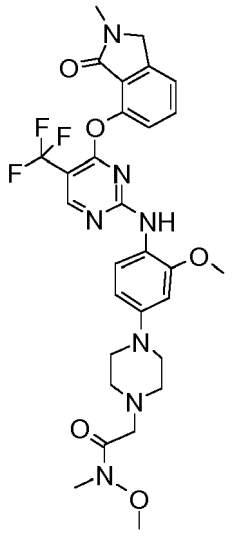
200	
201	
202	

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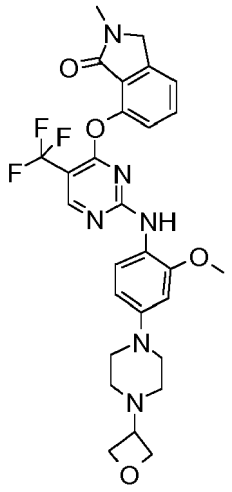
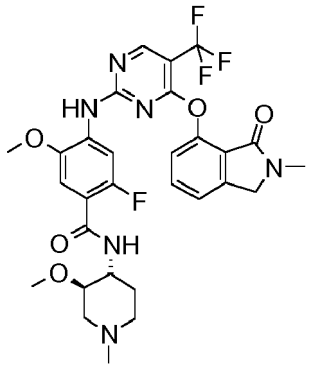
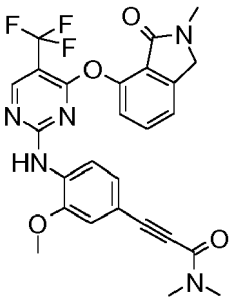
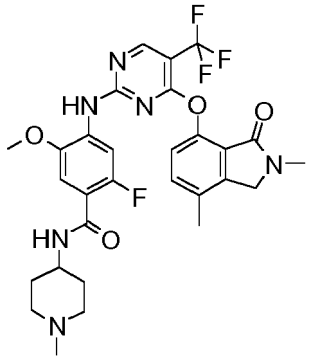
203	
204	
205	
206	

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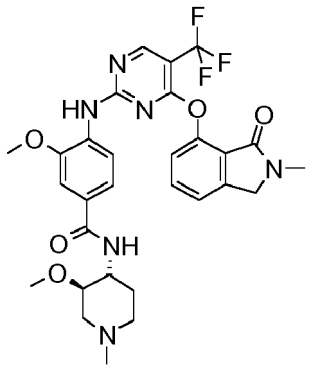
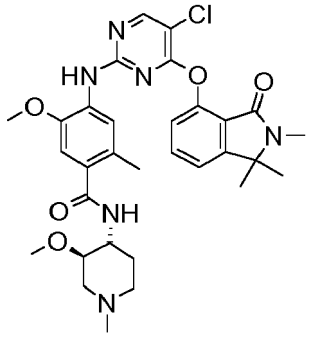
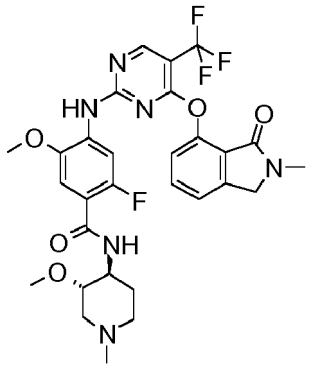
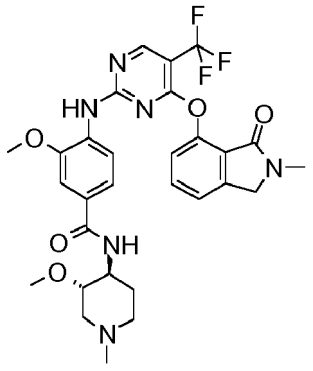
207	
208	
209	
210	

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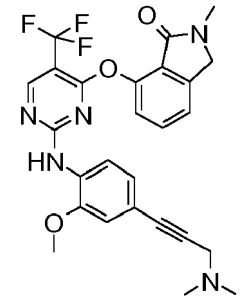
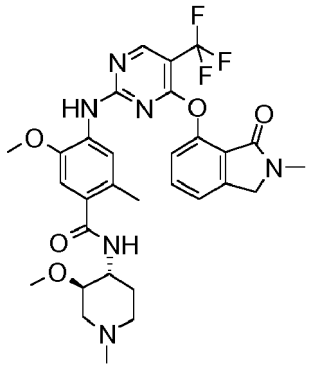
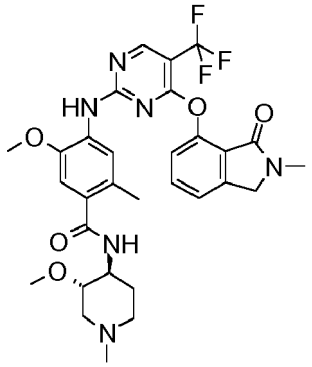
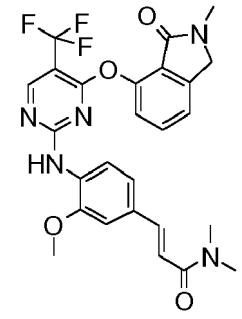
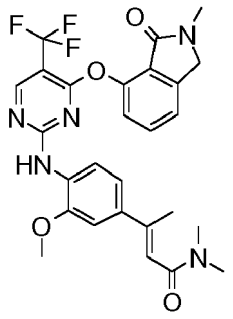
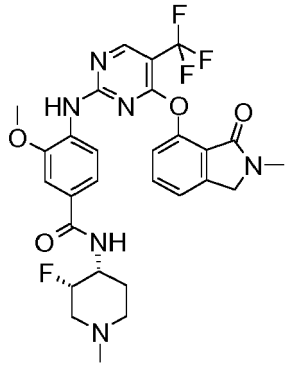
211	
212	
213	
214	

(continued)

215	

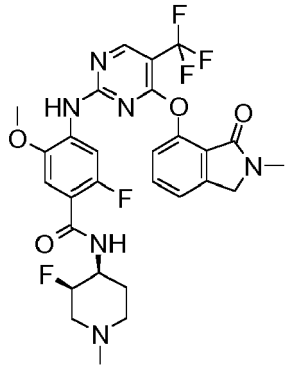
or a pharmacologically acceptable acid addition salt thereof.

8. A compound according to claim 7 of the formula

64	

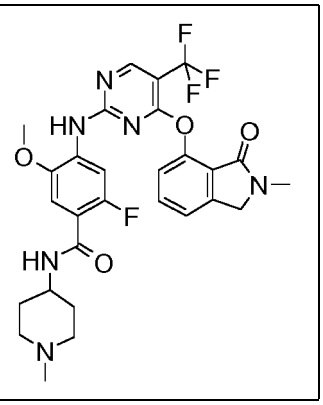
- or a pharmacologically acceptable acid addition salt thereof.

9. A compound according to claim 7 of the formula

65	

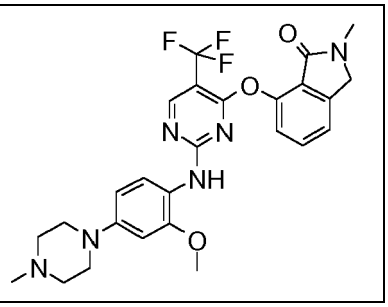
- or a pharmacologically acceptable acid addition salt thereof.

10. A compound according to claim 7 of the formula

69	

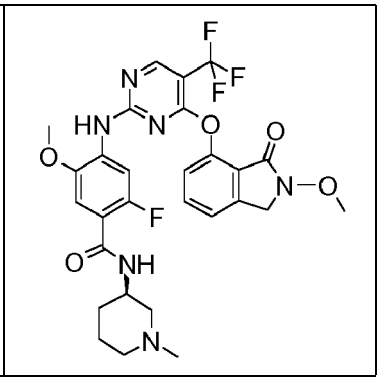
- or a pharmacologically acceptable acid addition salt thereof.

11. A compound according to claim 7 of the formula

101	

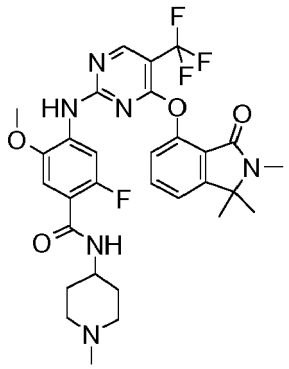
- or a pharmacologically acceptable acid addition salt thereof.

12. A compound according to claim 7 of the formula

116	

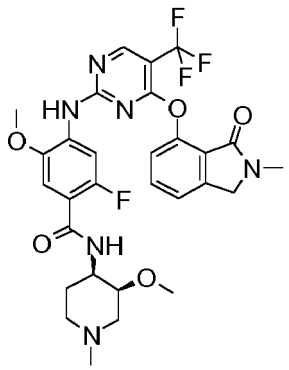
- or a pharmacologically acceptable acid addition salt thereof.

13. A compound according to claim 7 of the formula

118	

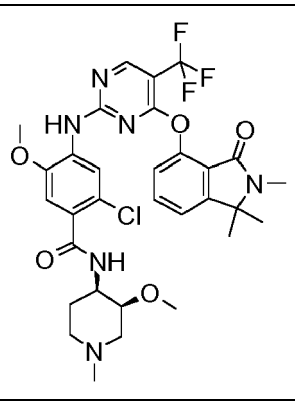
- or a pharmacologically acceptable acid addition salt thereof.

14. A compound according to claim 7 of the formula

119	

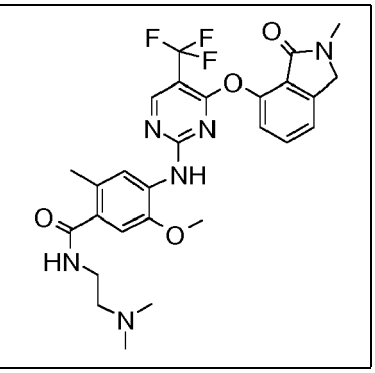
- or a pharmacologically acceptable acid addition salt thereof.

15. A compound according to claim 7 of the formula

121	

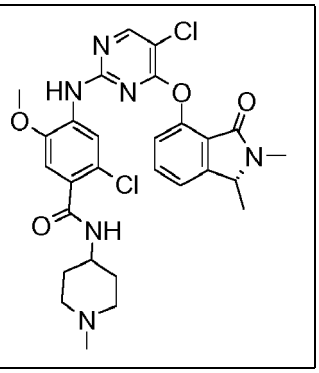
- or a pharmacologically acceptable acid addition salt thereof.

16. A compound according to claim 7 of the formula

139	

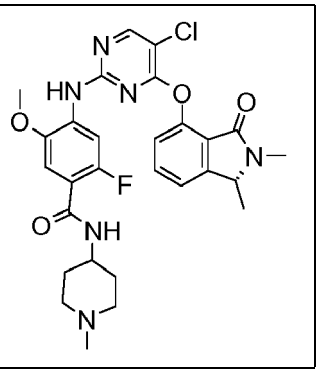
- or a pharmacologically acceptable acid addition salt thereof.

17. A compound according to claim 7 of the formula

146	

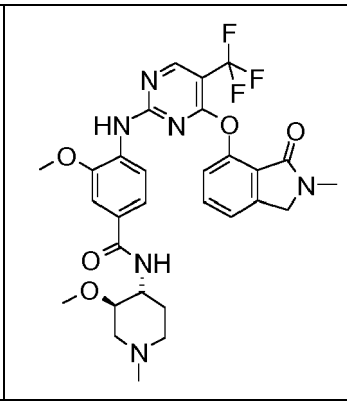
- or a pharmacologically acceptable acid addition salt thereof.

18. A compound according to claim 7 of the formula

148	

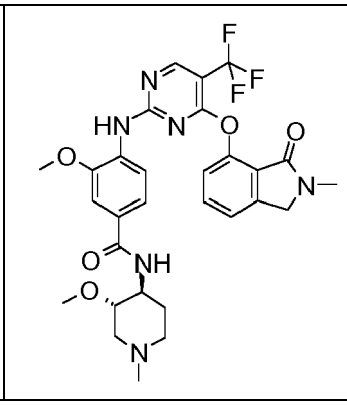
- or a pharmacologically acceptable acid addition salt thereof.

19. A compound according to claim 7 of the formula

207	

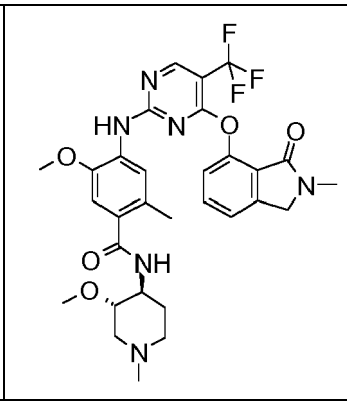
- or a pharmacologically acceptable acid addition salt thereof.

20. A compound according to claim 7 of the formula

210	

- or a pharmacologically acceptable acid addition salt thereof.

21. A compound according to claim 7 of the formula

213	

- or a pharmacologically acceptable acid addition salt thereof.

22. A compound - or the pharmaceutically effective salts thereof - according to one of claims 1 to 21 for use as medicament.

23. A compound - or the pharmaceutically effective salts thereof - according to one of claims 1 to 21 for preparing a medicament with an antiproliferative and/or pro-apoptotic activity.

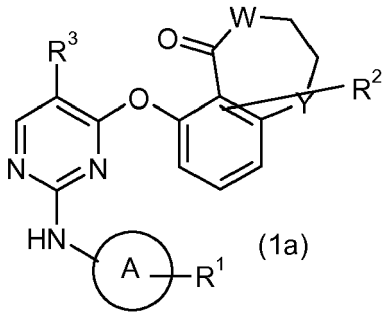
24. Pharmaceutical preparation, containing as active substance one or more compounds of general formulae **(1a)**, **(1b)**, **(1c)** or **(1d)** according to one of claims 1 to 21 or the physiologically acceptable salts thereof, optionally in combination with conventional excipients and/or carriers.

25. Use of a compound of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** according to one of claims 1 to 21 for preparing a pharmaceutical composition for the treatment and/or prevention of cancer, infections, inflammations and autoimmune diseases.

26. Pharmaceutical preparation comprising a compound of general formula **(1a)**, **(1b)**, **(1c)** or **(1d)** according to one of claims 1 to 21 and at least one further cytostatic or cytotoxic active substance different from formula **(1a)**, **(1b)**, **(1c)** or **(1d)**, optionally in the form of the tautomers, the racemates, the enantiomers, the diastereomers and the mixtures thereof, or the pharmacologically acceptable acid addition salts thereof.

Patentansprüche

1. Verbindung der allgemeinen Formel **(1a)**,



(1a)

wobei
A eine Gruppe bezeichnet, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen $\mathbf{R^1}$, ausgewählt aus C_{3-10}-Cycloalkyl, 3-8-gliedrigem Heterocycloalkyl, C_{6-15}-Aryl und 5-12-gliedrigem Heteroaryl;
$\mathbf{R^1}$ und $\mathbf{R^2}$ bezeichnen jeweils unabhängig voneinander Wasserstoff oder eine Gruppe, ausgewählt aus $\mathbf{R^a}$, $\mathbf{R^b}$ und $\mathbf{R^a}$, substituiert mit ein oder mehreren gleichen oder verschiedenen $\mathbf{R^c}$ und/oder $\mathbf{R^b}$;
$\mathbf{R^3}$ bezeichnet eine Gruppe, ausgewählt aus Wasserstoff, Halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}-Alkyl, C_{1-3}-Haloalkyl und C_{1-3}-Haloalkyloxy;
W und **Y** stellen jeweils unabhängig voneinander CH_2, O, N-R^e oder N-OR^e dar;
jedes $\mathbf{R^a}$ ist unabhängig voneinander ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-16}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes $\mathbf{R^b}$ stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, $-OR^c$, C_{1-3}-Haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, Halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^9)C(O)OR^c$, $-N(R^9)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ und $-N(R^g)C(NR^g)NR^cR^c$;
jedes $\mathbf{R^c}$ bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen $\mathbf{R^d}$ und/oder $\mathbf{R^e}$, ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes $\mathbf{R^d}$ stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, $-OR^e$, C_{1-3}-Haloalkyloxy, $-OCF_3$,

=S, -SR^e, =NR^e, =NOR^e, =NNR^eR^e, =$NN(R^g)C(O)NR^eR^e$, -NR^eR^e, -ONR^eR^e, -$N(R^g)NR^eR^e$, Halogen, -CF_3, -CN, -NC, -OCN, -SCN, -NO, -NO_2, =N_2, -N_3, -$S(O)R^e$, -$S(O)OR^e$, -$S(O)_2R^e$, -$S(O)_2OR^e$, -$S(O)NR^eR^e$, -$S(O)_2NR^eR^e$, -$OS(O)R^e$, -$OS(O)_2R^e$, -$OS(O)_2OR^e$, -$OS(O)NR^eR^e$, -$OS(O)_2NR^eR^e$, -$C(O)R^e$, -$C(O)OR^e$, -$C(O)SR^e$, -$C(O)NR^eR^e$, -$C(O)N(R^g)NR^eR^e$, -$C(O)N(R^g)OR^e$, -$C(NR^g)NR^eR^e$, -$C(NOH)R^e$, -$C(NOH)NR^eR^e$, -$OC(O)R^e$, -$OC(O)OR^e$, -$OC(O)SR^e$, -$OC(O)NR^eR^e$, -$OC(NR^g)NR^eR^e$, -$SC(O)R^e$, -$SC(O)OR^e$, -$SC(O)NR^eR^e$, -$SC(NR^g)NR^eR^e$, -$N(R^g)C(O)R^e$, -$N[C(O)R^e]_2$, -$N(OR^g)C(O)R^e$, -$N(R^g)C(NR^g)R^e$, -$N(R^g)N(R^g)C(O)R^e$, -$N[C(O)R^e]NR^eR^e$, -$N(R^g)C(S)R^e$, -$N(R^g)S(O)R^e$, -$N(R^g)S(O)OR^e$ -$N(R^g)S(O)_2R^e$, -$N[S(O)_2R^e]_2$, -$N(R^g)S(O)_2OR^e$, -$N(R^g)S(O)_2NR^eR^e$, -$N(R^g)[S(O)_2]_2R^e$, -$N(R^g)C(O)OR^e$, -$N(R^g)C(O)SR^e$, -$N(R^g)C(O)NR^eR^e$, -$N(R^g)C(O)NR^gNR^eR^e$, -$N(R^g)N(R^g)C(O)NR^eR^e$, -$N(R^g)C(S)NR^eR^e$, -$[N(R^g)C(O)]_2R^e$, -$N(R^g)[C(O)]_2R^e$, -$N\{[C(O)]_2R^e\}_2$, -$N(R^g)[C(O)]_2OR^e$, -$N(R^g)[C(O)]_2NR^eR^e$, -$N\{[C(O)]_2OR^e\}_2$, -$N\{[C(O)]_2NR^eR^e\}_2$, -$[N(R^g)C(O)]_2OR^e$, -$N(R^g)C(NR^g)OR^e$, -$N(R^g)C(NOH)R^e$, -$N(R^g)C(NR^g)SR^e$ und -$N(R^g)C(NR^g)NR^eR^e$;

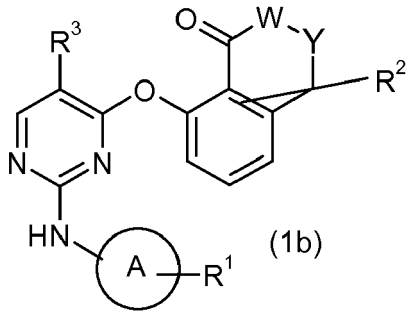
jedes **R^e** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^f** und/oder **R^g**, ausgewählt aus C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;

jedes **R^f** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus Halogen und -CF_3; und

jedes **R^g** bezeichnet unabhängig voneinander Wasserstoff, C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedriges Heteroalkyl, 3-8-gliedriges Heterocycloalkyl, 4-14-gliedriges Heterocycloalkyl, 5-12-gliedriges Heteroaryl oder 6-18-gliedriges Heteroarylalkyl;

gegebenenfalls in Form der Tautomeren, der Racemate, der Enantiomeren, der Diastereomeren und der Mischungen hiervon oder der pharmakologisch akzeptablen bzw. annehmbaren Säureadditionssalze hiervon.

2. Verbindung der allgemeinen Formel **(1b)**,



(1b)

wobei

A eine Gruppe bezeichnet, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^1**, ausgewählt aus C_{3-10}-Cycloalkyl, 3-8-gliedrigem Heterocycloalkyl, C_{6-15}-Aryl und 5-12-gliedrigem Heteroaryl;

R^1 und **R^2** bezeichnen jeweils unabhängig voneinander Wasserstoff oder eine Gruppe, ausgewählt aus **R^a**, **R^b** und **R^a**, substituiert mit ein oder mehreren gleichen oder verschiedenen **R^c** und/oder **R^b**;

R^3 bezeichnet eine Gruppe, ausgewählt aus Wasserstoff, Halogen, -OR^c, -OCF_3, -SR^c, -NR^cR^c, -CF_3, -CN, -OCN, -SCN, -NO, -NO_2, C_{1-3}-Alkyl, C_{1-3}-Haloalkyl und C_{1-3}-Haloalkyloxy;

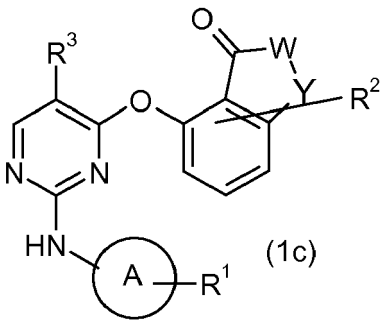
W und **Y** stellen jeweils unabhängig voneinander CH_2, O, N-R^e oder N-OR^e dar;

jedes **R^a** ist unabhängig voneinander ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-16}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;

jedes **R^b** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, -OR^c, C_{1-3}-Haloalkyloxy, -OCF3, =S, -SR^c, =NR^c, =NOR^c, =NNR^cR^c, =$NN(R^g)C(O)NR^cR^c$, -NR^cR^c, -ONR^cR^c, -$N(OR^c)R^c$, -$N(R^g)NR^cR^c$, Halogen, -CF_3, -CN, -NC, -OCN, -SCN, -NO, -NO_2, =N_2, -N_3, -$S(O)R^c$, -$S(O)OR^c$, -$S(O)_2R^c$, -$S(O)_2OR^c$, -$S(O)NR^cR^c$, -$S(O)_2NR^cR^c$, -$OS(O)R^c$, -$OS(O)_2R^c$, -$OS(O)_2OR^c$, -$OS(O)NR^cR^c$, -$OS(O)_2NR^cR^c$, -$C(O)R^c$, -$C(O)OR^c$, -$C(O)SR^c$, -$C(O)NR^cR^c$, -$C(O)N(R^g)NR^cR^c$, -$C(O)N(R^g)OR^c$, -$C(NR^g)NR^cR^c$, -$C(NOH)R^c$, -$C(NOH)NR^cR^c$, -$OC(O)R^c$, -$OC(O)OR^c$, -$OC(O)SR^c$, -$OC(O)NR^cR^c$, -$OC(NR^g)NR^cR^c$, -$SC(O)R^c$, -$SC(O)OR^c$, -$SC(O)NR^cR^c$, -$SC(NR^g)NR^cR^c$, -$N(R^g)C(O)R^c$, -$N[C(O)R^e]_2$, -$N(OR^g)C(O)R^c$, -$N(R^g)C(NR^g)R^c$, -$N(R^g)N(R^g)C(O)R^c$, -$N[C(O)R^c]NR^cR^c$, -$N(R^g)C(S)R^c$, -$N(R^g)S(O)R^c$, -$N(R^g)S(O)OR^c$, -$N(R^g)S(O)_2R^c$, -$N[S(O)_2R^c]_2$, -$N(R^g)S(O)_2OR^c$, -$N(R^g)S(O)_2NR^cR^c$, -$N(R^g)[S(O)_2]_2R^c$, -$N(R^9)C(O)OR^c$, -$N(R^9)C(O)SR^c$, -$N(R^g)C(O)NR^cR^c$, -$N(R^g)C(O)NR^gNR^cR^c$, -$N(R^g)N(R^g)C(O)NR^cR^c$, -$N(R^g)C(S)NR^cR^c$, -$[N(R^g)C(O)]_2R^c$, -$N(R^g)[C(O)_2R^c$, -$N\{[C(O)]_2R^c\}_2$, -$N(R^g)[C(O)]_2OR^c$, -$N(R^g)[C(O)]_2NR^cR^c$, -$N\{[C(O)]_2OR^c\}_2$, -$N\{[C(O)]_2NR^cR^c\}_2$, -$[N(R^g)C(O)]_2OR^c$, -$N(R^g)C(NR^g)OR^c$,

$-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ und $-N(R^g)C(NR^g)NR^cR^c$;
jedes **R^c** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^d** und/oder **R^e**, ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^d** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, $-OR^e$, C_{1-3}-Haloalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, Halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_{2O}R^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ und $-N(R^g)C(NR^g)NR^eR^e$;
jedes **R^e** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^f** und/oder **R^g**, ausgewählt aus C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^f** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus Halogen und $-CF_3$; und
jedes **R^g** bezeichnet unabhängig voneinander Wasserstoff, C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedriges Heteroalkyl, 3-8-gliedriges Heterocycloalkyl, 4-14-gliedriges Heterocycloalkyl, 5-12-gliedriges Heteroaryl oder 6-18-gliedriges Heteroarylalkyl;
gegebenenfalls in Form der Tautomeren, der Racemate, der Enantiomeren, der Diastereomeren und der Mischungen hiervon, oder der pharmakologisch akzeptablen bzw. annehmbaren Säureadditionssalze hiervon.

3. Verbindung der allgemeinen Formel **(1c)**,



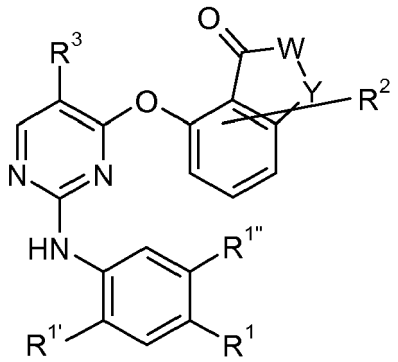
(1c)

wobei
A eine Gruppe bezeichnet, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^1**, ausgewählt aus C_{3-10}-Cycloalkyl, 3-8-gliedrigem Heterocycloalkyl, C_{6-15}-Aryl und 5-12-gliedrigem Heteroaryl;
R^1 und **R^2** bezeichnen jeweils unabhängig voneinander Wasserstoff oder eine Gruppe, ausgewählt aus **R^a**, **R^b** und **R^a**, substituiert mit ein oder mehreren gleichen oder verschiedenen **R^c** und/oder **R^b**;
R^3 bezeichnet eine Gruppe, ausgewählt aus Wasserstoff, Halogen, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, C_{1-3}-Alkyl, C_{1-3}-Haloalkyl und C_{1-3}-Haloalkyloxy;
W und Y stellen jeweils unabhängig voneinander CH_2, O, N-R^e oder N-OR^e dar;
jedes **R^a** ist unabhängig voneinander ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-16}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^b** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, $-OR^c$, C_{1-3}-Haloalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, Halogen, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$,

-OC(O)OR^c, -OC(O)SR^c, -OC(O)NR^{c}R^c, -OC(NR^g)NR^{c}R^c, -SC(O)R^c, -SC(O)OR^c, -SC(O)NR^{c}R^c, -SC(NR^g)NR^{c}R^c, -N(R^g)C(O)R^c, -N[C(O)R^c]$_2$, -N(OR^g)C(O)^c, -N(R^g)C(NR^g)R^c, -N(R^g)N(R^g)C(O)R^c, -N[C(O)R^c]NR^{c}R^c, -N(R^g)C(S)R^c, -N(R^g)S(O)R^c, -N(R^g)S(O)OR^c, -N(R^g)S(O)$_2$R^c, -N[S(O)$_2$R^c]$_2$, -N(R^g)S(O)$_2$OR^c, -N(R^g)S(O)$_2$NR^{c}R^c, -N(R^g)[S(O)$_2$]$_2$R^c, -N(R^g)C(O)OR^c, -N(R^g)C(O)SR^c, -N(R^g)C(O)NR^{c}R^c, -N(R^g)C(O)NR^{g}NR^{c}R^c, -N(R^g)N(R^g)C(O)NR^{c}R^c, -N(R^g)C(S)NR^{c}R^c, -[N(R^g)C(O)]$_2$R^c, -N(R^g)[C(O)$_2$R^c, -N{[C(O)]$_2$R^c}$_2$, -N(R^g)[C(O)]$_2$OR^c, -N(R^g)[C(O)]$_2$NR^{c}R^c, -N{[C(O)]$_2$OR^c}$_2$, -N{[C(O)]$_2$NR^{c}R^c}$_2$, -[N(R^g)C(O)]$_2$OR^c, -N(R^g)C(NR^g)OR^c, -N(R^g)C(NOH)R^c, -N(R^g)C(NR^g)SR^c und -N(R^g)C(NR^g)NR^{c}R^c;
jedes **R^c** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^d** und/oder **R^e**, ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^d** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, -OR^e, C_{1-3}-Haloalkyloxy, -OCF$_3$, =S, -SR^e, =NR^e, =NOR^e, =NNR^{e}R^e, =NN(R^g)C(O)NR^{e}R^e, -NR^{e}R^e, -ONR^{e}R^e, -N(R^g)NR^{e}R^e, Halogen, -CF$_3$, -CN, -NC, -OCN, -SCN, -NO, -NO$_2$, =N$_2$, -N$_3$, -S(O)R^e, -S(O)OR^e, -S(O)$_2$R^e, -S(O)$_2$OR^e, -S(O)NR^{e}R^e, -S(O)$_2$NR^{e}R^e, -OS(O)R^e, -OS(O)$_2$R^e, -OS(O)$_2$OR^e, -OS(O)NR^{e}R^e, -OS(O)$_2$NR^{e}R^e, -C(O)R^e, -C(O)OR^e, -C(O)SR^e, -C(O)NR^{e}R^e, -C(O)N(R^g)NR^{e}R^e, -C(O)N(R^g)OR^e, -C(NR^g)NR^{e}R^e, -C(NOH)R^e, -C(NOH)NR^{e}R^e, -OC(O)R^e, -OC(O)OR^e, -OC(O)SR^e, -OC(O)NR^{e}R^e, -OC(NR^g)NR^{e}R^e, -SC(O)R^e, -SC(O)OR^e, -SC(O)NR^{e}R^e, -SC(NR^g)NR^{e}R^e, -N(R^g)C(O)R^e, -N[C(O)R^e]$_2$, -N(OR^g)C(O)R^e, -N(R^g)C(NR^g)R^e, -N(R^g)N(R^g)C(O)R^e, -N[C(O)R^e]NR^{e}R^e, -N(R^g)C(S)R^e, -N(R^g)S(O)R^e, -N(R^g)S(O)OR^e -N(R^g)S(O)$_2$R^e, -N[S(O)$_2$R^c]$_2$, -N(R^g)S(O)$_2$OR^e, -N(R^g)S(O)$_2$NR^{e}R^e, -N(R^g)[S(O)$_2$]$_2$R^e, -N(R^g)C(O)OR^e, -N(R^g)C(O)SR^e, -N(R^g)C(O)NR^{e}R^e, -N(R^g)C(O)NR^{g}NR^{e}R^e, -N(R^g)N(R^g)C(O)NR^{e}R^e, -N(R^g)C(S)NR^{e}R^e, -[N(R^g)C(O)]$_2$R^e, -N(R^g)[C(O)]$_2$R^e, -N{[C(O)]$_2$R^c}$_2$, -N(R^g)[C(O)]$_2$OR^e, -N(R^g)[C(O)]$_2$NR^{e}R^e, -N{[C(O)]$_{2O}$R^e}$_2$, -N{[C(O)]$_2$NR^{e}R^e}$_2$, -[N(R^g)C(O)]$_2$OR^e, -N(R^g)C(NR^g)OR^e, -N(R^g)C(NOH)R^e, -N(R^g)C(NR^g)SR^e und -N(R^g)C(NR^g)NR^{e}R^e;
jedes **R^e** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^f** und/oder **R^g**, ausgewählt aus C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^f** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus Halogen und -CF$_3$; und
jedes **R^g** bezeichnet unabhängig voneinander Wasserstoff, C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedriges Heteroalkyl, 3-8-gliedriges Heterocycloalkyl, 4-14-gliedriges Heterocycloalkyl, 5-12-gliedriges Heteroaryl oder 6-18-gliedriges Heteroarylalkyl;
gegebenenfalls in Form der Tautomeren, der Racemate, der Enantiomeren, der Diastereomeren und der Mischungen hiervon oder der pharmakologisch akzeptablen bzw. annehmbaren Säureadditionssalze hiervon.

4. Verbindung nach einem der Ansprüche 1 bis 3, wobei **A** Phenyl darstellt.

5. Verbindung der allgemeinen Formel **(1d)** nach Anspruch 3,



(1d)

wobei **W** und **Y** jeweils unabhängig voneinander CH$_2$, O, N-R^e oder N-OR^e darstellen, und
R^1 bezeichnet Wasserstoff oder eine Gruppe, ausgewählt aus **R^a**, **R^b** und **R^a**, substituiert mit ein oder mehreren gleichen oder verschiedenen **R^c** und/oder **R^b**,
jedes **R^a** ist unabhängig voneinander ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-16}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;
jedes **R^b** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, -OR^c, C_{1-3}-Haloalkyloxy, -OCF$_3$,

=S, -SR^c, =NR^c, =NOR^c, =NNR^{c}R^c, =NN(R^g)C(O)NR^{c}R^c, -NR^{c}R^c, -ONR^{c}R^c, -N(OR^c)R^c, -N(R^g)NR^{c}R^c, Halogen, -CF_3, -CN, -NC, -OCN, -SCN, -NO, -NO_2, =N_2, -N_3, -S(O)R^c, -S(O)OR^c, -$S(O)_2$R^c, -$S(O)_2$OR^c, -S(O)NR^{c}R^c, -$S(O)_2$NR^{c}R^c, -OS(O)R^c, -$OS(O)_2$R^c, -$OS(O)_2$OR^c, -OS(O)NR^{c}R^c, -$OS(O)_2$NR^{c}R^c, -C(O)R^c, -C(O)OR^c, -C(O)SR^c, -C(O)NR^{c}R^c, -C(O)N(R^g)NR^{c}R^c, -C(O)N(R^g)OR^c, -C(NR^g)NR^{c}R^c, -C(NOH)R^c, -C(NOH)NR^{c}R^c, -OC(O)R^c, -OC(O)OR^c, -OC(O)SR^c, -OC(O)NR^{c}R^c, -OC(NR^g)NR^{c}R^c, -SC(O)R^c, -SC(O)OR^c, -SC(O)NR^{c}R^c, -SC(NR^g)NR^{c}R^c, -N(R^g)C(O)R^c, -N[C(O)R^e]$_2$, -N(OR^g)C(O)R^c, -N(R^g)C(NR^g)R^c, -N(R^g)N(R^g)C(O)R^c, -N[C(O)R^c]NR^{c}R^c, -N(R^g)C(S)R^c, -N(R^g)S(O)R^c, -N(R^g)S(O)OR^c, -N(R^g)$S(O)_2$R^c, -N[$S(O)_2$R^c]$_2$, -N(R^g)$S(O)_2$OR^c, -N(R^g)$S(O)_2$NR^{c}R^c, -N(R^g)[$S(O)_2$]$_2$R^c, -N(R^9)C(O)OR^c, -N(R^9)C(O)SR^c, -N(R^g)C(O)NR^{c}R^c, -N(R^g)C(O)NR^{g}NR^{c}R^c, -N(R^g)N(R^g)C(O)NR^{c}R^c, -N(R^g)C(S)NR^{c}R^c, -[N(R^g)C(O)]$_2$R^c, -N(R^g)[C(O)$_2$R^c, -N{[C(O)]$_2$R^c}$_2$, -N(R^g)[C(O)]$_2$OR^c, -N(R^g)[C(O)]$_2$NR^{c}R^c, -N{[C(O)]$_2$OR^c}$_2$, -N{[C(O)]$_2$NR^{c}R^c}$_2$, -[N(R^g)C(O)]$_2$OR^c, -N(R^g)C(NR^g)OR^c, -N(R^g)C(NOH)R^c, -N(R^g)C(NR^g)SR^c und -N(R^g)C(NR^g)NR^{c}R^c,

jedes **R^c** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^d** und/oder **R^e**, ausgewählt aus C_{1-6}-Alkyl, C_{3-10}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;

jedes **R^d** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus =O, -OR^e, C_{1-3}-Haloalkyloxy, -OCF_3, =S, -SR^e, =NR^e, =NOR^e, =NNR^{e}R^e, =NN(R^g)C(O)NR^{e}R^e, -NR^{e}R^e, -ONR^{e}R^e, -N(R^g)NR^{e}R^e, Halogen, -CF_3, -CN, -NC, -OCN, -SCN, -NO, -NO_2, =N_2, -N_3, -S(O)R^e, -S(O)OR^e, -$S(O)_2$R^e, -$S(O)_2$OR^e, -S(O)NR^{e}R^e, -$S(O)_2$NR^{e}R^e, -OS(O)R^e, -$OS(O)_2$R^e, -$OS(O)_2$OR^e, -OS(O)NR^{e}R^e, -$OS(O)_2$NR^{e}R^e, -C(O)R^e, -C(O)OR^e, -C(O)SR^e, -C(O)NR^{e}R^e, -C(O)N(R^g)NR^{e}R^e, -C(O)N(R^g)OR^e, -C(NR^g)NR^{e}R^e, -C(NOH)R^e, -C(NOH)NR^{e}R^e, -OC(O)R^e, -OC(O)OR^e, -OC(O)SR^e, -OC(O)NR^{e}R^e, -OC(NR^g)NR^{e}R^e, -SC(O)R^e, -SC(O)OR^e, -SC(O)NR^{e}R^e, -SC(NR^g)NR^{e}R^e, -N(R^g)C(O)R^e, -N[C(O)R^e]$_2$, -N(OR^g)C(O)R^e, -N(R^g)C(NR^g)R^e, -N(R^g)N(R^g)C(O)R^e, -N[C(O)R^e]NR^{e}R^e, -N(R^g)C(S)R^e, -N(R^g)S(O)R^e, -N(R^g)S(O)OR^e -N(R^g)$S(O)_2$R^e, -N[$S(O)_2$R^c]$_2$, -N(R^g)$S(O)_2$OR^e, -N(R^g)$S(O)_2$NR^{e}R^e, -N(R^g)[$S(O)_2$]$_2$R^e, -N(R^g)C(O)OR^e, -N(R^g)C(O)SR^e, -N(R^g)C(O)NR^{e}R^e, -N(R^g)C(O)NR^{g}NR^{e}R^e, -N(R^g)N(R^g)C(O)NR^{e}R^e, -N(R^g)C(S)NR^{e}R^e, -[N(R^g)C(O)]$_2$R^e, -N(R^g)[C(O)]$_2$R^e, -N{[C(O)]$_2$R^e}$_2$, -N(R^g)[C(O)]$_2$OR^e, -N(R^g)[C(O)]$_2$NR^{e}R^e, -N{[C(O)]$_{2O}$R^e}$_2$, -N{[C(O)]$_2$NR^{e}R^e}$_2$, -[N(R^g)C(O)]$_2$OR^e, -N(R^g)C(NR^g)OR^e, -N(R^g)C(NOH)R^e, -N(R^g)C(NR^g)SR^e und -N(R^g)C(NR^g)NR^{e}R^e,

jedes **R^e** bezeichnet unabhängig voneinander Wasserstoff oder eine Gruppe, gegebenenfalls substituiert mit ein oder mehreren gleichen oder verschiedenen **R^f** und/oder **R^g**, ausgewählt aus C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, C_{4-11}-Cycloalkylalkyl, C_{6-10}-Aryl, C_{7-16}-Arylalkyl, 2-6-gliedrigem Heteroalkyl, 3-8-gliedrigem Heterocycloalkyl, 4-14-gliedrigem Heterocycloalkylalkyl, 5-12-gliedrigem Heteroaryl und 6-18-gliedrigem Heteroarylalkyl;

jedes **R^f** stellt eine geeignete Gruppe dar und ist unabhängig ausgewählt aus Halogen und -CF_3; und

jedes **R^g** bezeichnet unabhängig voneinander Wasserstoff, C_{1-6}-Alkyl, C_{3-8}-Cycloalkyl, und

R$^{1'}$ und **R$^{1''}$** bezeichnen jeweils unabhängig voneinander eine Gruppe, ausgewählt aus Wasserstoff, Halogen und -OR^c,

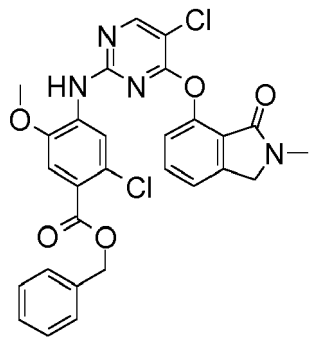
R^2 bezeichnet Wasserstoff oder eine Gruppe, ausgewählt aus **R^a**, **R^b** und **R^a**, substituiert mit ein oder mehreren gleichen oder verschiedenen **R^c** und/oder **R^b**, und

R^3 bezeichnet eine Gruppe, ausgewählt aus Wasserstoff, Halogen, -OR^c, -OCF_3, -SR^c, -NR^{c}R^c, -CF_3, -CN, -OCN, -SCN, -NO, -NO_2, C_{1-3}-Alkyl, C_{1-3}-Haloalkyl und C_{1-3}-Haloalkyloxy;

gegebenenfalls in Form der Tautomeren, der Racemate, der Enantiomeren, der Diastereomeren und der Mischungen hiervon oder der pharmakologisch akzeptablen bzw. annehmbaren Säureadditionssalze hiervon.

6. Verbindung nach einem der Ansprüche 1 bis 5, wobei **R^3** Cl oder CF_3 darstellt.

7. Verbindung ausgewählt aus

1	

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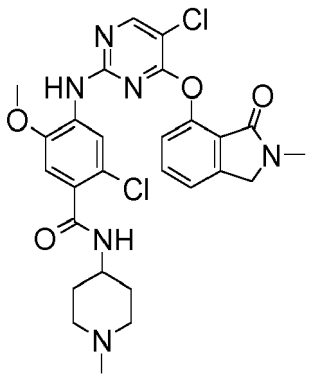
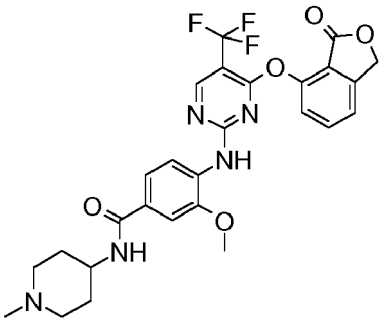
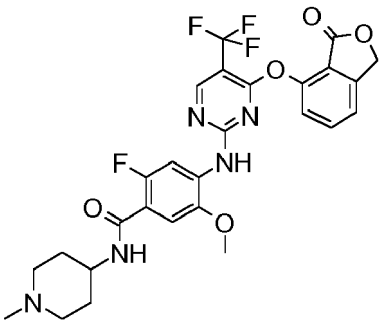
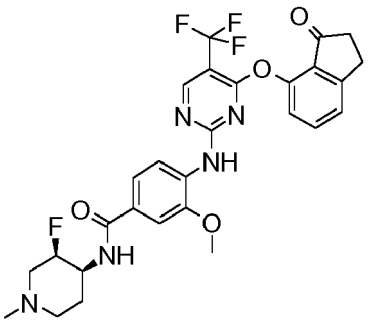
2	
3	
4	
5	

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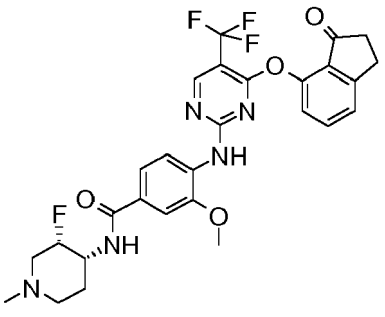
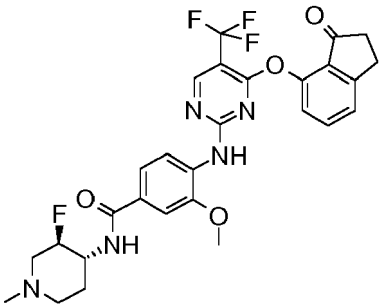
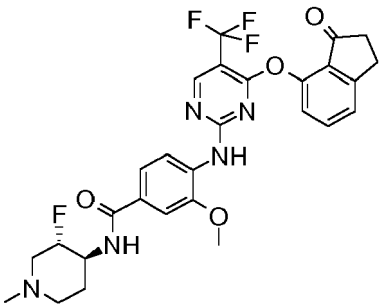
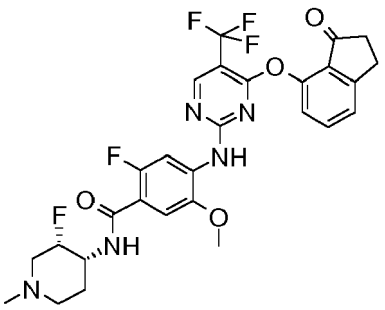
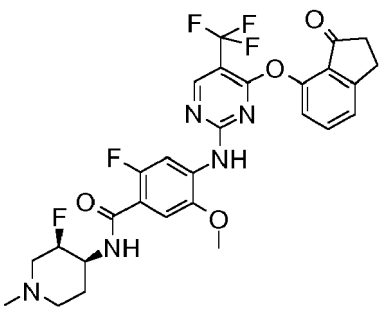
6	
7	
8	
9	
10	

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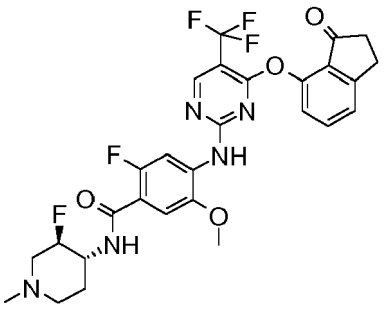
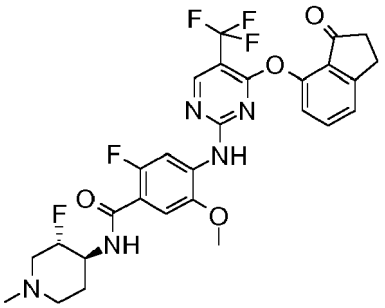
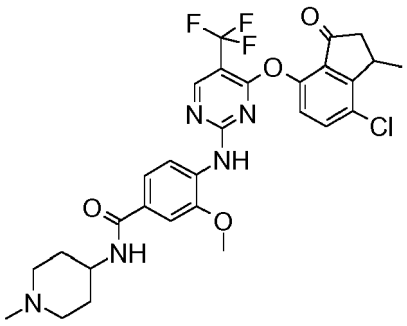
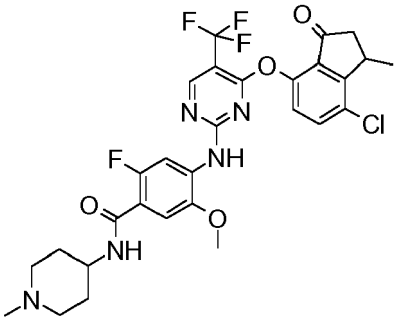
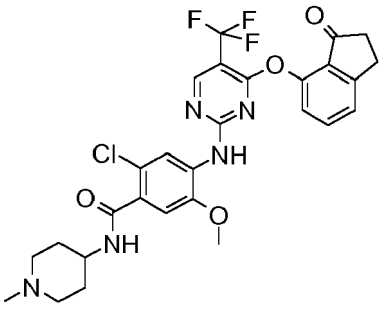
11	
12	
13	
14	
15	

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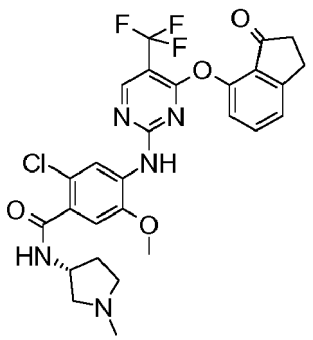
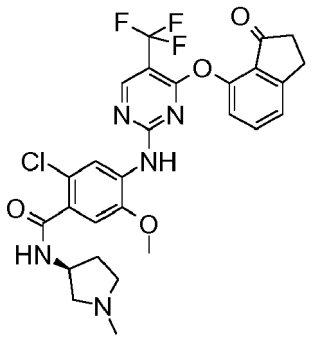
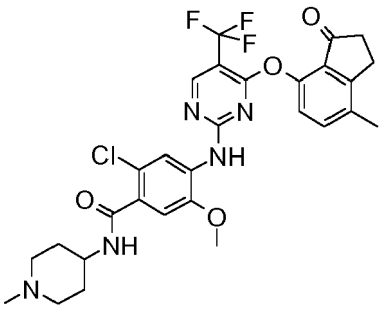
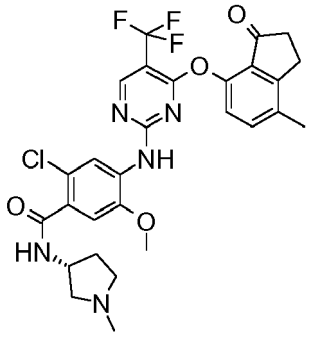
16	
17	
18	
19	

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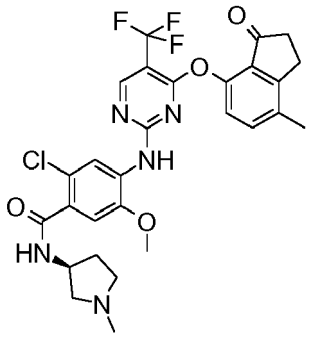
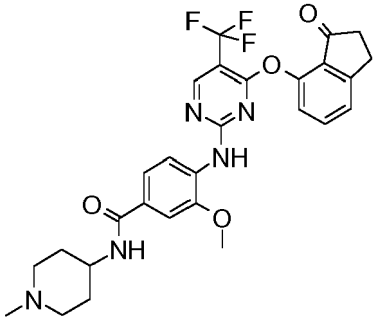
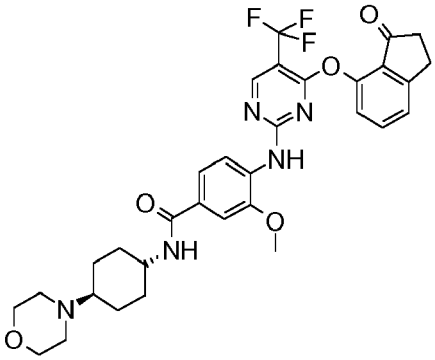
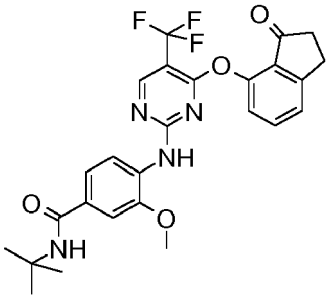
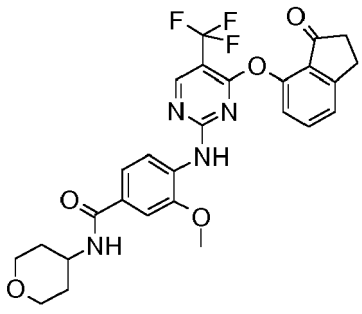
20	
21	
22	
23	
24	

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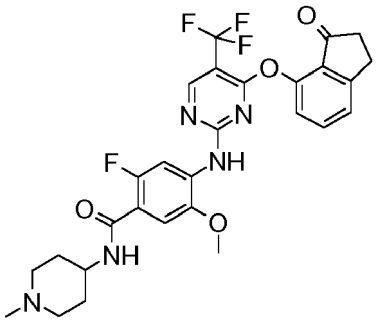
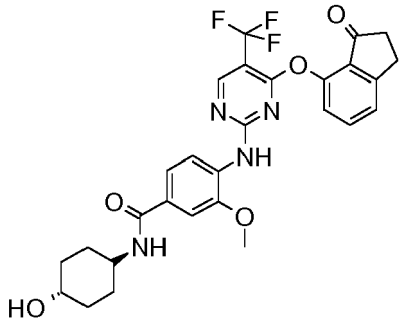
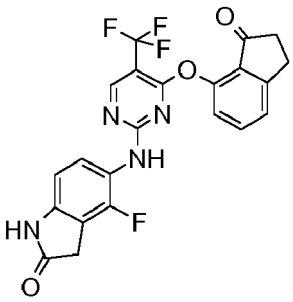
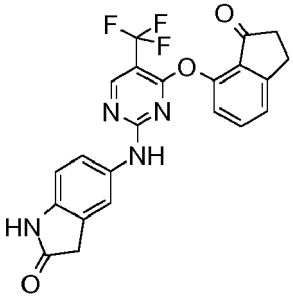
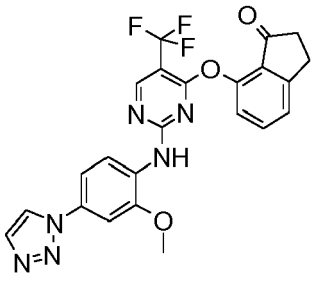
25	
26	
27	
28	
29	

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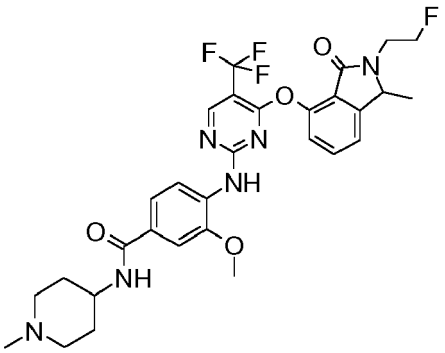
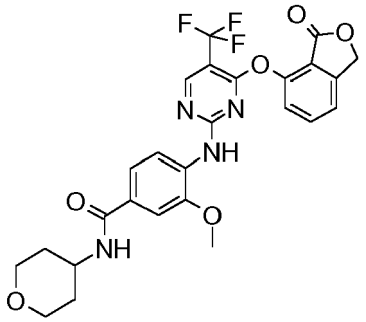
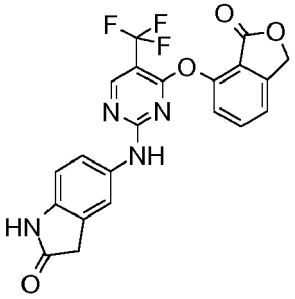
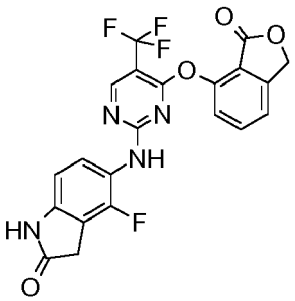
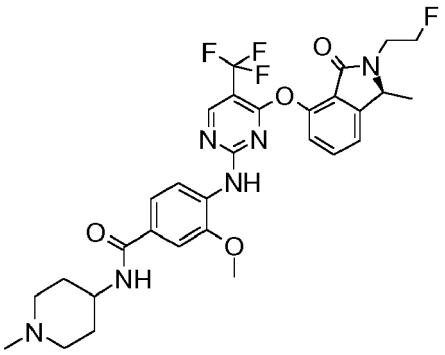
30	
31	
32	
33	
34	

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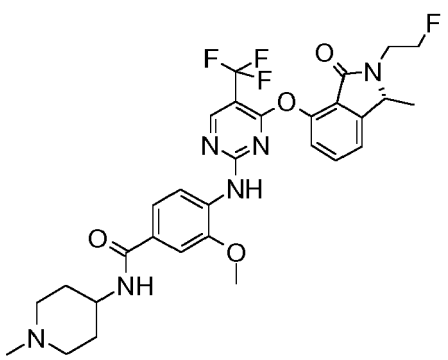
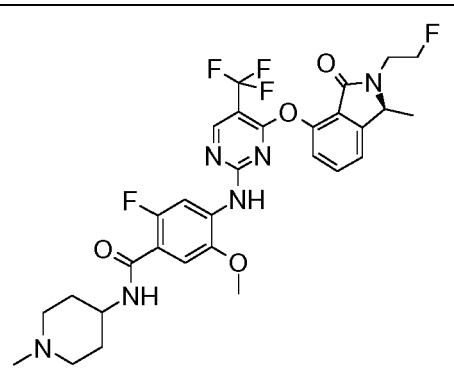
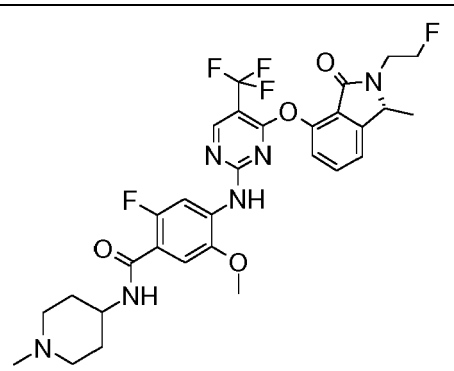
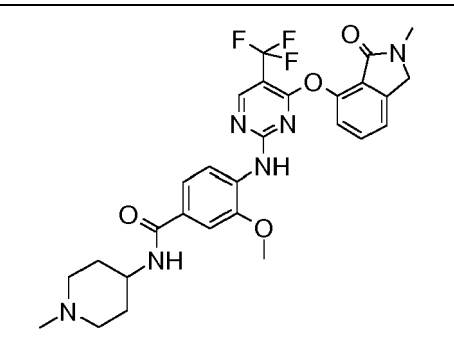
35	
36	
37	
38	

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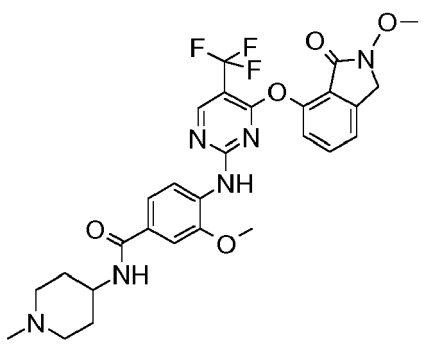
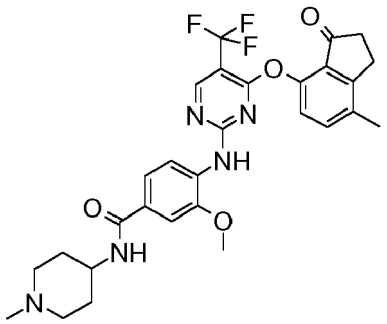
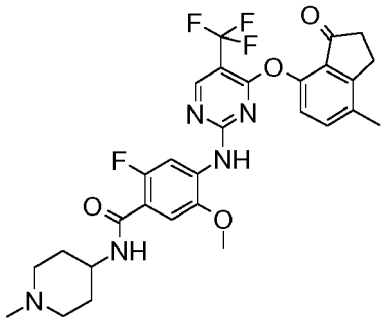
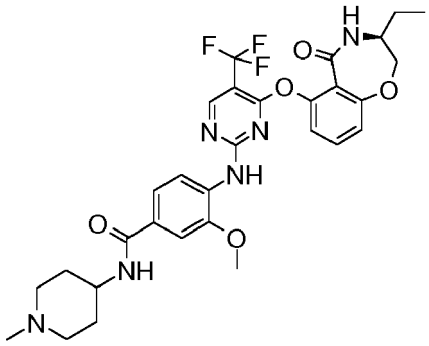
39	
40	
41	
42	

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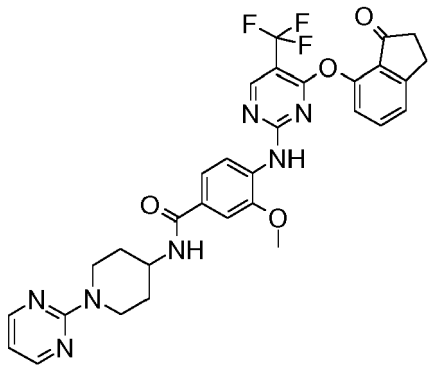
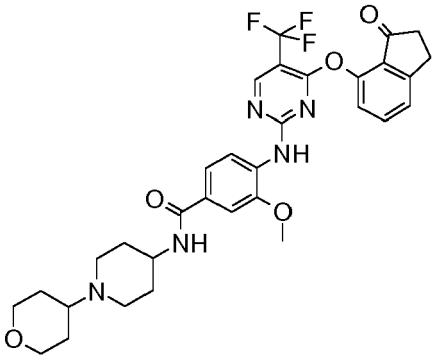
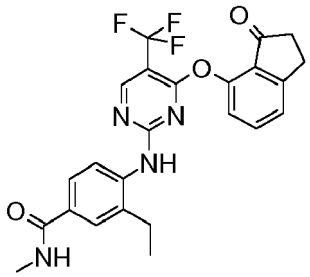
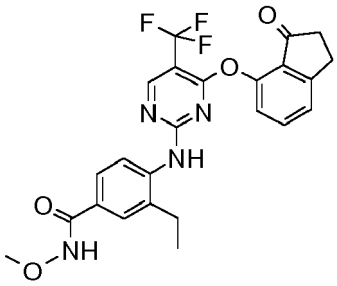
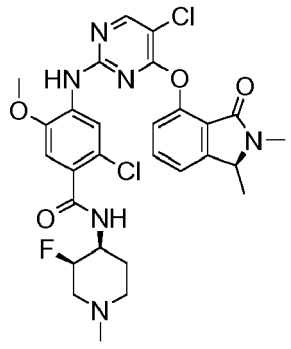
43	
44	
45	
46	
47	

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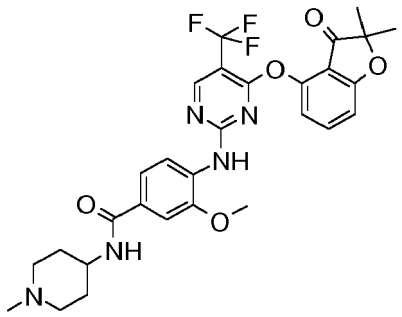
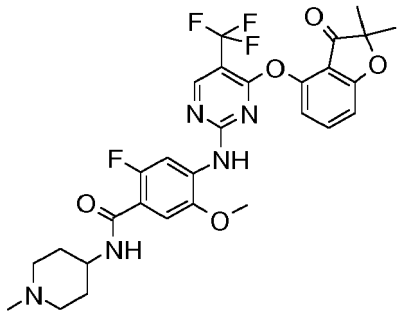
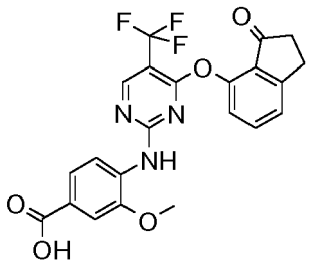
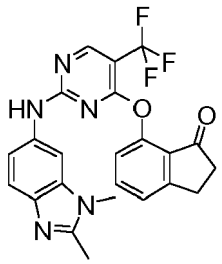
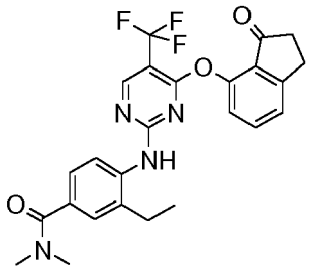
48	
49	
50	
51	
52	

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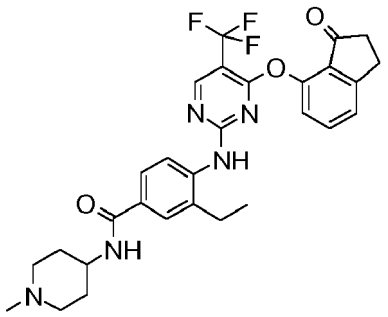
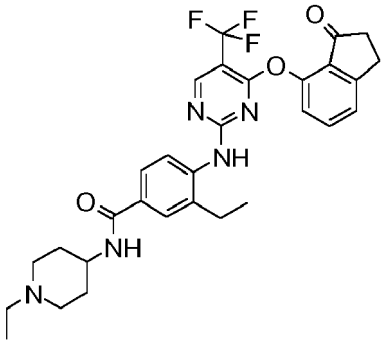
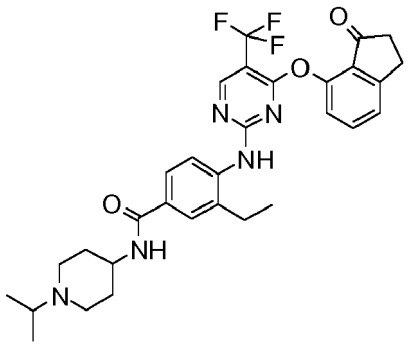
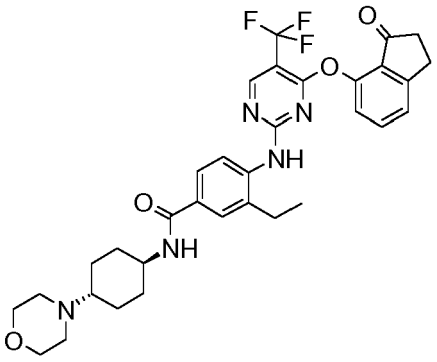
53	
54	
55	
56	

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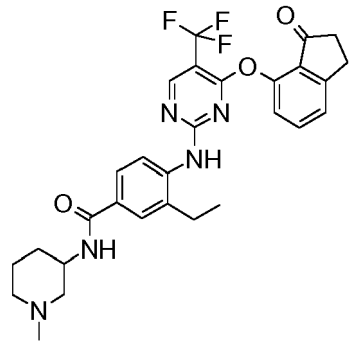
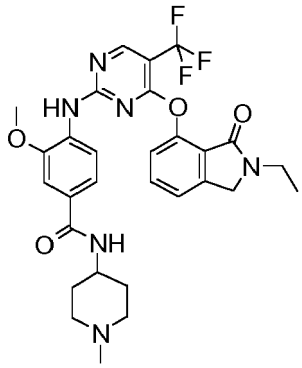
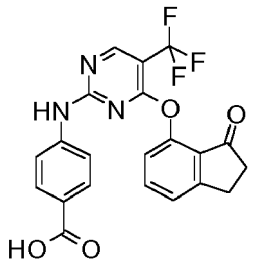
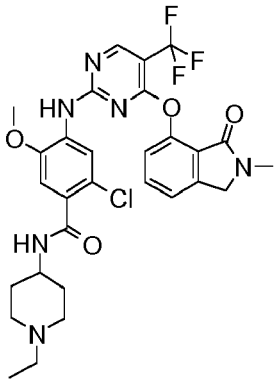
57	
58	
59	
60	

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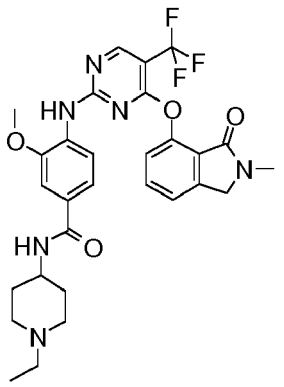
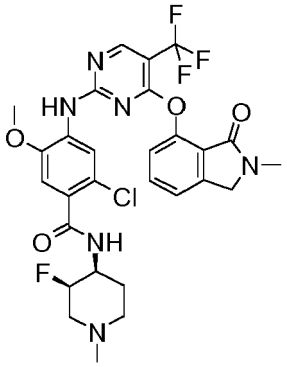
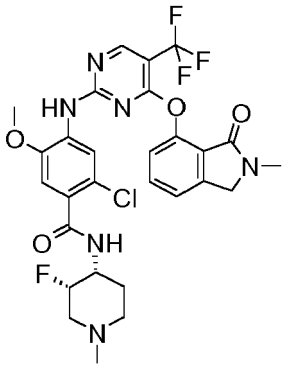
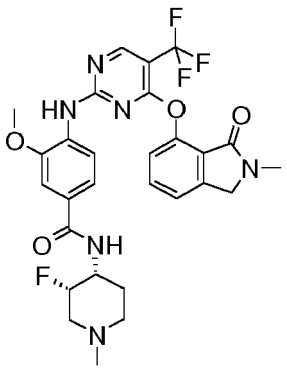
61	
62	
63	
64	

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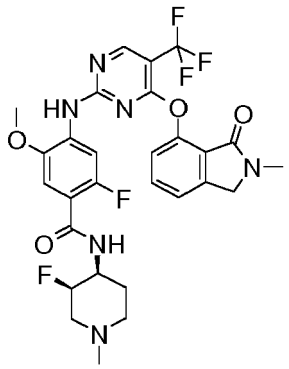
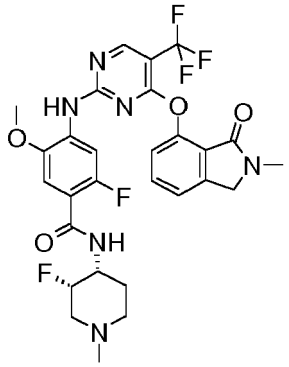
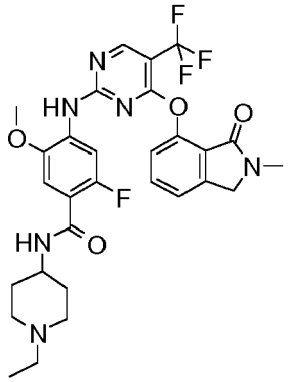
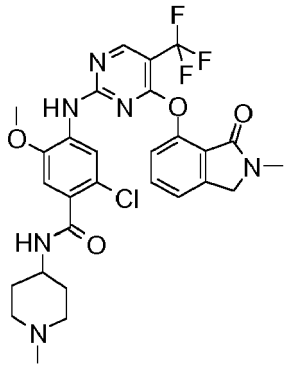
65	
66	
67	
68	

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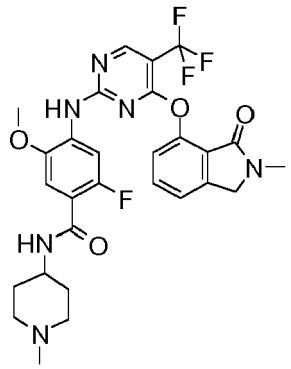
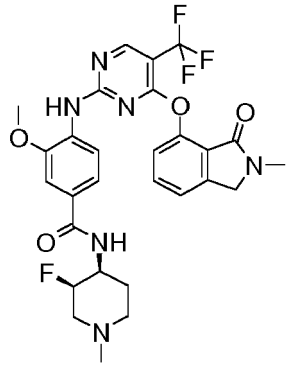
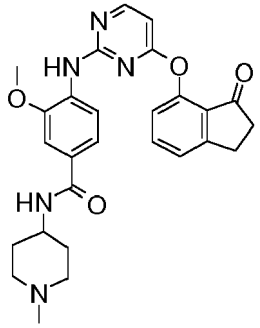
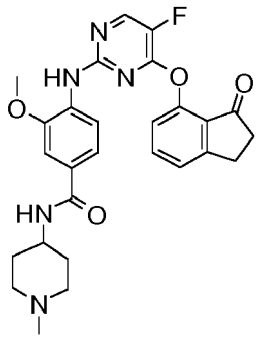
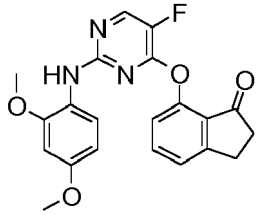
69	
70	
71	
72	
73	

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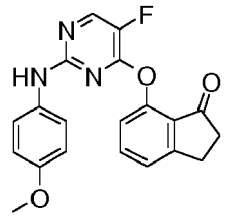
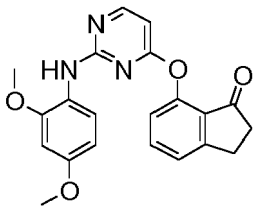
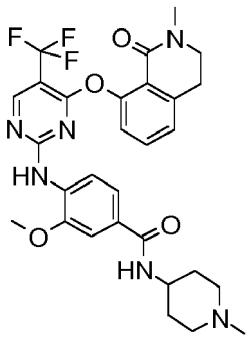
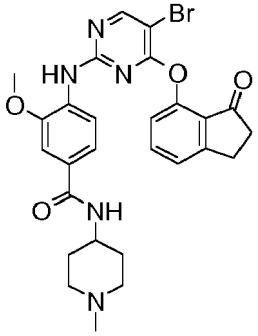
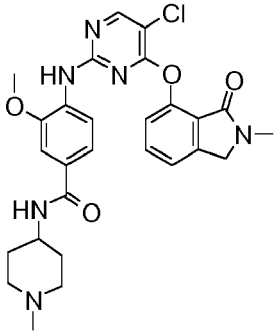
74	
75	
76	
77	
78	

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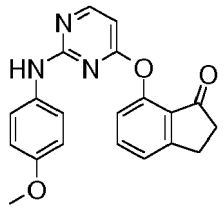
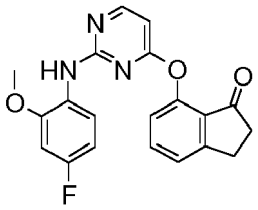
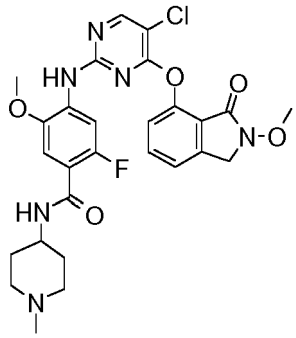
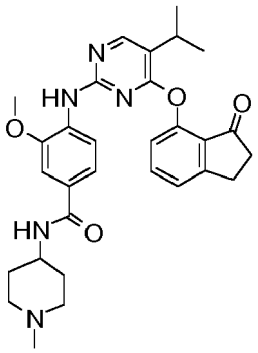
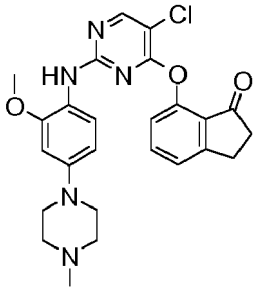
79	
80	
81	
82	
83	

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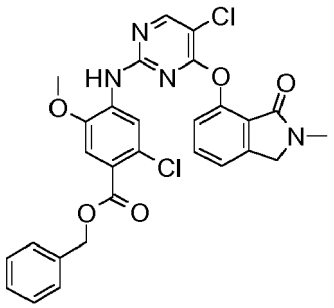
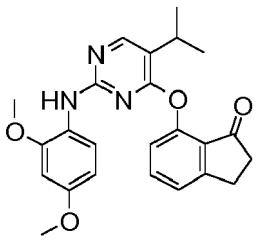
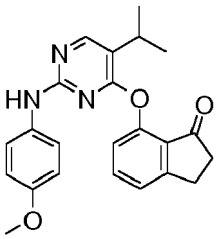
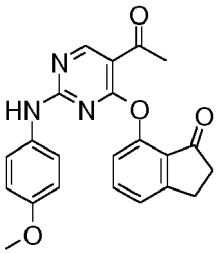
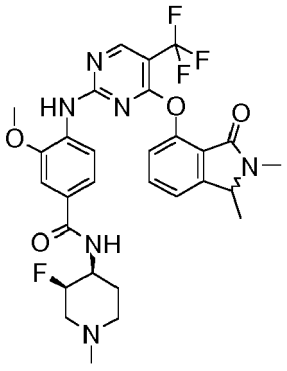
84	
85	
86	
87	
88	

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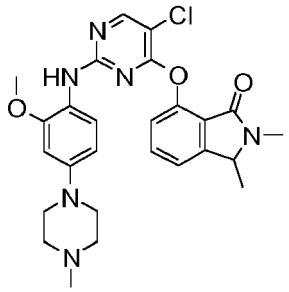
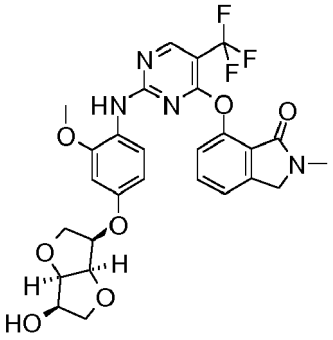
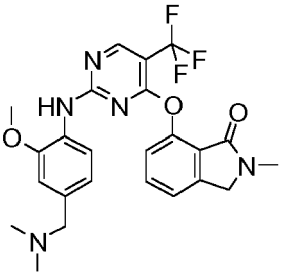
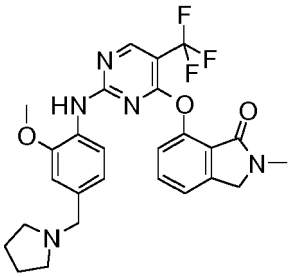
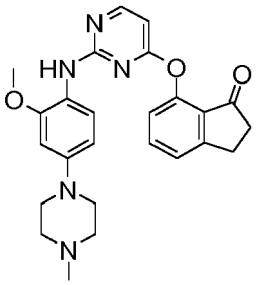
89	
91	
93	
94	
95	

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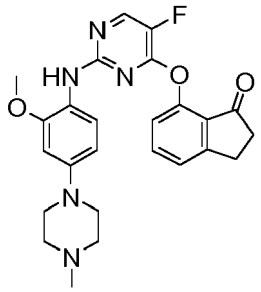
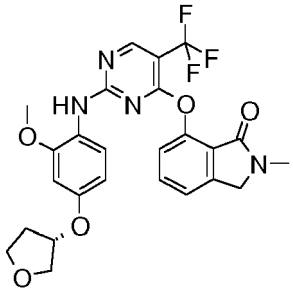
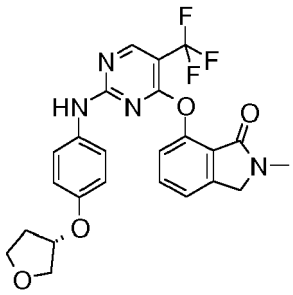
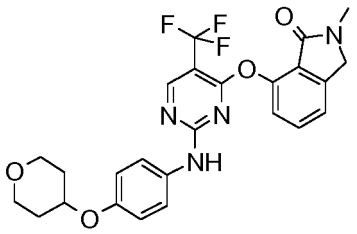
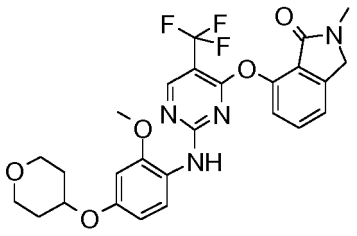
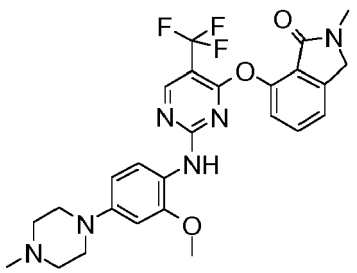
96	
97	
98	
99	
100	
101	

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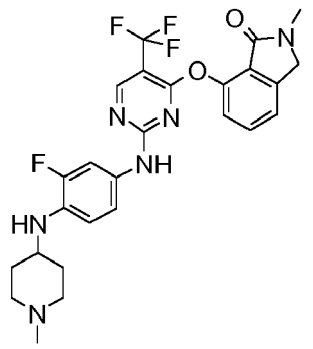
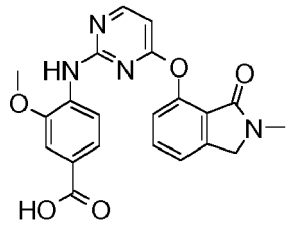
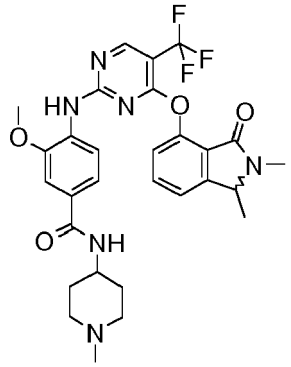
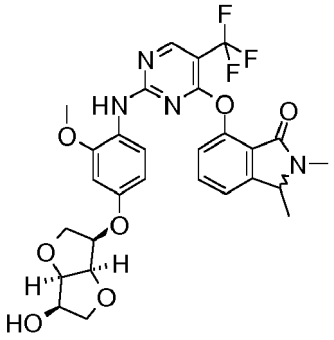
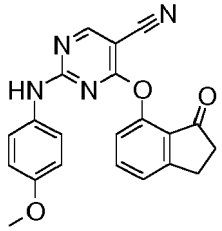
102	
103	
104	
105	
106	

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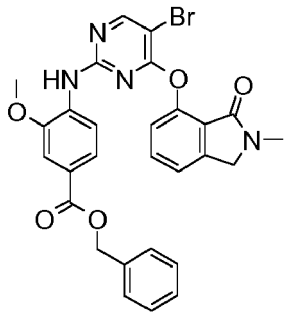
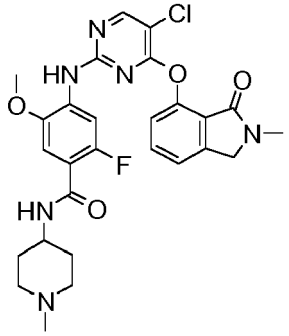
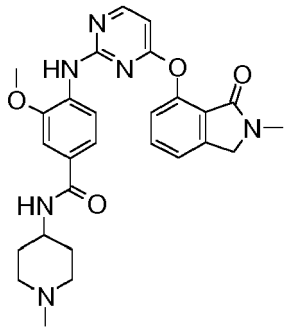
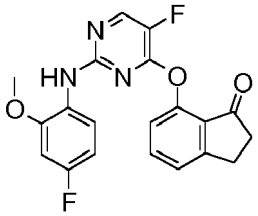
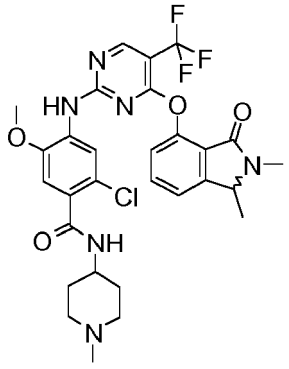
107	
108	
109	
110	
111	

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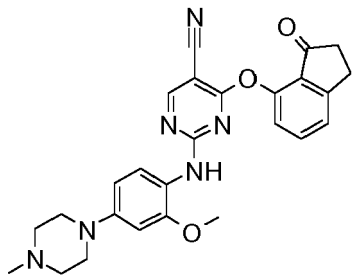
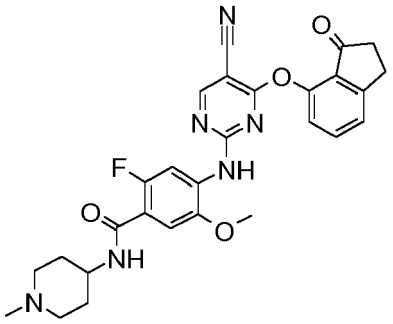
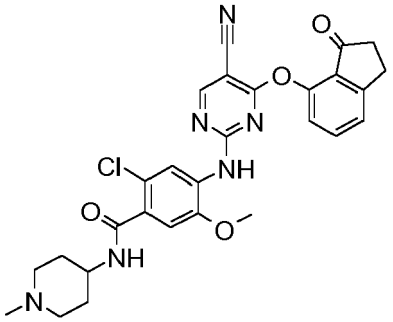
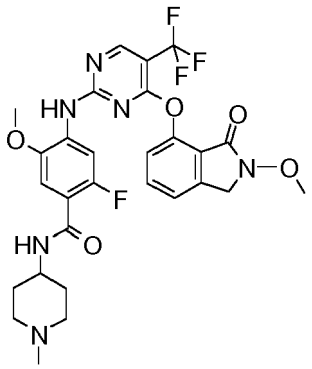
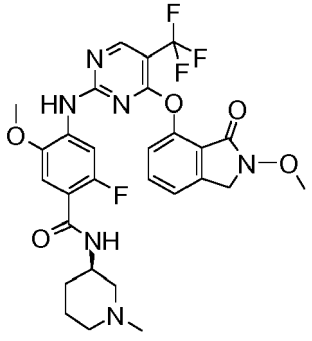
112	
113	
114	
115	
116	

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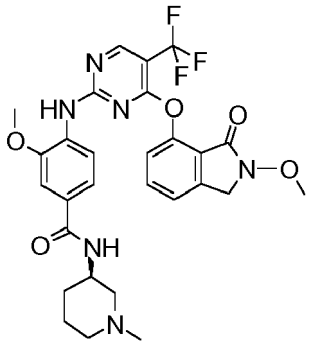
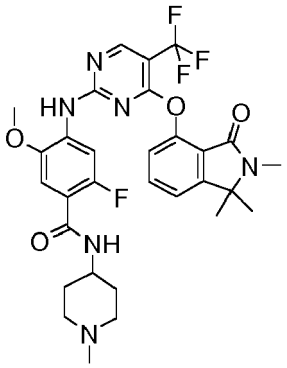
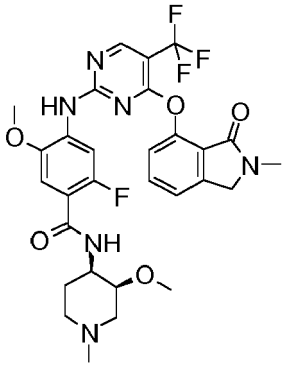
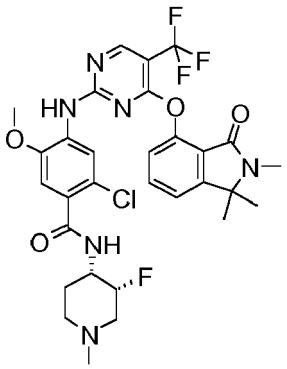
117	
118	
119	
120	

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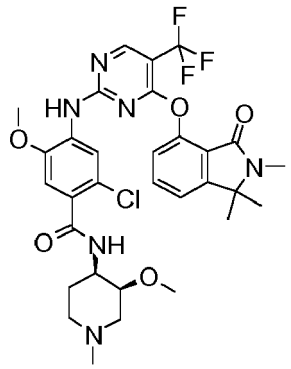
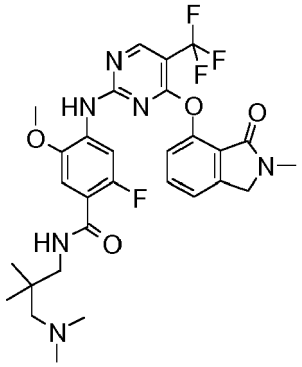
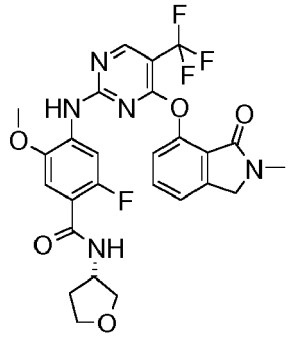
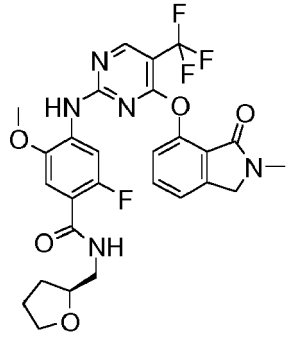
121	
122	
123	
124	

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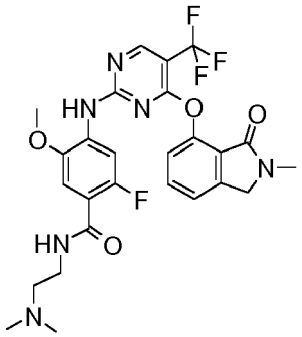
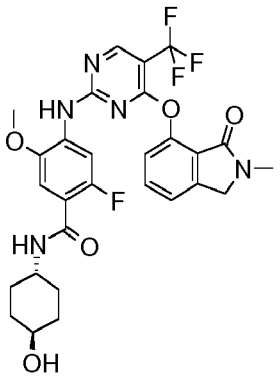
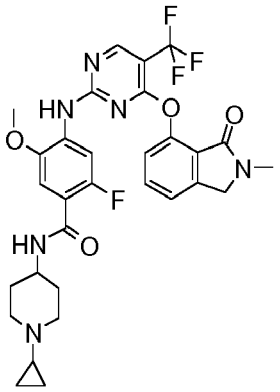
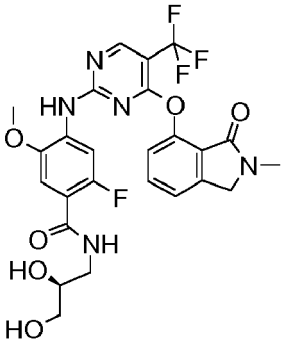
125	
126	
127	
128	

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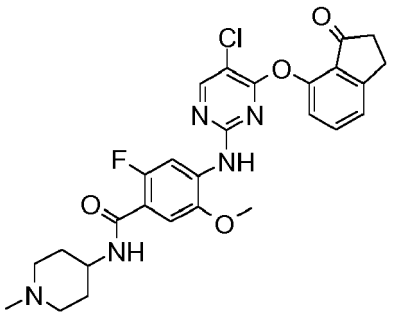
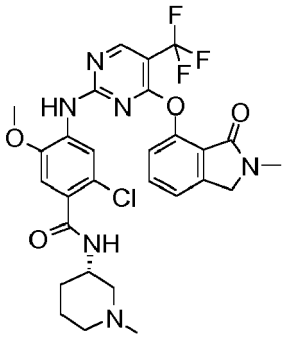
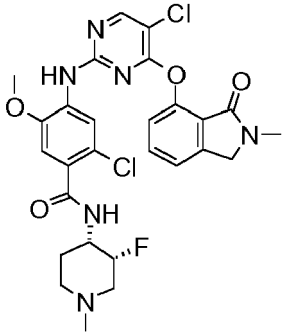
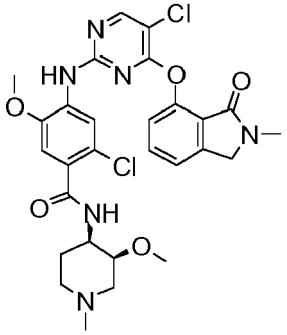
129	
130	
131	
132	

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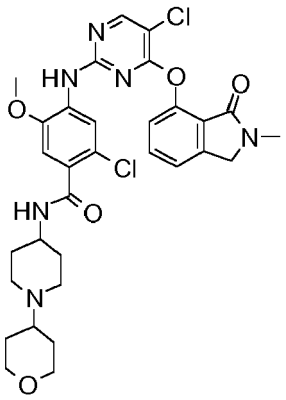
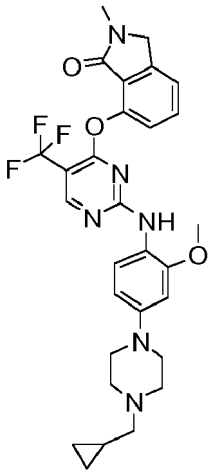
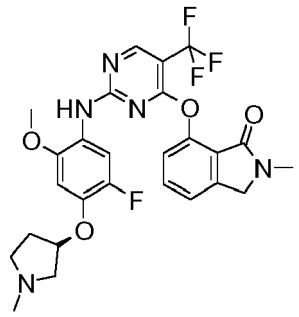
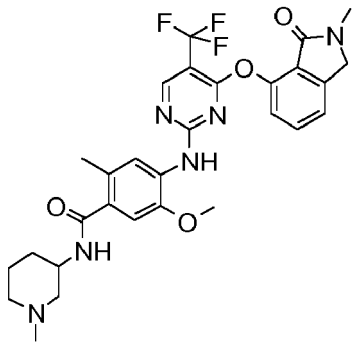
133	
134	
135	
136	

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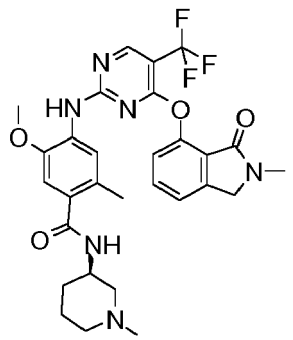
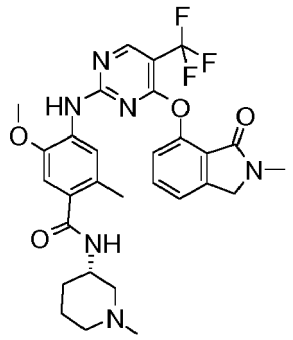
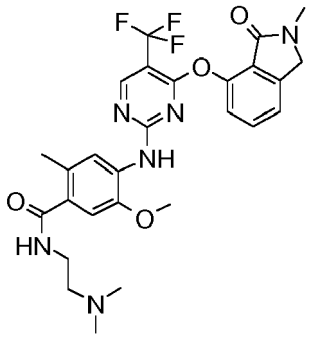
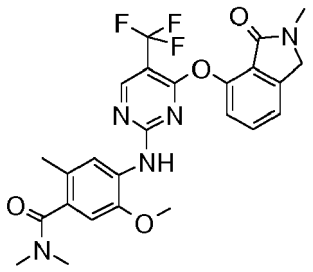
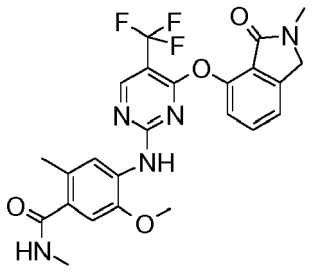
137	
138	
139	
140	
141	

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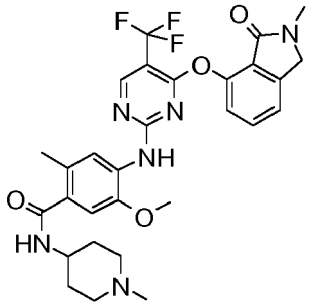
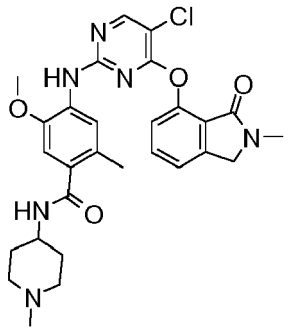
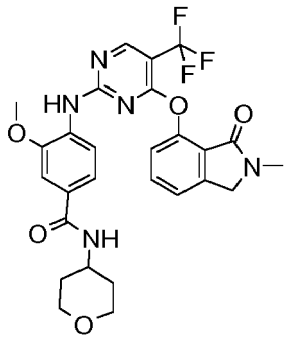
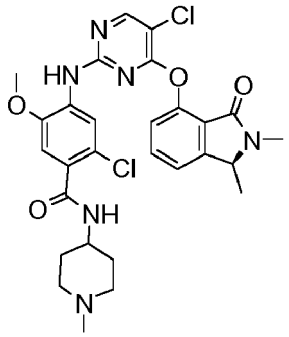
142	
143	
144	
145	

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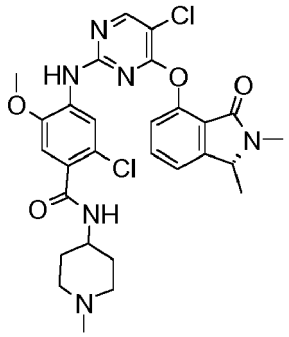
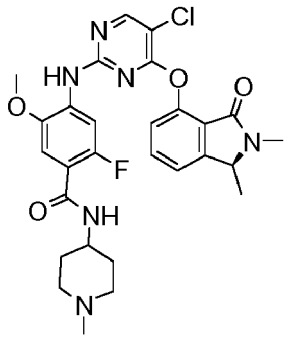
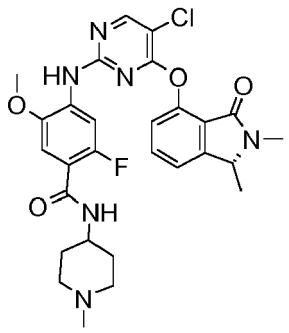
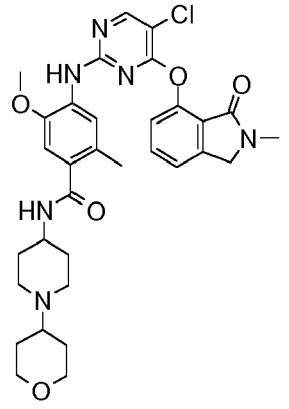
146	
147	
148	
149	

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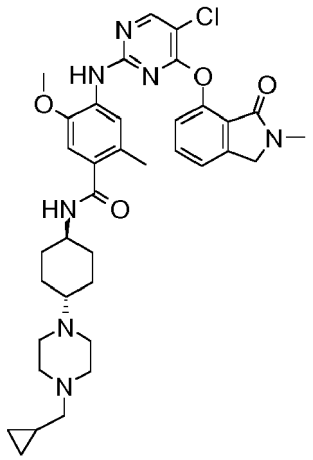
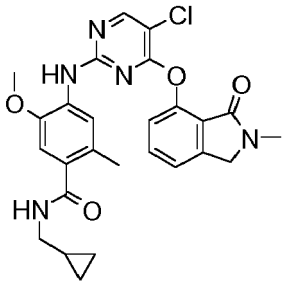
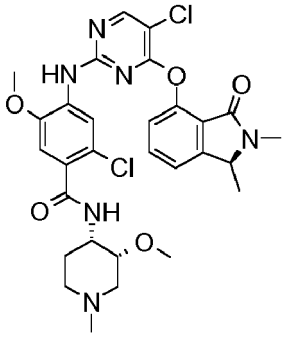
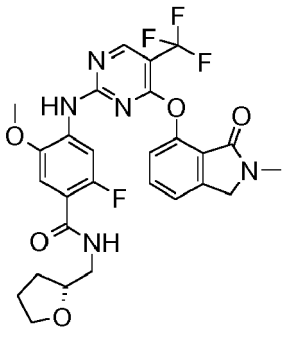
150	
151	
152	
153	

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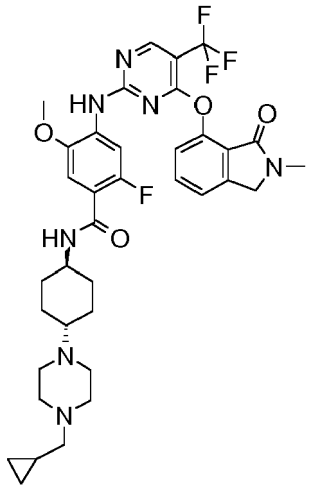
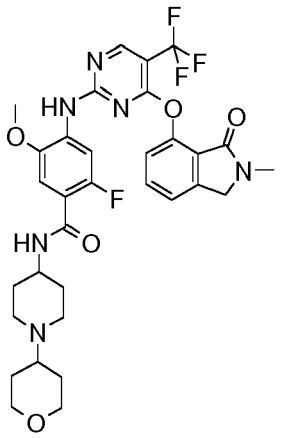
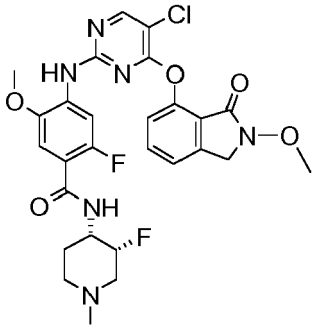
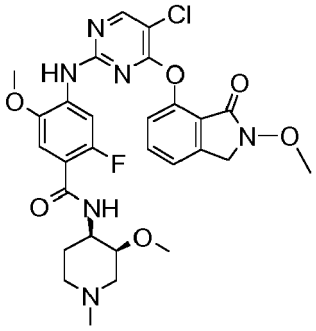
154	
155	
157	
158	

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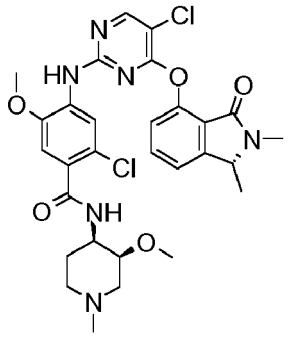
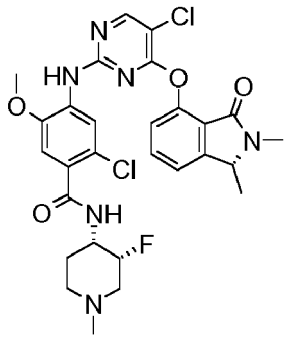
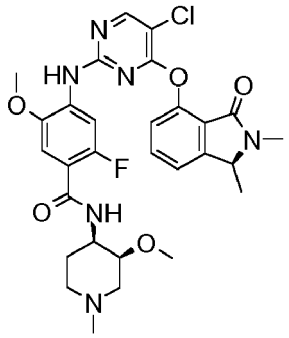
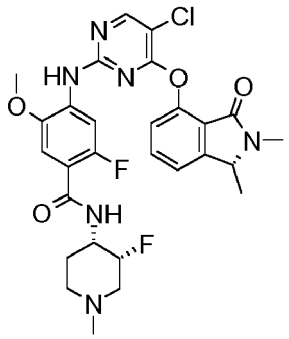
159	
160	
161	
162	

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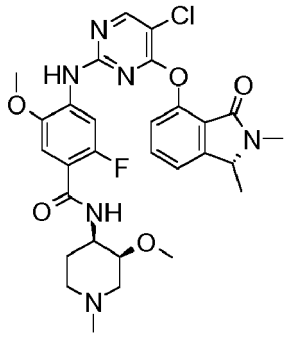
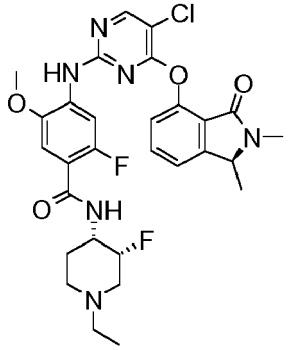
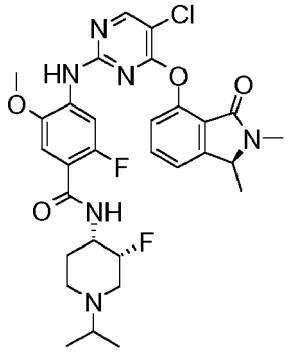
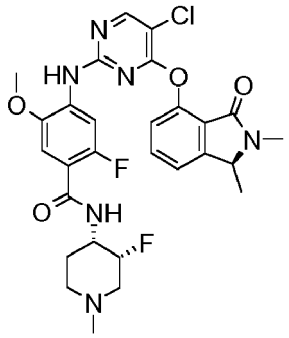
163	
164	
165	
166	

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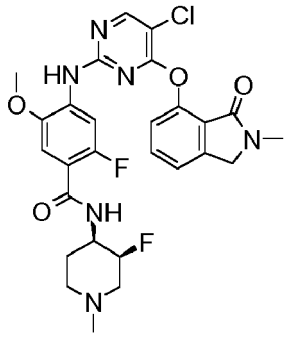
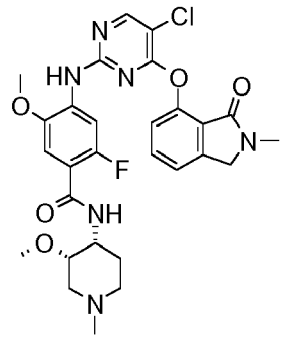
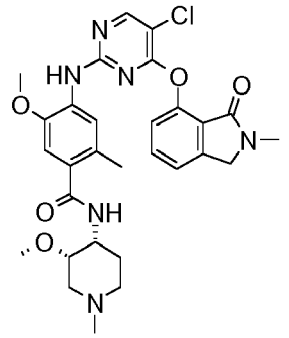
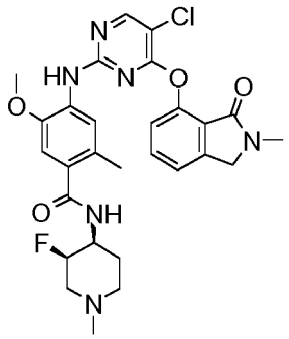
167	
168	
169	
170	

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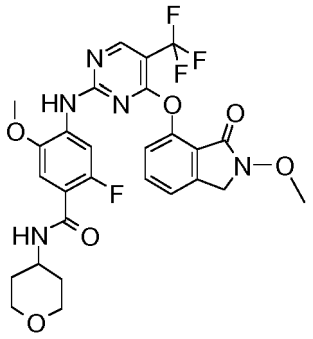
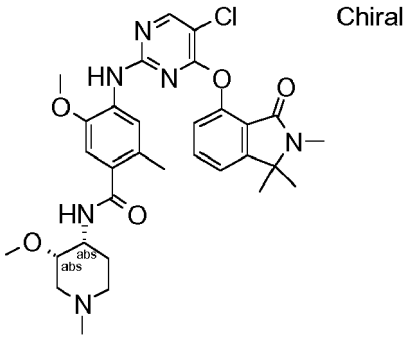
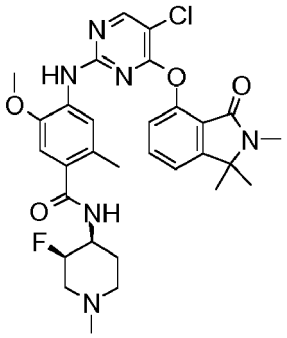
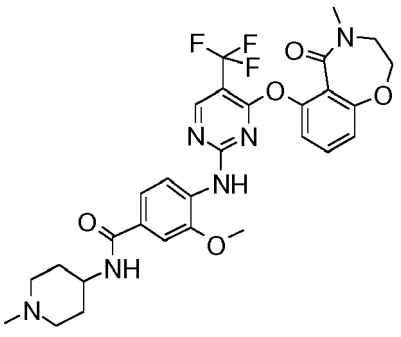
171	
172	 Chiral
173	
174	

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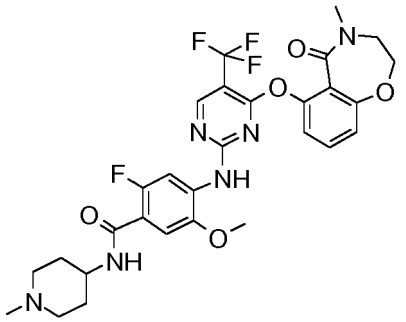
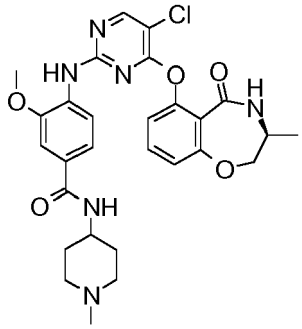
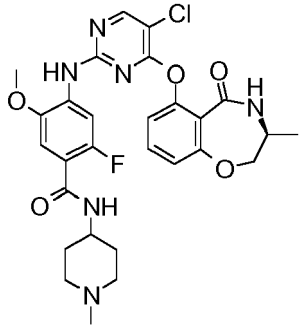
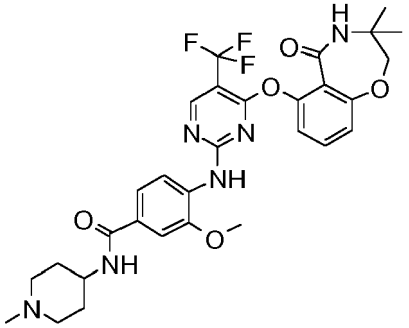
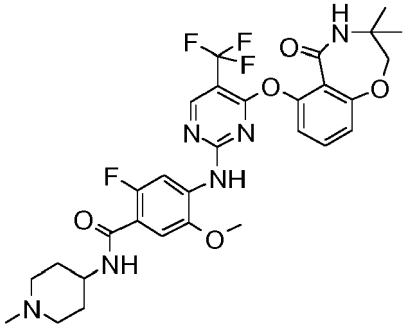
175	
176	
177	
178	
179	

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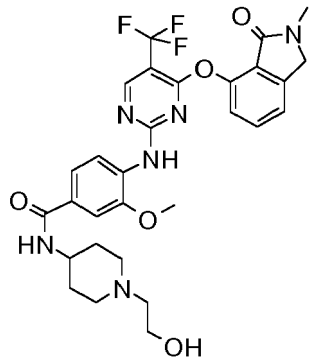
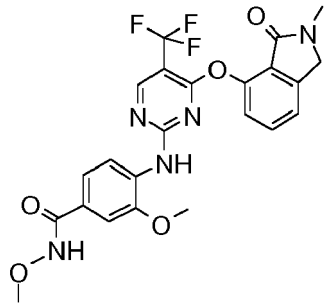
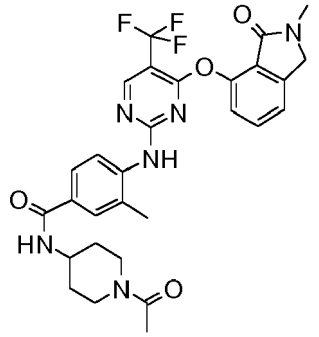
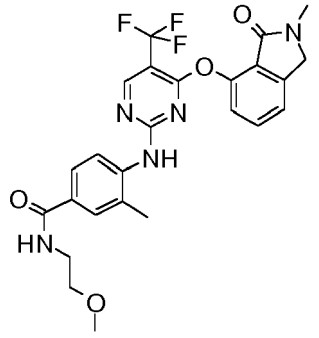
180	
181	
182	
183	

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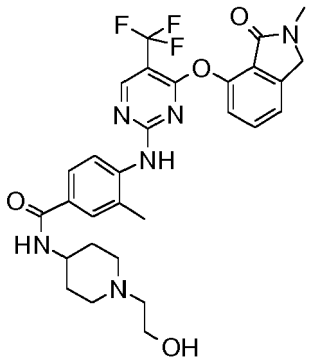
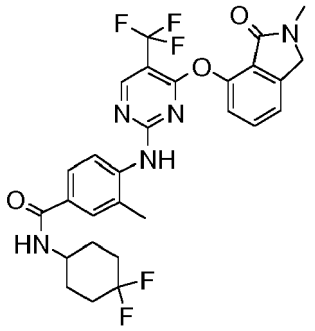
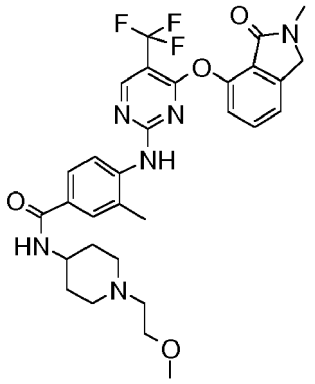
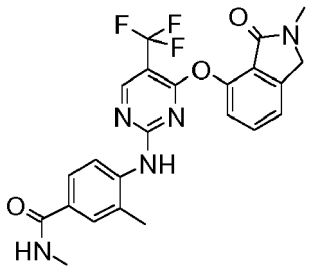
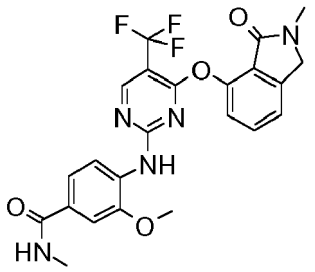
184	
185	
186	
187	
188	

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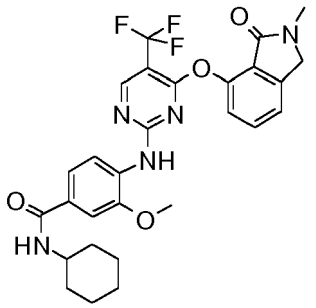
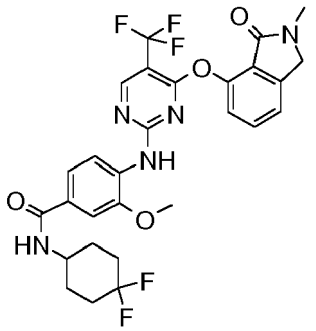
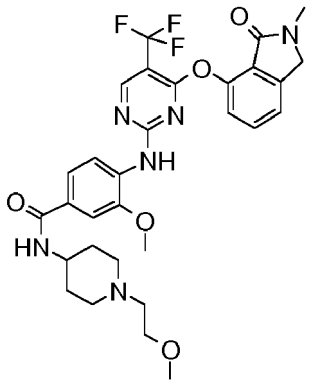
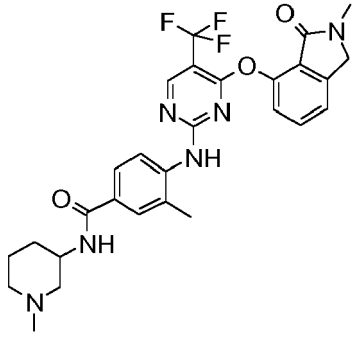
189	
190	
191	
192	

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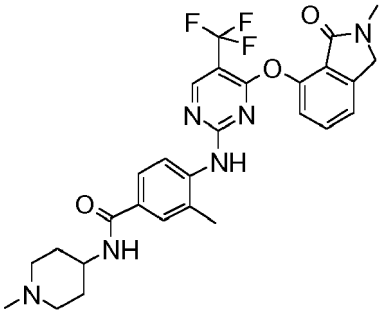
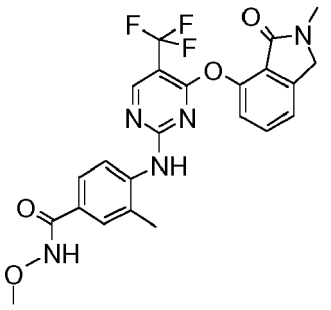
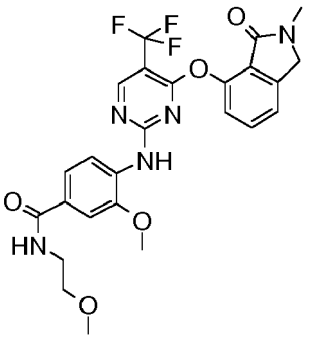
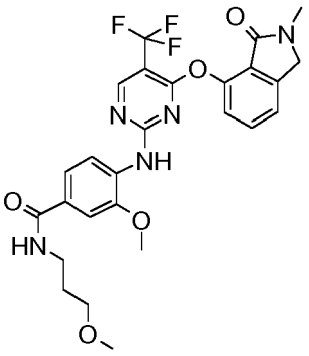
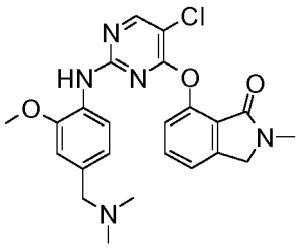
193	
194	
195	
196	
197	

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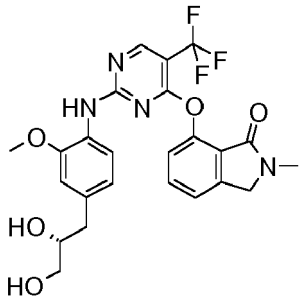
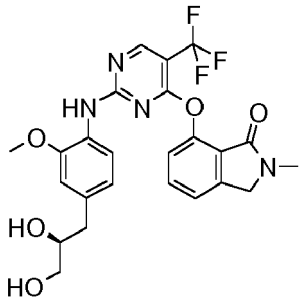
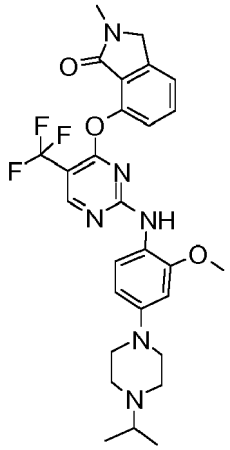
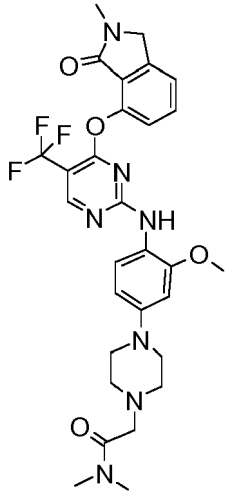
198	
199	
200	
201	

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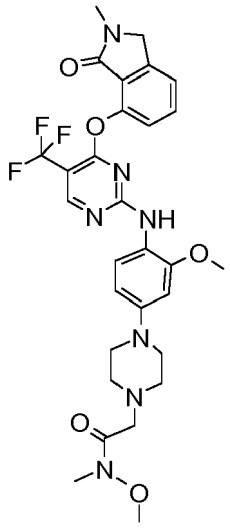
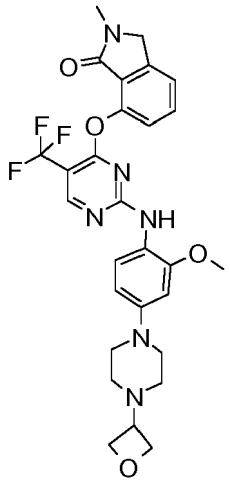
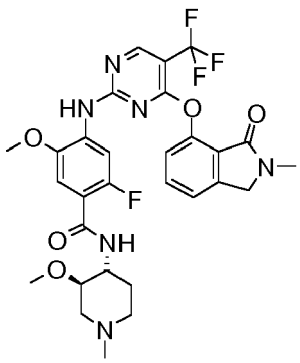
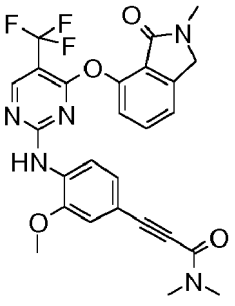
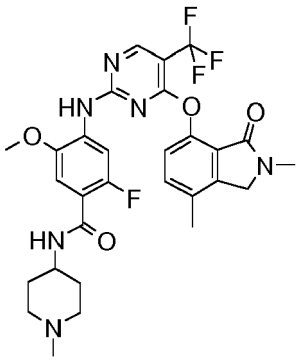
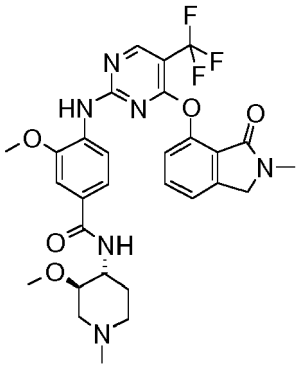
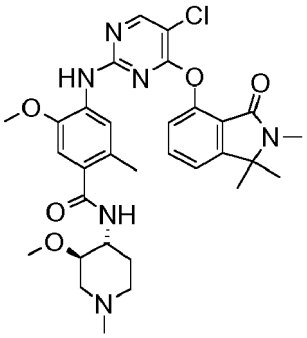
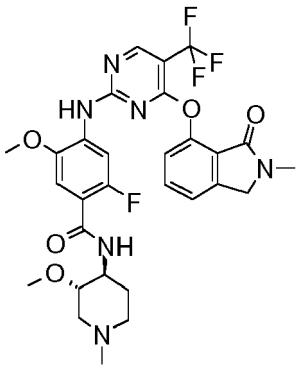
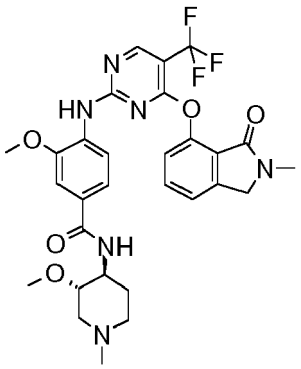
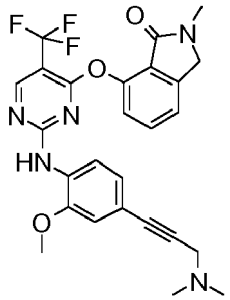
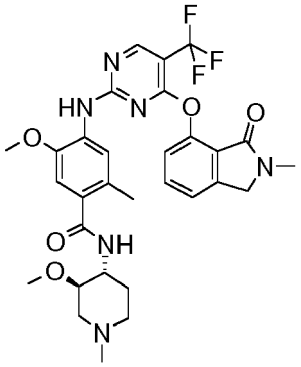
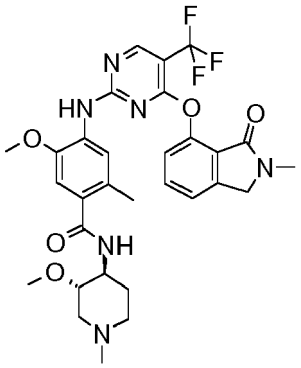
202	
203	
204	
205	

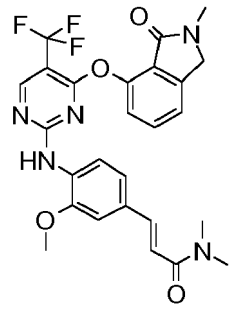
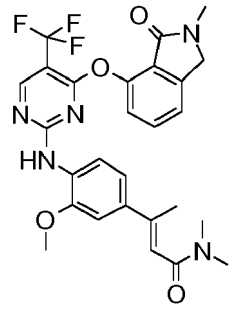
(fortgesetzt)

206	
207	
208	
209	

(fortgesetzt)

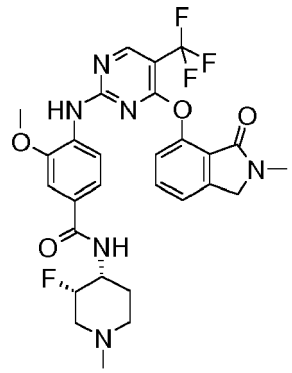
210	
211	
212	
213	

(fortgesetzt)

214	
215	

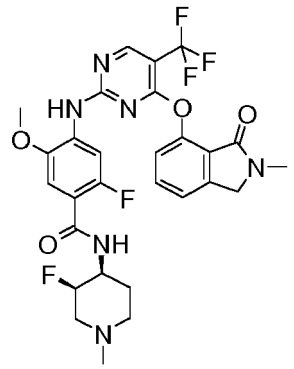
oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

8. Verbindung nach Anspruch 7 der Formel

64	

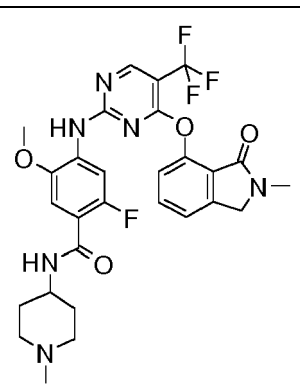
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

9. Verbindung nach Anspruch 7 der Formel

65	

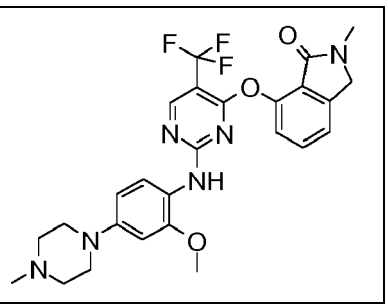
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

10. Verbindung nach Anspruch 7 der Formel

69	

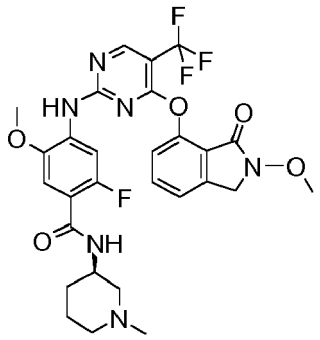
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

11. Verbindung nach Anspruch 7 der Formel

101	

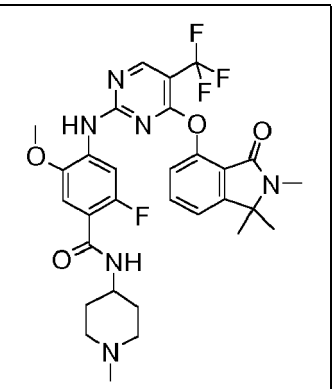
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

12. Verbindung nach Anspruch 7 der Formel

116	

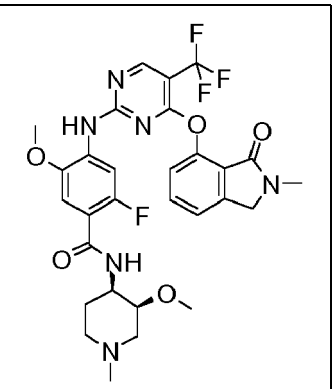
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

13. Verbindung nach Anspruch 7 der Formel

118	

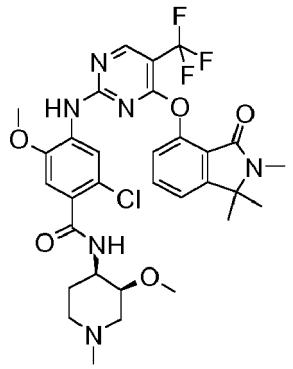
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

14. Verbindung nach Anspruch 7 der Formel

119	

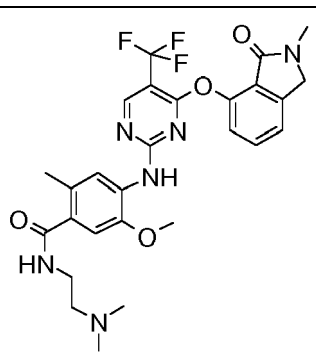
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

15. Verbindung nach Anspruch 7 der Formel

121	

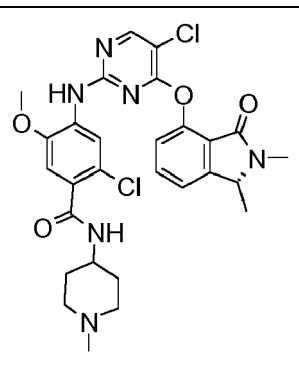
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

16. Verbindung nach Anspruch 7 der Formel

139	

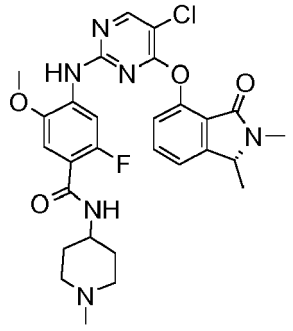
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

17. Verbindung nach Anspruch 7 der Formel

146	

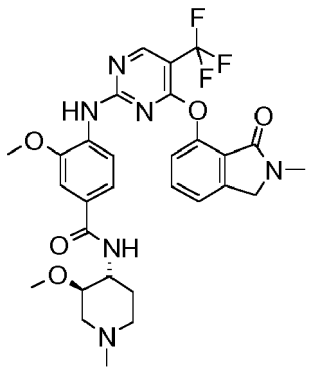
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

18. Verbindung nach Anspruch 7 der Formel

148	

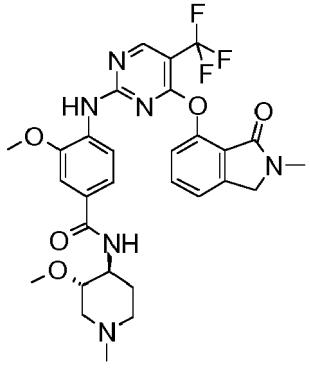
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

19. Verbindung nach Anspruch 7 der Formel

207	

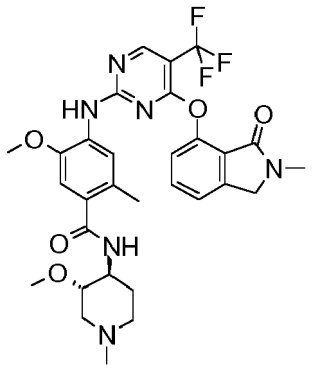
- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

20. Verbindung nach Anspruch 7 der Formel

210	

- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

21. Verbindung nach Anspruch 7 der Formel

213	

- oder ein pharmakologisch akzeptables bzw. annehmbares Säureadditionssalz hiervon.

22. Verbindung - oder die pharmazeutisch wirksamen Salze hiervon - nach einem der Ansprüche 1 bis 21 zur Verwendung als Medikament.

23. Verbindung - oder die pharmazeutisch wirksamen Salze hiervon - nach einem der Ansprüche 1 bis 21 zur Herstellung eines Medikaments mit einer antiproliferativen und/oder pro-apoptotischen Aktivität.

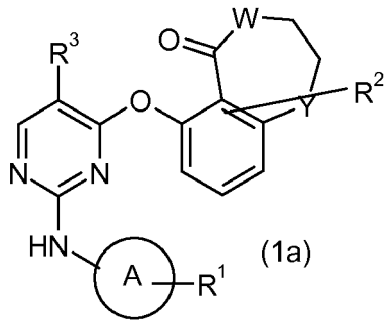
24. Pharmazeutische Zubereitung, enthaltend als aktive Substanz bzw. Wirksubstanz eine oder mehrere Verbindungen der allgemeinen Formeln **(1a)**, **(1b)**, **(1c)** oder **(1d)** nach einem der Ansprüche 1 bis 21 oder die physiologisch akzeptablen bzw. annehmbaren Salze hiervon, gegebenenfalls in Kombination mit herkömmlichen Hilfsstoffen und/oder Trägern.

25. Verwendung der Verbindung der allgemeinen Formel **(1a)**, **(1b)**, **(1c)** oder **(1d)** nach einem der Ansprüche 1 bis 21 zur Herstellung einer pharmazeutischen Zusammensetzung zur Behandlung und/oder Vorbeugung bzw. Prävention von Krebs, Infektionen, Inflammationen bzw. Entzündungen und Autoimmunerkrankungen.

26. Pharmazeutische Zubereitung, umfassend eine Verbindung der allgemeinen Formel **(1a)**, **(1b)**, **(1c)** oder **(1d)** nach einem der Ansprüche 1 bis 21 und mindestens eine weitere zytostatisch oder zytotoxisch wirksame Substanz unterschiedlich zu Formel **(1a)**, **(1b)**, **(1c)** oder **(1d)**, gegebenenfalls in Form der Tautomeren, der Racemate, der Enantiomeren, der Diastereomeren und der Mischungen hiervon oder der pharmakologisch akzeptablen bzw. annehmbaren Säureadditionssalze hiervon.

Revendications

1. Composé de formule générale (Ia),

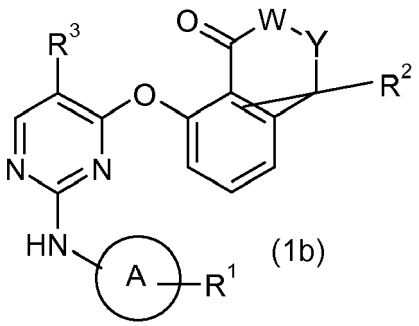


(1a)

dans lequel
A désigne un groupe, éventuellement substitué par un ou plusieurs R^1 identiques ou différents, sélectionné parmi un C_{3-10} cycloalkyle, un hétérocycloalkyle de 3 à 8 chaînons, un C_{6-15} aryle et un hétéroaryle de 5 à 12 chaînons ;

R^1 et R^2 désignent chacun indépendamment l'un de l'autre un hydrogène ou un groupe sélectionné parmi un R^a, R^b et R^a substitué par un ou plusieurs R^c et/ou R^b identiques ou différents ;
R^3 désigne un groupe sélectionné parmi un hydrogène, un halogène, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SC N, -NO, $-NO_2$, un C_{1-3} alkyle, un C_{1-3} halogénoalkyle et un C_{1-3} halogénoalkyloxy ;
W et Y représentent chacun indépendamment l'un de l'autre CH_2, O, N-R^e ou N-OR^e ;
chaque R^a est indépendamment sélectionné l'un de l'autre parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-16} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^b est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^c$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^c$, =NR^c, =NOR^c, =NNR^cR^c, =$NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^cR^c$, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ et $-N(R^g)C(NR^g)NR^cR^c$;
chaque R^c indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^d et/ou R^e identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^d est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^e$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^e$, =NR^e, =NOR^e, =NNR^eR^e, =$NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^eR^e$, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ et $-N(R^g)C(NR^g)NR^eR^e$;
chaque R^e indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^f et/ou R^g identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^f est un groupe adéquat et est indépendamment sélectionné parmi un halogène et $-CF_3$; et
chaque R^g indépendamment l'un de l'autre désigne un hydrogène, un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons ou un hétéroarylalkyle de 6 à 18 chaînons ;
éventuellement sous la forme des tautomères, des racémates, des énantiomères, des diastéréomères et des mélanges de ceux-ci, ou des sels d'addition d'acide pharmacologiquement acceptables de ceux-ci.

2. Composé de formule générale (1b),



(1b)

dans lequel

A désigne un groupe, éventuellement substitué par un ou plusieurs R^1 identiques ou différents, sélectionné parmi un C_{3-10}cycloalkyle, un hétérocycloalkyle de 3 à 8 chaînons, un C_{6-15} aryle et un hétéroaryle de 5 à 12 chaînons ;

R^1 et R^2 désignent chacun indépendamment l'un de l'autre un hydrogène ou un groupe sélectionné parmi un R^a, R^b et R^a substitué par un ou plusieurs R^c et/ou R^b identiques ou différents ;

R^3 désigne un groupe sélectionné parmi un hydrogène, un halogène, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SC N, -NO, $-NO_2$, un C_{1-3} alkyle, un C_{1-3} halogénoalkyle et un C_{1-3} halogénoalkyloxy ;

W et Y représentent chacun indépendamment l'un de l'autre CH_2, O, N-R^e ou N-OR^e ;

chaque R^a est indépendamment sélectionné l'un de l'autre parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-16} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;

chaque R^b est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^c$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)$ NR^cR^c, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^c$ R^c, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR$ $^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)$ NR^cR^c, $-C(O)N(R^g)$ OR^c, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR$ ^{c}, $-OC(NR^g)$ NR^cR^c, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(N$ $R^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)$ $C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g$ $)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^c$ R^c, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g$ $)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)$ $C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR$ ^{c} et $-N(R^g)C(NR^g)NR^cR^c$;

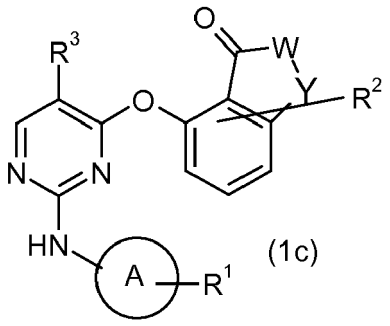
chaque R^c indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^d et/ou R^e identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;

chaque R^d est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^e$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^e$ R^e, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR$ $^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR$ ^{e}, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(N$ $R^g)NR^e$-R^e, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)$ $C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)$ $C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR$ ^{e}, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$, $-N(R^g)$ $[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C$ $(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ et $-N(R^g)C(NR^g)NR^eR^e$;

chaque R^e indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^f et/ou R^g identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;

chaque R^f est un groupe adéquat et est indépendamment sélectionné parmi un halogène et $-CF_3$; et
chaque R^g indépendamment l'un de l'autre désigne un hydrogène, un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons ou un hétéroarylalkyle de 6 à 18 chaînons ;
éventuellement sous la forme des tautomères, des racémates, des énantiomères, des diastéréomères et des mélanges de ceux-ci, ou des sels d'addition d'acide pharmacologiquement acceptables de ceux-ci.

3. Composé de formule générale (1c),



(1c)

dans lequel
A désigne un groupe, éventuellement substitué par un ou plusieurs R^1 identiques ou différents, sélectionné parmi un C_{3-10} cycloalkyle, un hétérocycloalkyle de 3 à 8 chaînons, un C_{6-15} aryle et un hétéroaryle de 5 à 12 chaînons ;
R^1 et R^2 désignent chacun indépendamment l'un de l'autre un hydrogène ou un groupe sélectionné parmi un R^a, R^b et R^a substitué par un ou plusieurs R^c et/ou R^b identiques ou différents ;
R^3 désigne un groupe sélectionné parmi un hydrogène, un halogène, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SC N, -NO, $-NO_2$, un C_{1-3} alkyle, un C_{1-3} halogénoalkyle et un C_{1-3} halogénoalkyloxy ;
W et Y représentent chacun indépendamment l'un de l'autre CH_2, O, N-R^e ou N-OR^e ;
chaque R^a est indépendamment sélectionné l'un de l'autre parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-16} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^b est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^c$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^c$ R^c, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)OR^c$, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR^c$, $-OC(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(NR^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^cNR^cR^c$, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cR^c\}_2$, $-[N(R^g)C(O)]_2OR^c$, $-N(R^g)C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR^c$ et $-N(R^g)C(NR^g)NR^cR^c$;
chaque R^c indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^d et/ou R^e identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^d est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^e$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^e$ R^e, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^c$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$,

$-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)$ $S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R^e]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)$ $C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)$ $C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$-$N(R^g)$ $[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C$ $(O)]_2OR^e$, $-N(R^g)$ $C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ et $-N(R^g)C(NR^g)NR^eR^e$;

chaque R^e indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^f et/ou R^g identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;

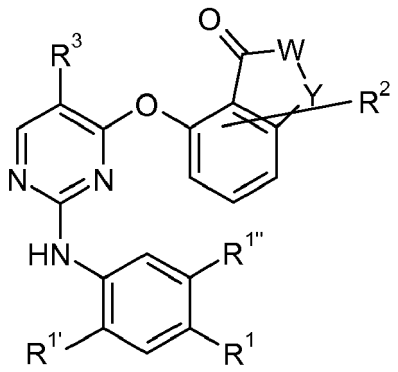
chaque R^f est un groupe adéquat et est indépendamment sélectionné parmi un halogène et $-CF_3$; et

chaque R^g indépendamment l'un de l'autre désigne un hydrogène, un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons ou un hétéroarylalkyle de 6 à 18 chaînons ;

éventuellement sous la forme des tautomères, des racémates, des énantiomères, des diastéréomères et des mélanges de ceux-ci, ou des sels d'addition d'acide pharmacologiquement acceptables de ceux-ci.

4. Composé selon l'une quelconque des revendications 1 à 3, dans lequel A est un phényle.

5. Composé de formule générale (1d) selon la revendication 3,



(1d)

dans lequel

W et Y représentent chacun indépendamment l'un de l'autre CH_2, O, N-R^e ou N-OR^e, et

R^1 désigne un hydrogène ou un groupe sélectionné parmi un R^a, R^b et R^a substitué par un ou plusieurs R^c et/ou R^b identiques ou différents,

chaque R^a est indépendamment sélectionné l'un de l'autre parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-16} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;

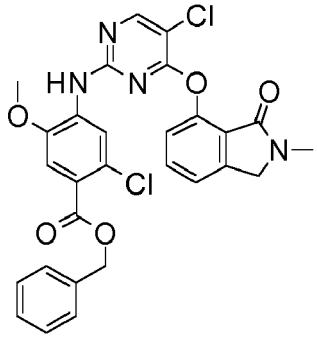
chaque R^b est un groupe adéquat et est indépendamment sélectionné parmi = O, $-OR^c$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^c$, $=NR^c$, $=NOR^c$, $=NNR^cR^c$, $=NN(R^g)C(O)NR^cR^c$, $-NR^cR^c$, $-ONR^cR^c$, $-N(OR^c)R^c$, $-N(R^g)NR^cR^c$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^c$, $-S(O)OR^c$, $-S(O)_2R^c$, $-S(O)_2OR^c$, $-S(O)NR^c$ R^c, $-S(O)_2NR^cR^c$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)_2OR^c$, $-OS(O)NR$ $^cR^c$, $-OS(O)_2NR^cR^c$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)SR^c$, $-C(O)NR^cR^c$, $-C(O)N(R^g)NR^cR^c$, $-C(O)N(R^g)$ OR^c, $-C(NR^g)NR^cR^c$, $-C(NOH)R^c$, $-C(NOH)NR^cR^c$, $-OC(O)R^c$, $-OC(O)OR^c$, $-OC(O)SR^c$, $-OC(O)NR^cR$ ^{c}, $-OC$ $(NR^g)NR^cR^c$, $-SC(O)R^c$, $-SC(O)OR^c$, $-SC(O)NR^cR^c$, $-SC(N$ $R^g)NR^cR^c$, $-N(R^g)C(O)R^c$, $-N[C(O)R^c]_2$, $-N(OR^g)C(O)R^c$, $-N(R^g)$ $C(NR^g)R^c$, $-N(R^g)N(R^g)C(O)R^c$, $-N[C(O)R^c]NR^cR^c$, $-N(R^g)C(S)R^c$, $-N(R^g)S(O)R^c$, $-N(R^g)S(O)OR^c$, $-N(R^g)S(O)_2R^c$, $-N[S(O)_2R^c]_2$, $-N(R^g)S(O)_2OR^c$, $-N(R^g)S(O)_2NR^cR^c$, $-N(R^g)[S(O)_2]_2R^c$, $-N(R^g$ $)C(O)OR^c$, $-N(R^g)C(O)SR^c$, $-N(R^g)C(O)NR^cR^c$, $-N(R^g)C(O)NR^gNR^c$ R^c, $-N(R^g)N(R^g)C(O)NR^cR^c$, $-N(R^g)C(S)NR^cR^c$, $-[N(R^g)C(O)]_2R^c$, $-N(R^g)[C(O)]_2R^c$, $-N\{[C(O)]_2R^c\}_2$, $-N(R^g)[C(O)]_2OR^c$, $-N(R^g$ $)[C(O)]_2NR^cR^c$, $-N\{[C(O)]_2OR^c\}_2$, $-N\{[C(O)]_2NR^cRc\}_2$, $-[N(R^g)$ $C(O)]_2OR^c$, $-N(R^g)$ $C(NR^g)OR^c$, $-N(R^g)C(NOH)R^c$, $-N(R^g)C(NR^g)SR$ ^{c} et $-N(R^g)C(NR^g)NR^cR^c$,

chaque R^c indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^d et/ou R^e identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-10} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à

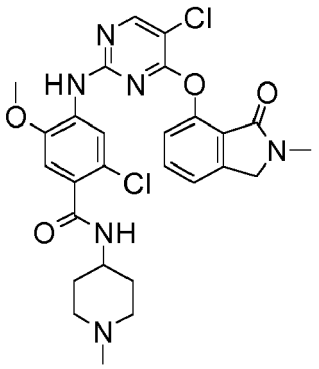
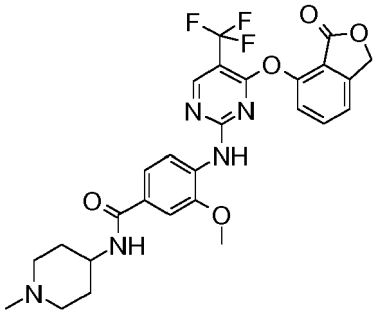
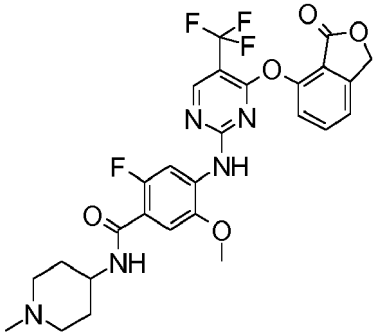
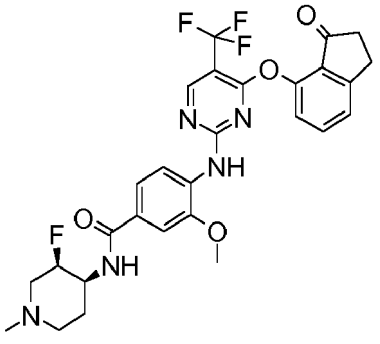
8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^d est un groupe adéquat et est indépendamment sélectionné parmi =O, $-OR^e$, un C_{1-3} halogénoalkyloxy, $-OCF_3$, =S, $-SR^e$, $=NR^e$, $=NOR^e$, $=NNR^eR^e$, $=NN(R^g)C(O)NR^eR^e$, $-NR^eR^e$, $-ONR^eR^e$, $-N(R^g)NR^eR^e$, un halogène, $-CF_3$, -CN, -NC, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)R^e$, $-S(O)OR^e$, $-S(O)_2R^e$, $-S(O)_2OR^e$, $-S(O)NR^e$ R^e, $-S(O)_2NR^eR^e$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)_2OR^e$, $-OS(O)NR^eR^e$, $-OS(O)_2NR^eR^e$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)SR^e$, $-C(O)NR^eR^e$, $-C(O)N(R^g)NR^eR^e$, $-C(O)N(R^g)OR^e$, $-C(NR^g)NR^eR^e$, $-C(NOH)R^e$, $-C(NOH)NR^eR^e$, $-OC(O)R^e$, $-OC(O)OR^e$, $-OC(O)SR^e$, $-OC(O)NR^eR^e$, $-OC(NR^g)NR^eR^e$, $-SC(O)R^e$, $-SC(O)OR^e$, $-SC(O)NR^eR^e$, $-SC(NR^g)NR^eR^e$, $-N(R^g)C(O)R^e$, $-N[C(O)R^e]_2$, $-N(OR^g)C(O)R^e$, $-N(R^g)C(NR^g)R^e$, $-N(R^g)N(R^g)C(O)R^e$, $-N[C(O)R^e]NR^eR^e$, $-N(R^g)C(S)R^e$, $-N(R^g)S(O)R^e$, $-N(R^g)S(O)OR^e$ $-N(R^g)S(O)_2R^e$, $-N[S(O)_2R]_2$, $-N(R^g)S(O)_2OR^e$, $-N(R^g)S(O)_2NR^eR^e$, $-N(R^g)[S(O)_2]_2R^e$, $-N(R^g)C(O)OR^e$, $-N(R^g)C(O)SR^e$, $-N(R^g)C(O)NR^eR^e$, $-N(R^g)C(O)NR^gNR^eR^e$, $-N(R^g)N(R^g)C(O)NR^eR^e$, $-N(R^g)C(S)NR^eR^e$, $-[N(R^g)C(O)]_2R^e$, $-N(R^g)[C(O)]_2R^e$, $-N\{[C(O)]_2R^e\}_2$, $-N(R^g)[C(O)]_2OR^e$-$N(R^g)[C(O)]_2NR^eR^e$, $-N\{[C(O)]_2OR^e\}_2$, $-N\{[C(O)]_2NR^eR^e\}_2$, $-[N(R^g)C(O)]_2OR^e$, $-N(R^g)C(NR^g)OR^e$, $-N(R^g)C(NOH)R^e$, $-N(R^g)C(NR^g)SR^e$ et $-N(R^g)C(NR^g)NR^eR^e$,
chaque R^e indépendamment l'un de l'autre désigne un hydrogène ou un groupe éventuellement substitué par un ou plusieurs R^f et/ou R^g identiques ou différents sélectionné parmi un C_{1-6} alkyle, un C_{3-8} cycloalkyle, un C_{4-11} cycloalkylalkyle, un C_{6-10} aryle, un C_{7-16} arylalkyle, un hétéroalkyle de 2 à 6 chaînons, un hétérocycloalkyle de 3 à 8 chaînons, un hétérocycloalkylalkyle de 4 à 14 chaînons, un hétéroaryle de 5 à 12 chaînons et un hétéroarylalkyle de 6 à 18 chaînons ;
chaque R^f est un groupe adéquat et est indépendamment sélectionné parmi un halogène et $-CF_3$; et
chaque R^g indépendamment l'un de l'autre désigne un hydrogène, un C_{1-6} alkyle, un C_{3-8} cycloalkyle, et
$R^{1'}$ et $R^{1''}$ désignent chacun indépendamment l'un de l'autre un groupe sélectionné parmi un hydrogène, un halogène et $-OR^c$,
R^2 désigne un hydrogène ou un groupe sélectionné parmi un R^a, R^b et R^a substitué par un ou plusieurs identiques ou différents R^c et/ou R^b, et
R^3 désigne un groupe sélectionné parmi un hydrogène, un halogène, $-OR^c$, $-OCF_3$, $-SR^c$, $-NR^cR^c$, $-CF_3$, -CN, -OCN, -SC N, -NO, $-NO_2$, un C_{1-3} alkyle, un C_{1-3} halogénoalkyle et un C_{1-3} halogénoalkyloxy ;
éventuellement sous la forme des tautomères, des racémates, des énantiomères, des diastéréomères et des mélanges de ceux-ci, ou des sels d'addition d'acide pharmacologiquement acceptables de ceux-ci.

6. Composé selon l'une quelconque des revendications 1 à 5, dans lequel R^3 est Cl ou CF_3.

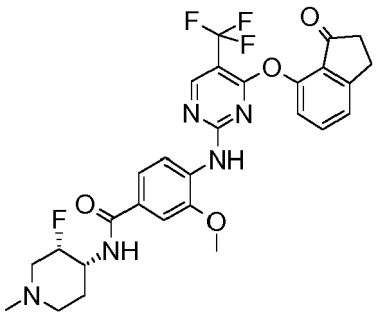
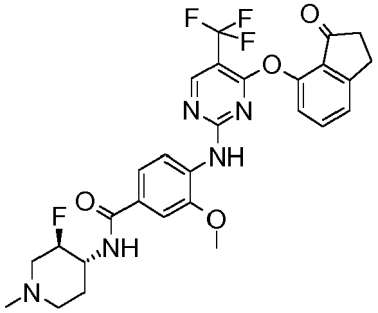
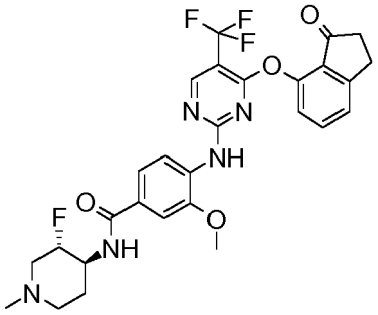
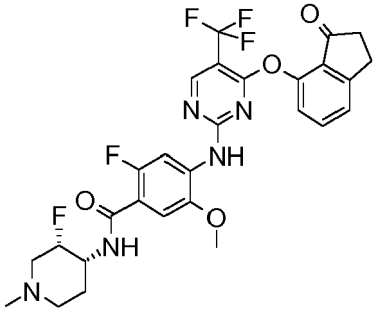
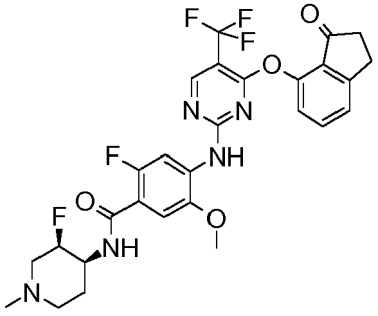
7. Composé sélectionné parmi

1	

(suite)

2	
3	
4	
5	

(suite)

6	
7	
8	
9	
10	

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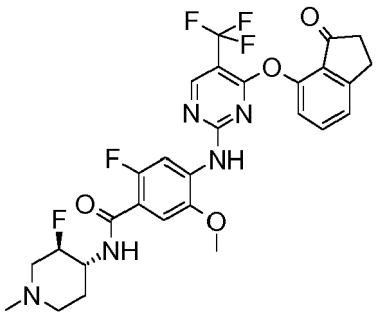
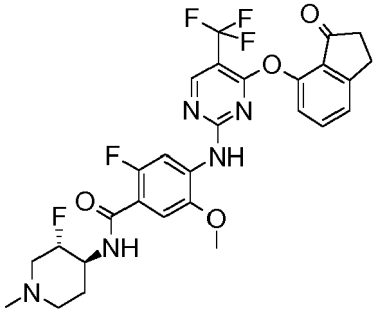
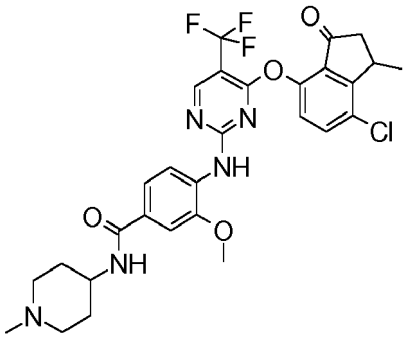
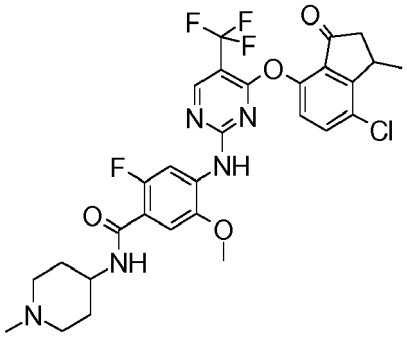
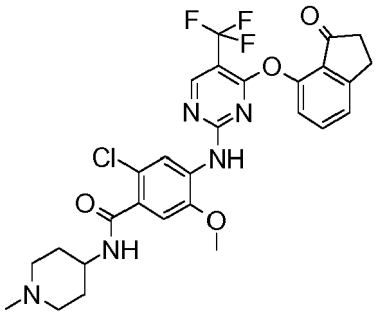
11	
12	
13	
14	
15	

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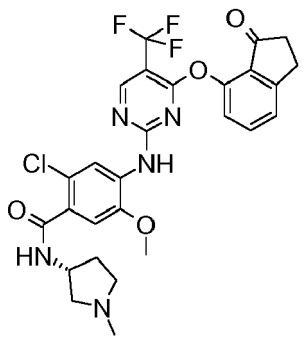
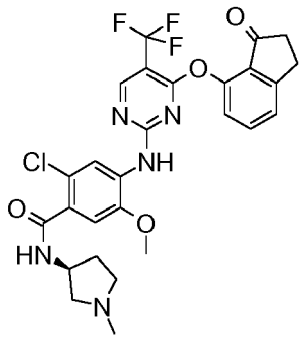
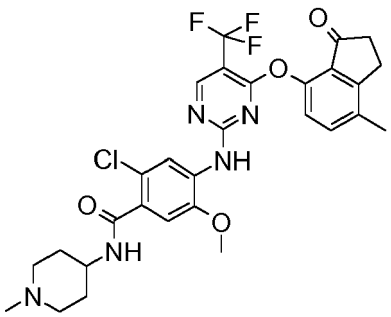
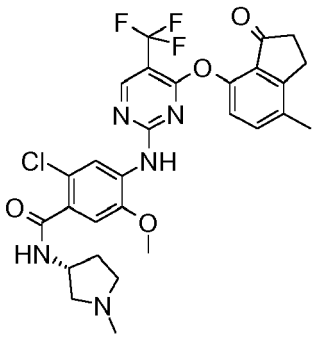
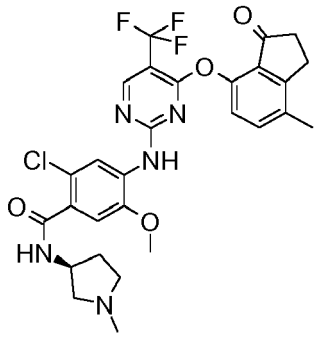
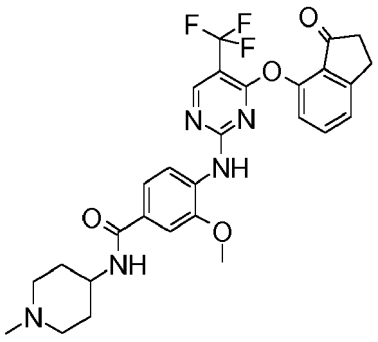
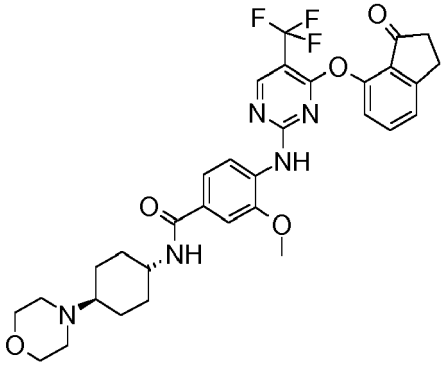
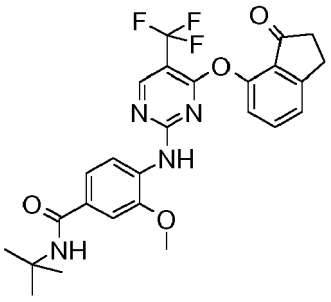
16	
17	
18	
19	

(suite)

20	
21	
22	
23	

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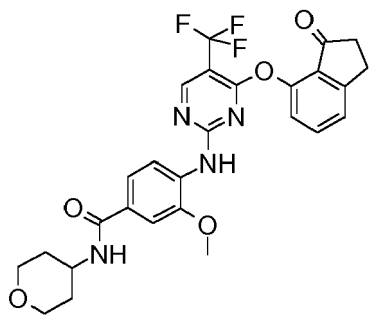
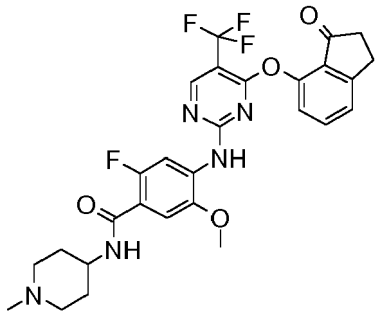
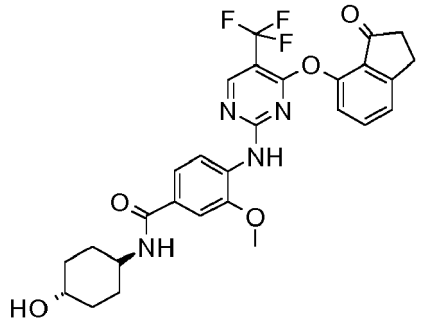
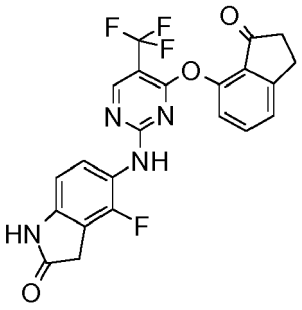
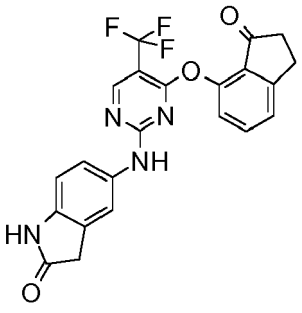
24	
25	
26	
27	
28	

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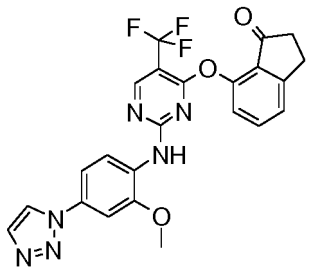
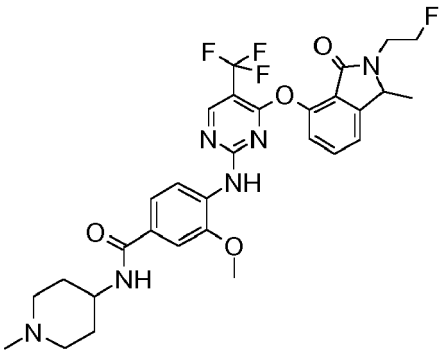
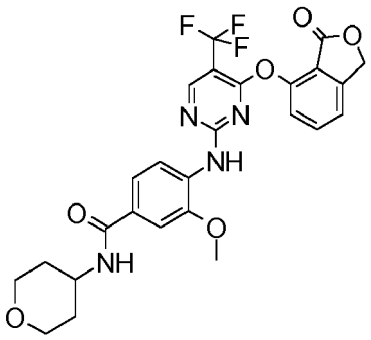
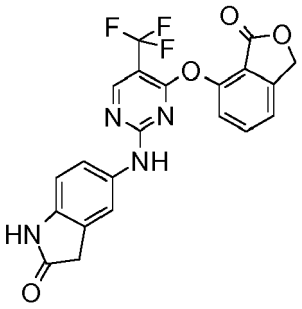
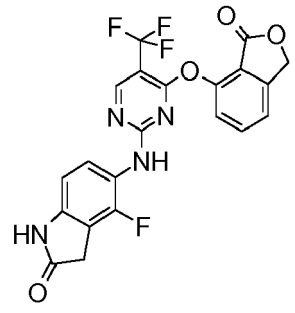
29	
30	
31	
32	
33	

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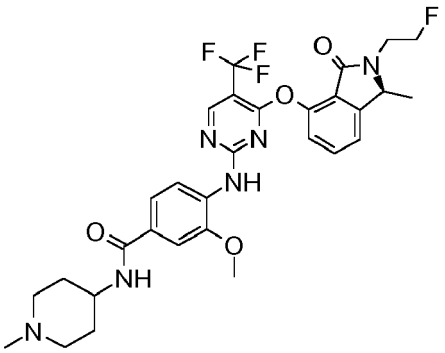
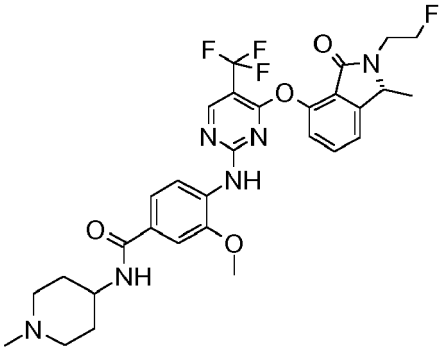
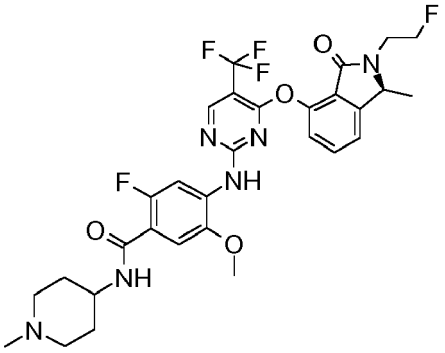
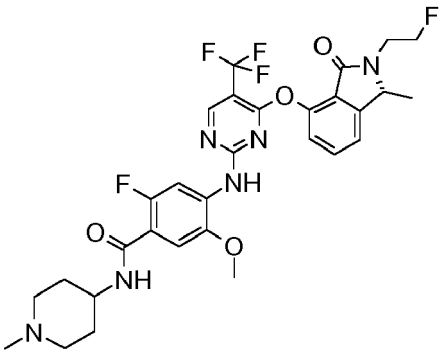
34	
35	
36	
37	

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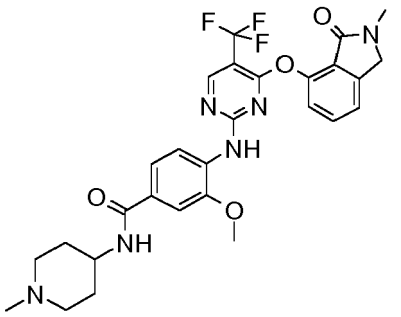
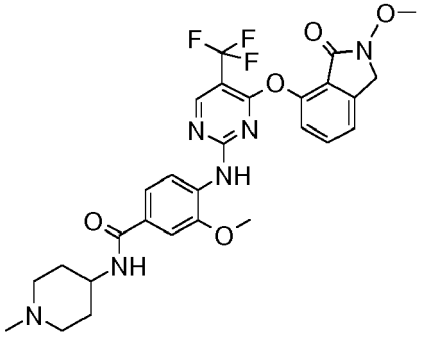
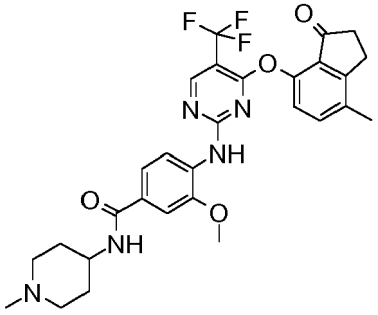
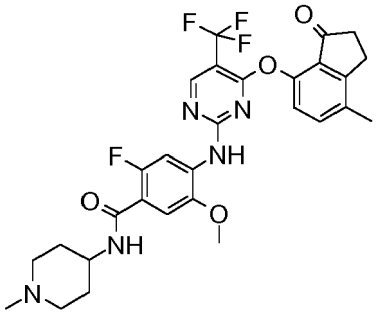
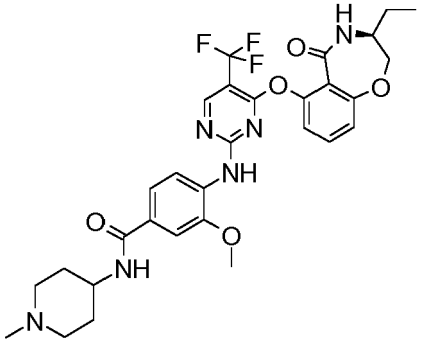
38	
39	
40	
41	
42	

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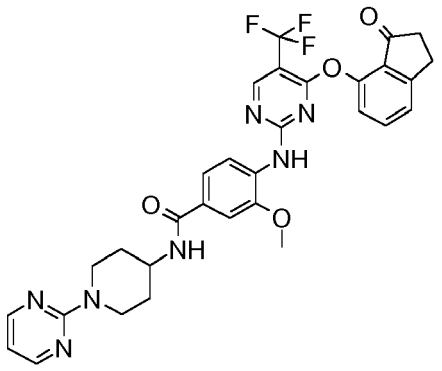
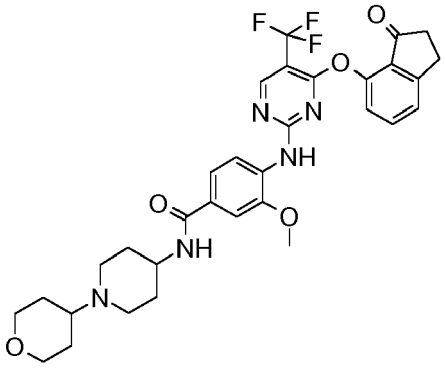
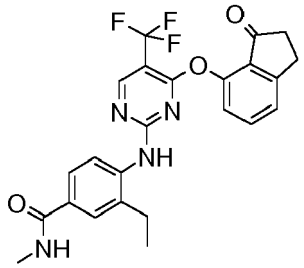
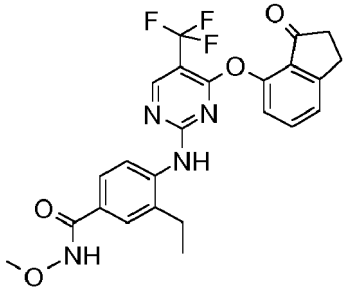
43	
44	
45	
46	

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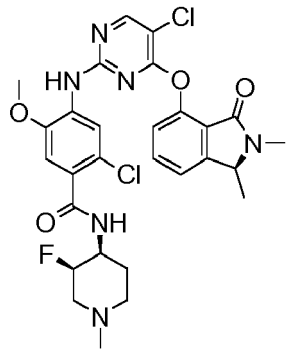
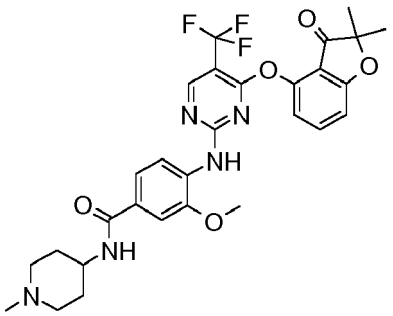
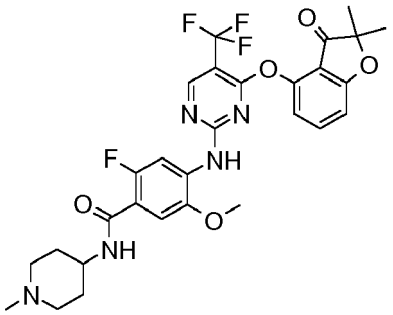
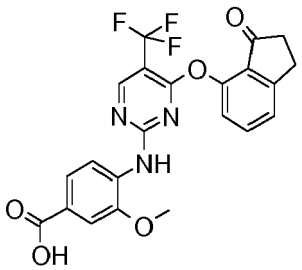
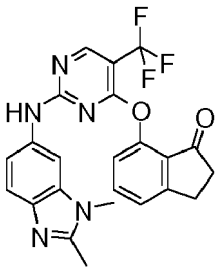
47	
48	
49	
50	
51	

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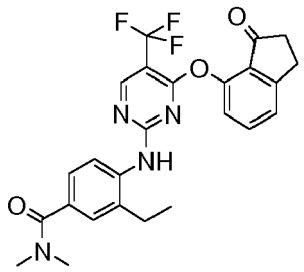
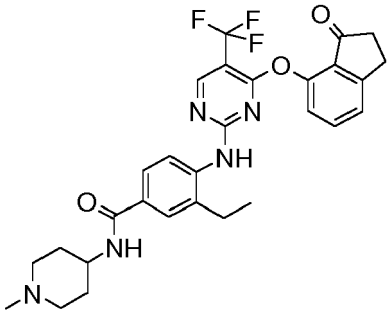
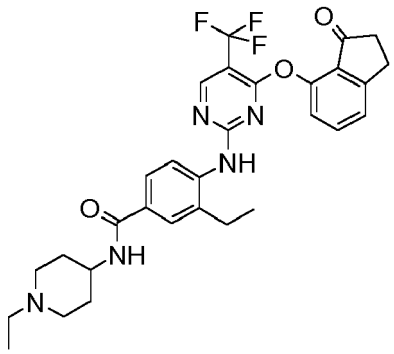
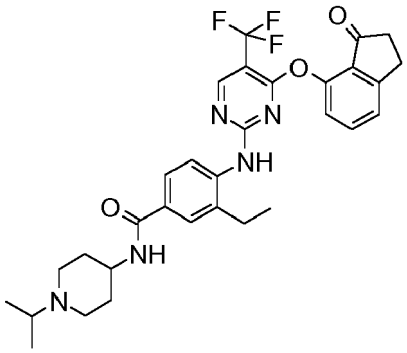
52	
53	
54	
55	

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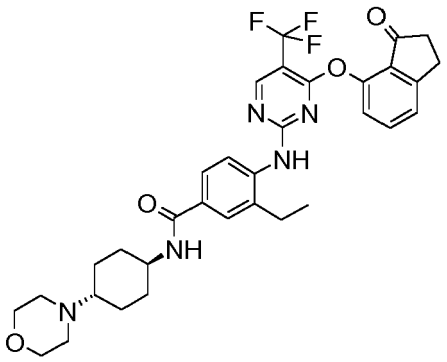
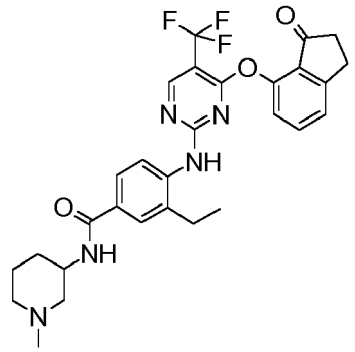
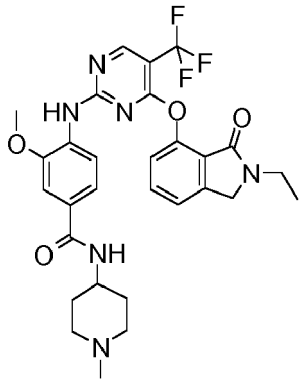
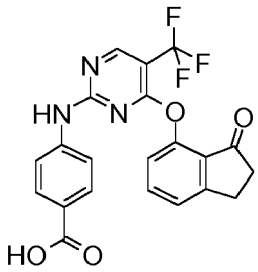
56	
57	
58	
59	

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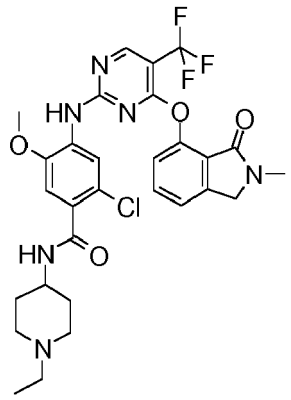
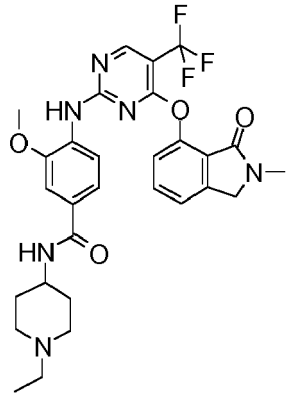
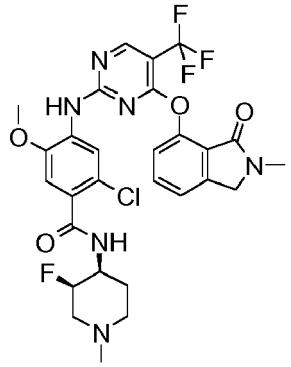
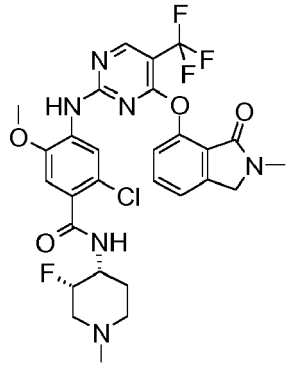
60	
61	
62	
63	

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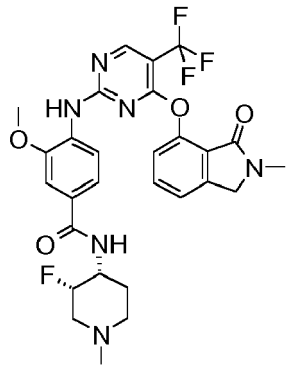
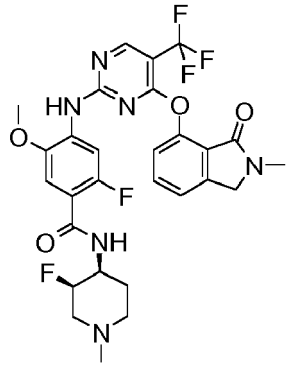
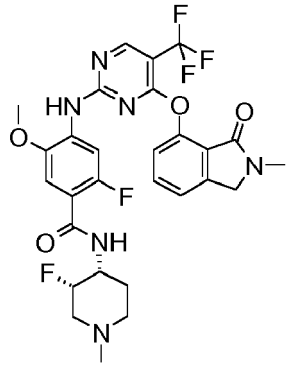
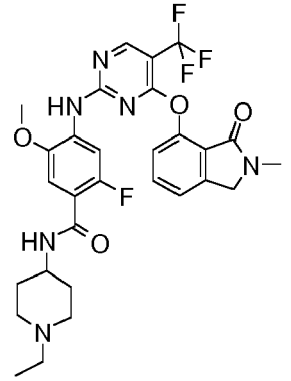
64	
65	
66	
67	

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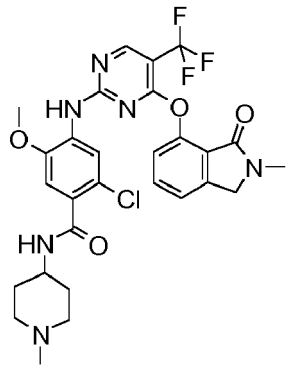
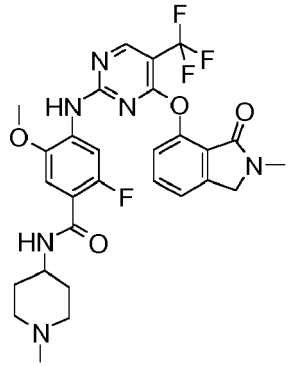
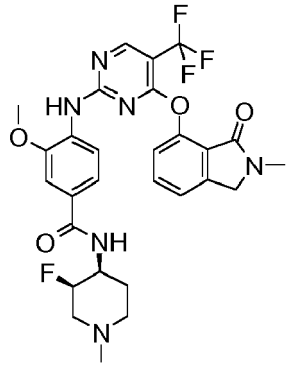
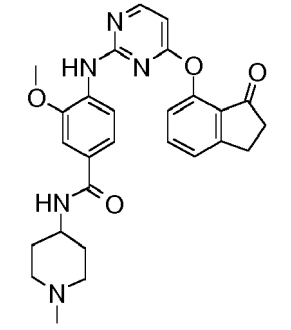
68	
69	
70	
71	

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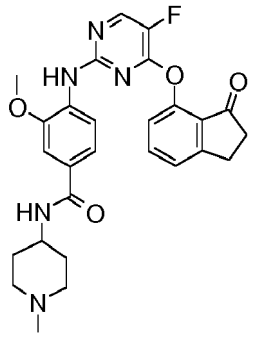
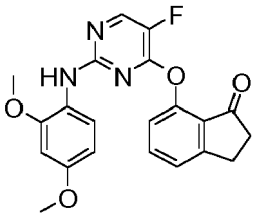
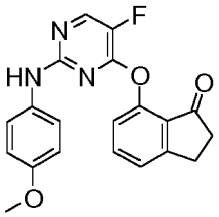
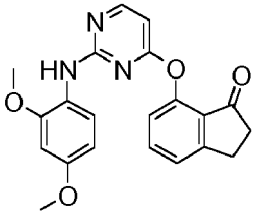
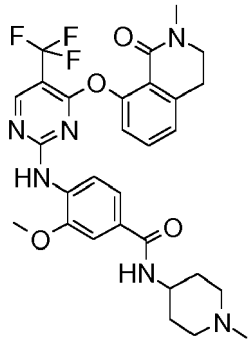
72	
73	
74	
75	
76	

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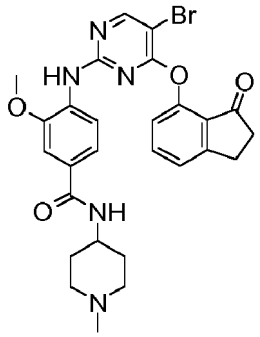
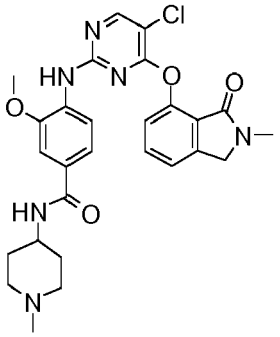
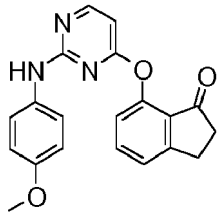
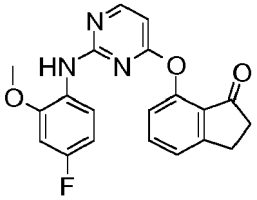
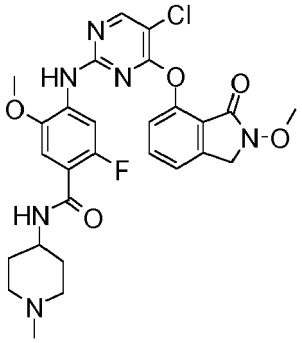
77	
78	
79	
80	
81	

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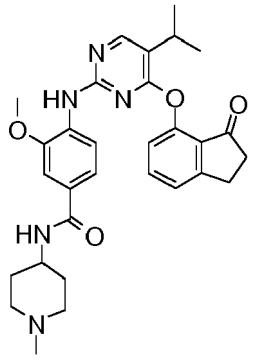
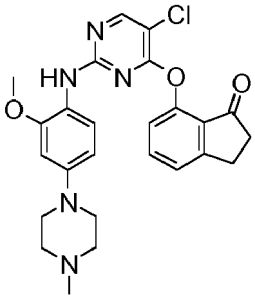
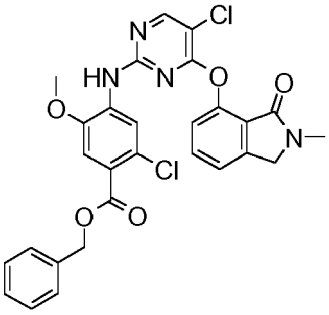
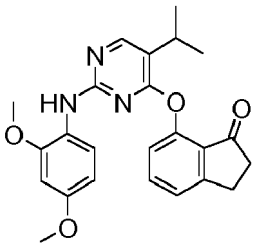
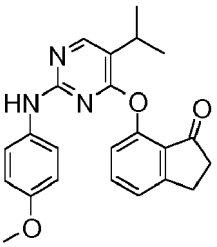
82	
83	
84	
85	
86	

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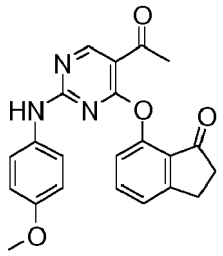
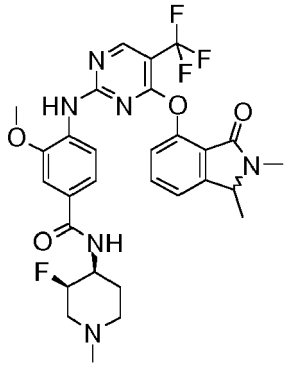
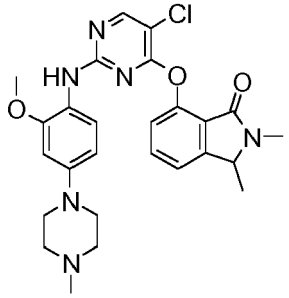
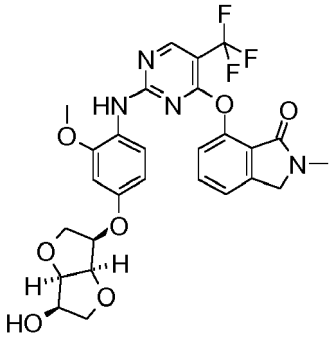
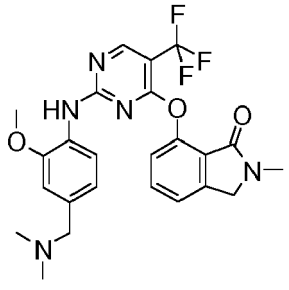
87	
88	
89	
91	
93	

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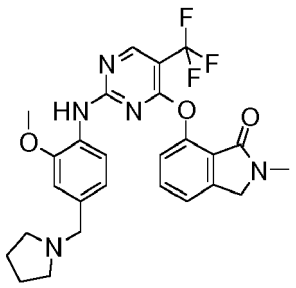
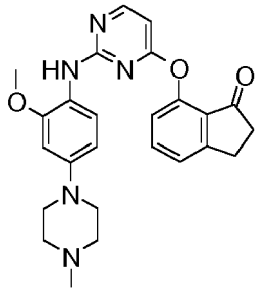
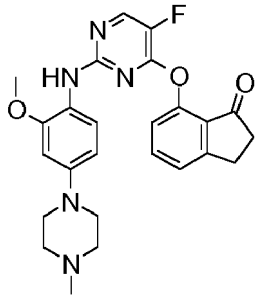
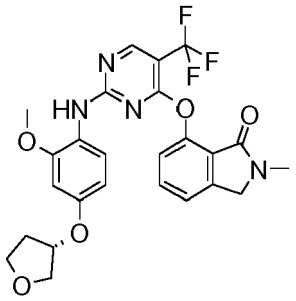
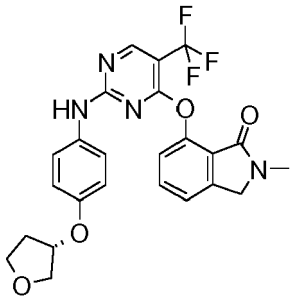
94	
95	
96	
97	
98	

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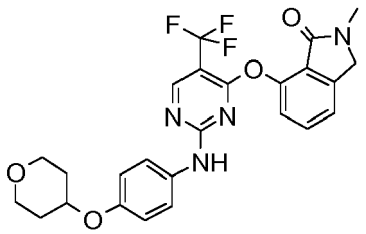
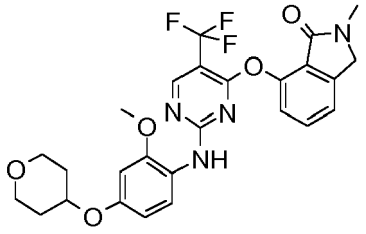
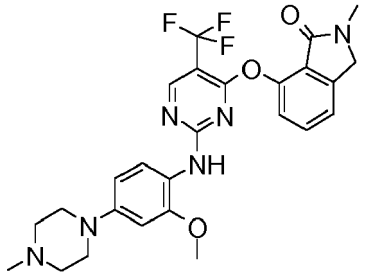
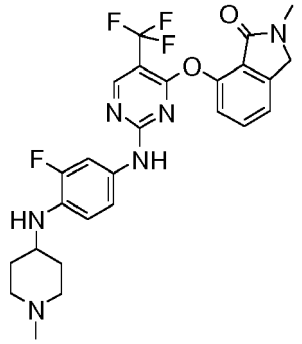
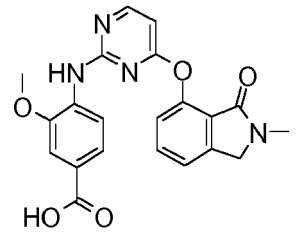
99	
100	
101	
102	
103	

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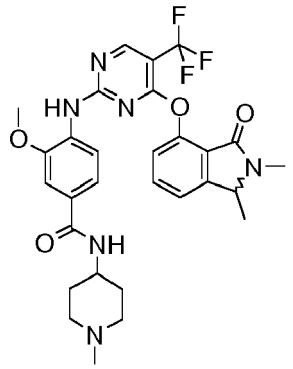
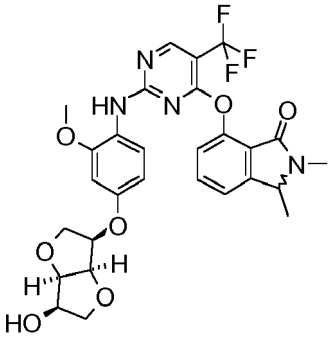
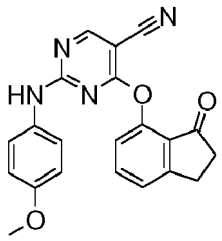
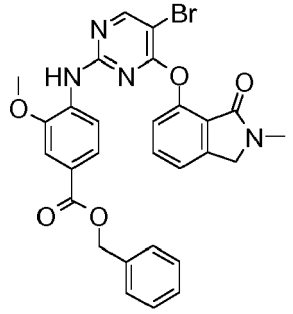
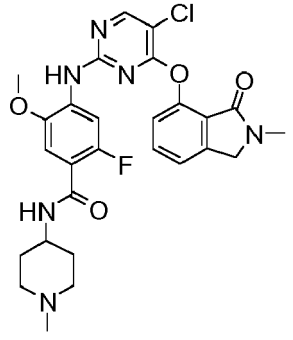
104	
105	
106	
107	
108	

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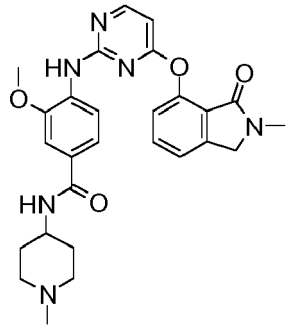
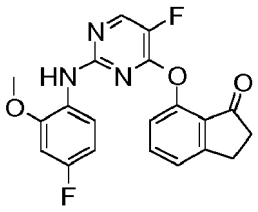
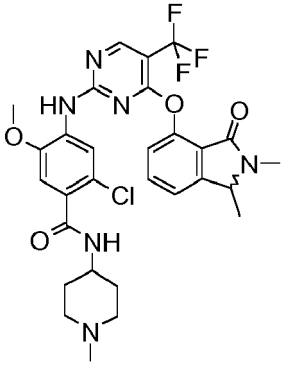
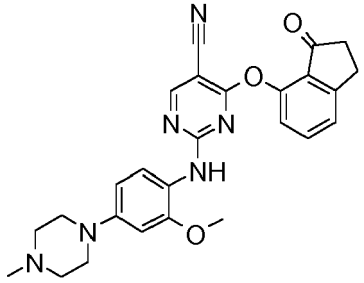
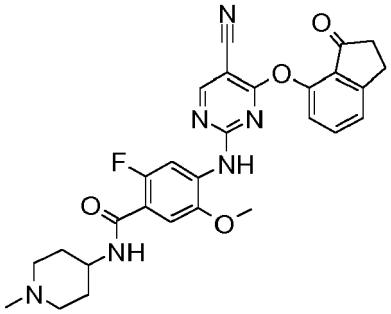
109	
110	
111	
112	
113	

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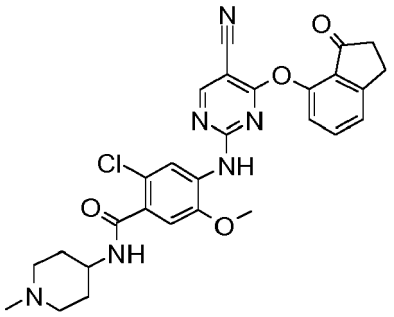
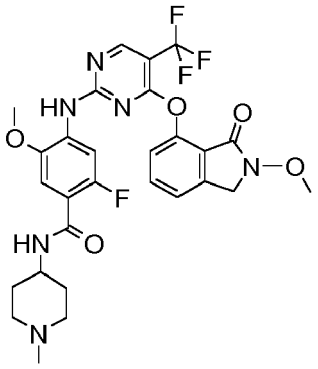
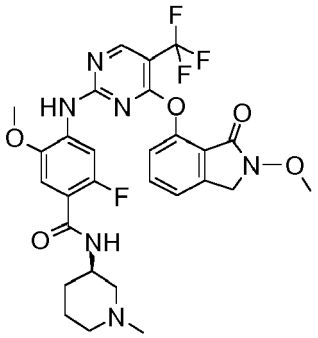
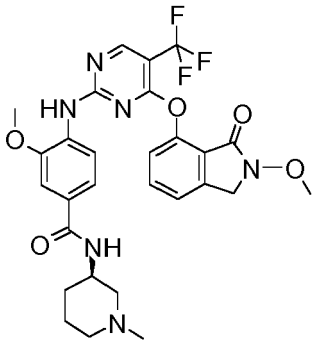
114	
115	
116	
117	

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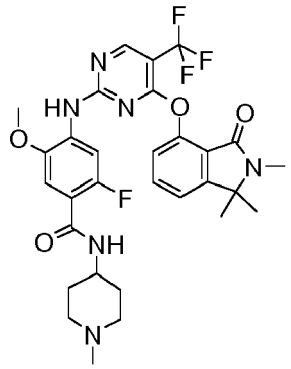
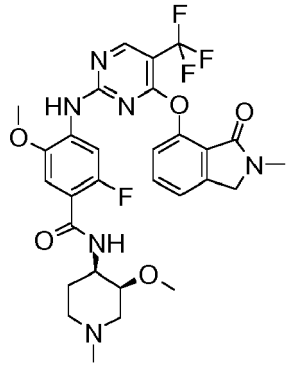
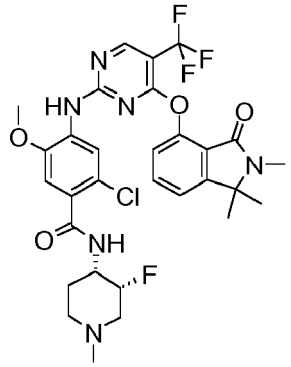
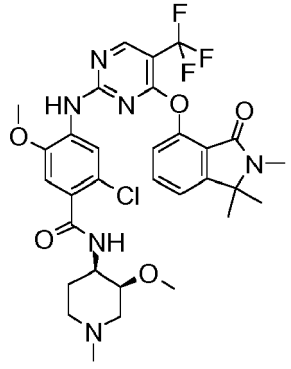
118	
119	
120	
121	

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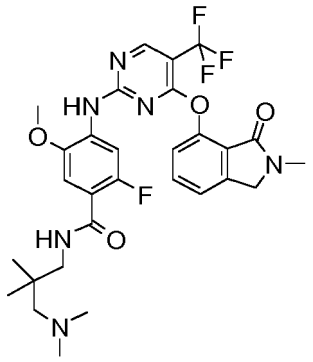
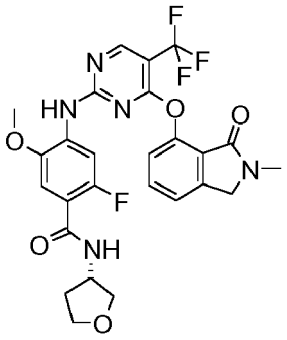
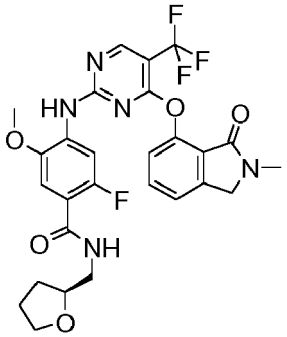
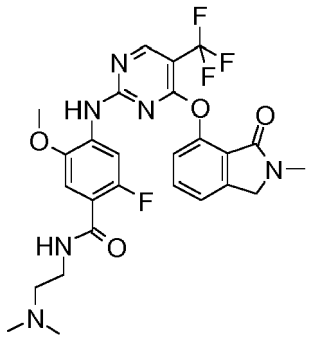
122	
123	
124	
125	

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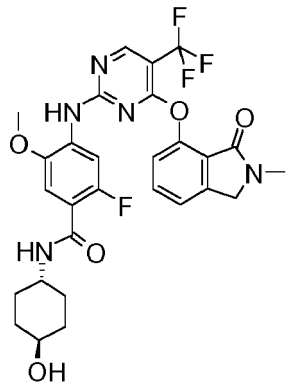
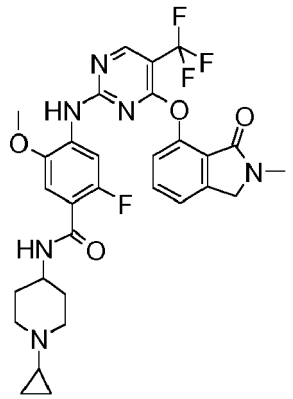
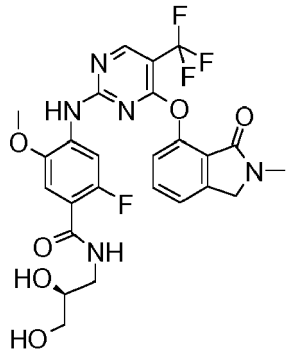
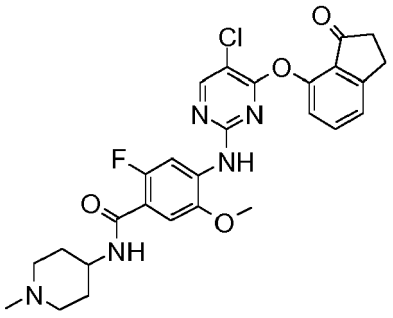
126	
127	
128	
129	

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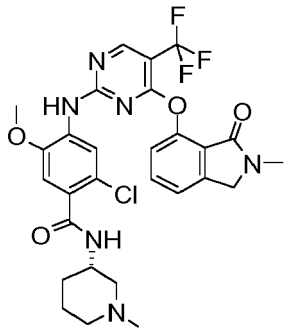
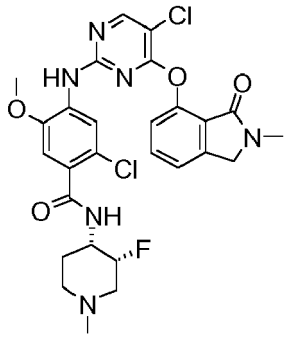
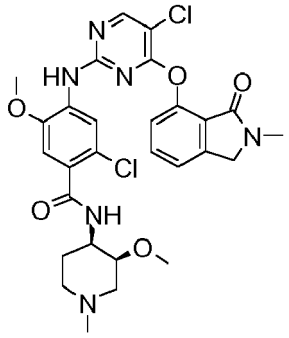
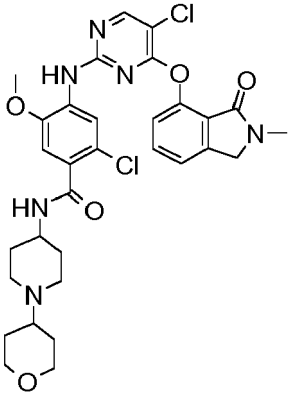
130	
131	
132	
133	

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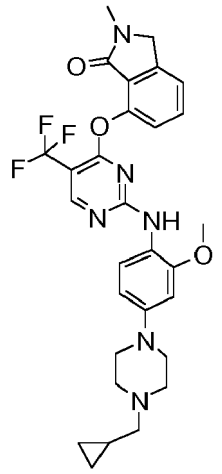
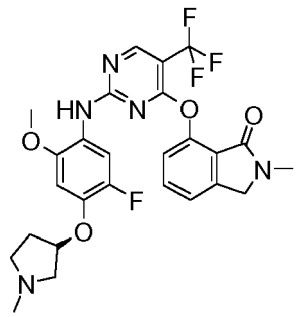
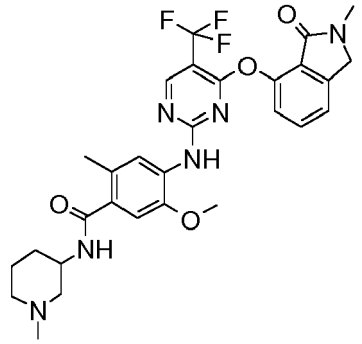
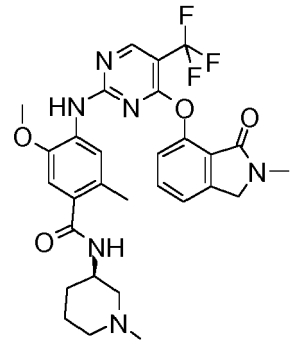
134	
135	
136	
137	

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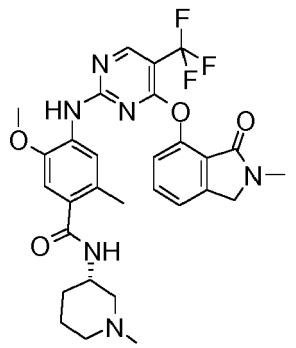
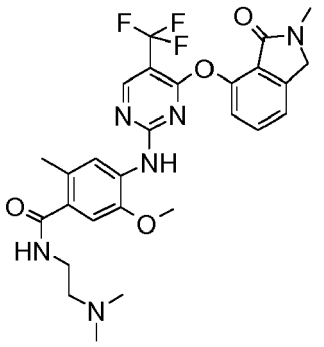
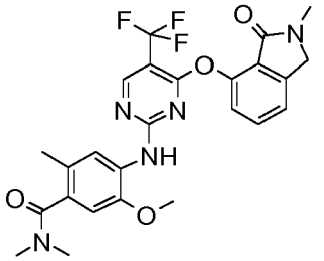
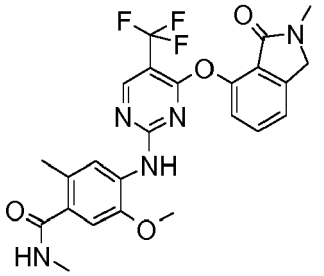
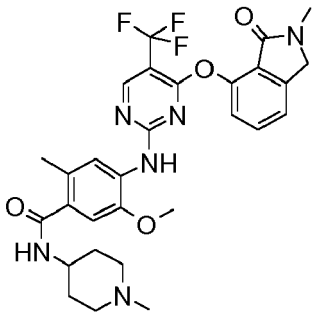
138	
139	
140	
141	
142	

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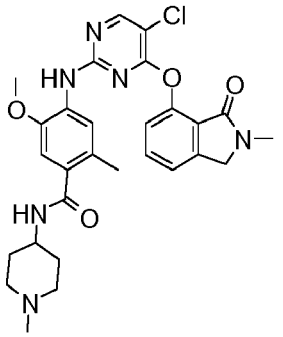
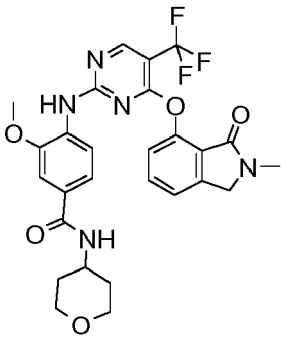
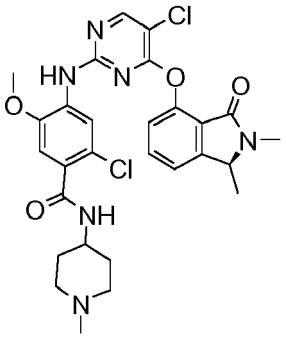
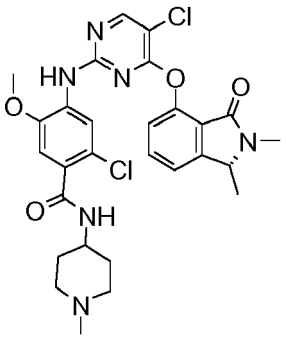
143	
144	
145	
146	

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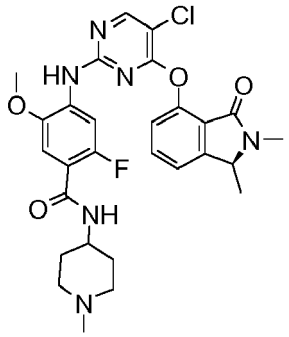
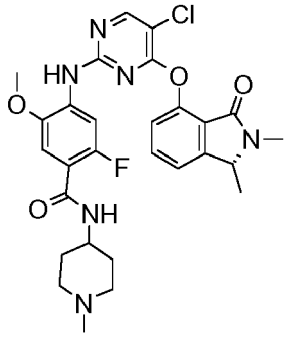
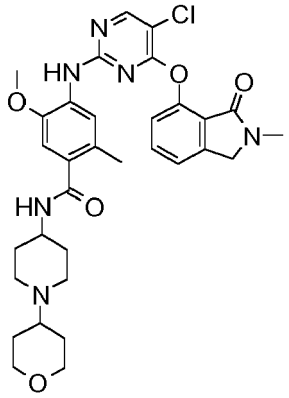
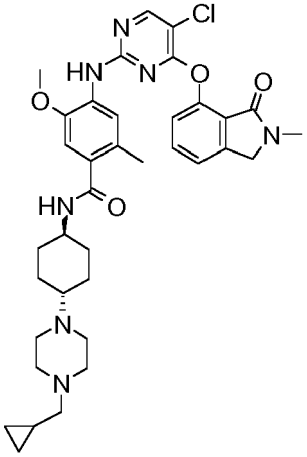
147	
148	
149	
150	

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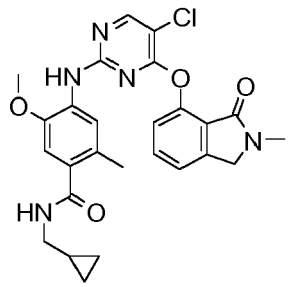
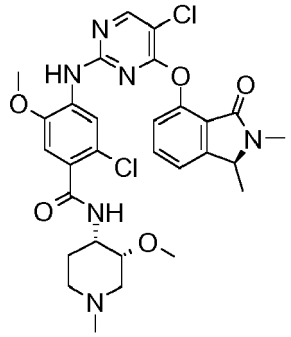
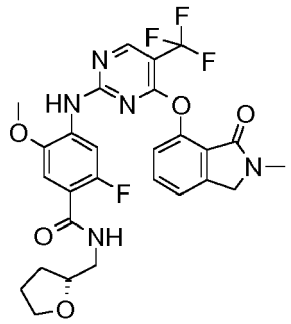
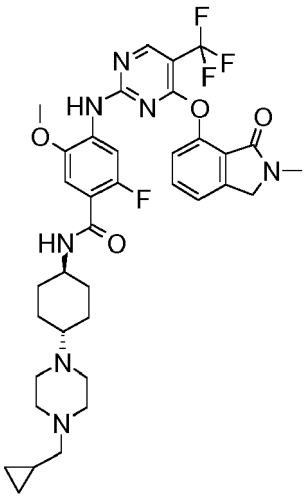
151	
152	
153	
154	

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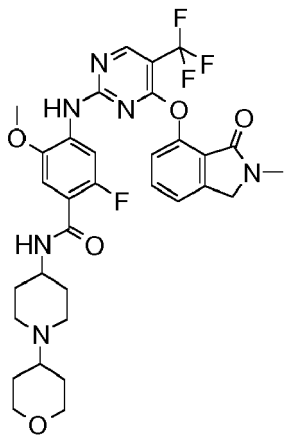
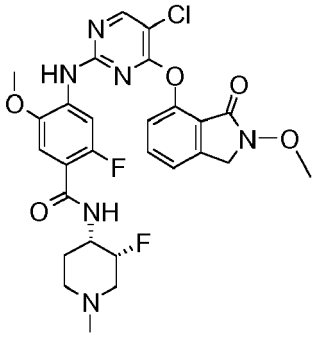
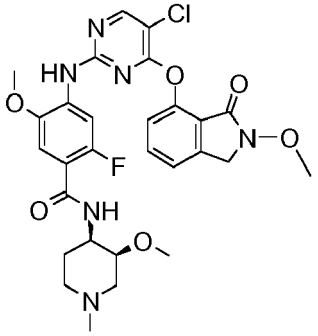
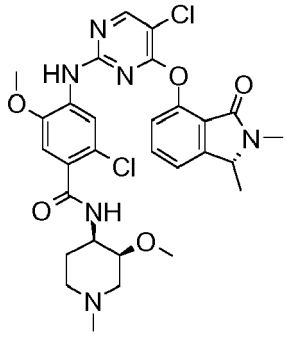
155	
157	
158	
159	

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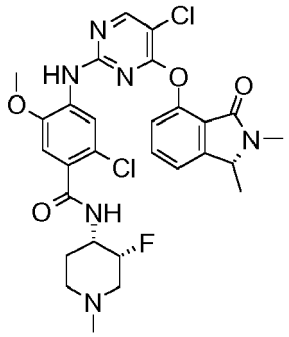
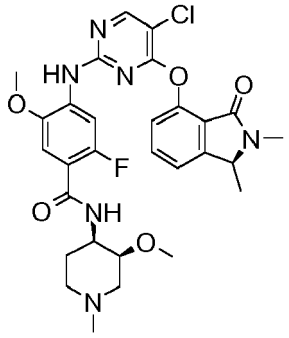
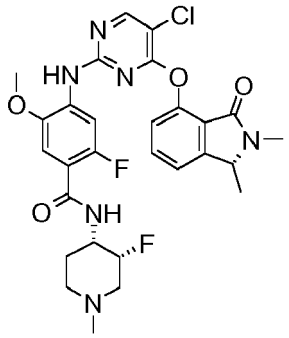
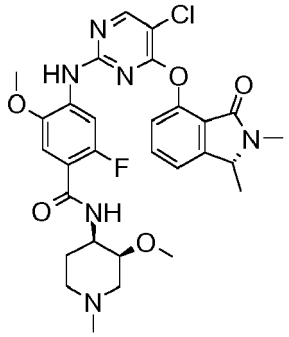
160	
161	
162	
163	

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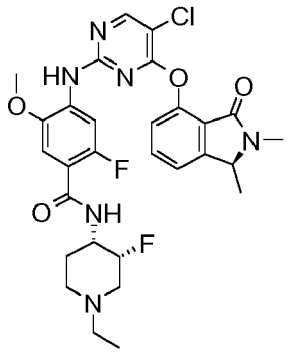
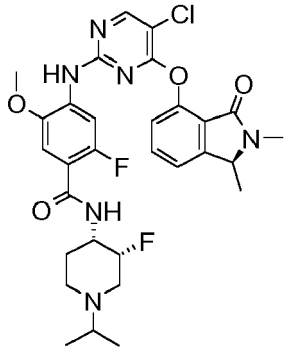
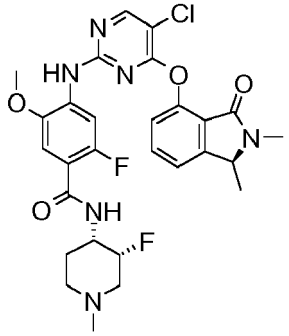
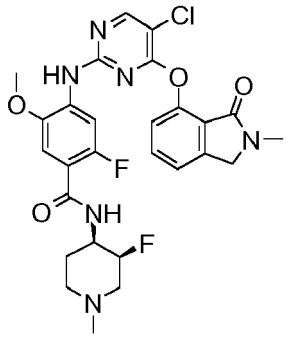
164	
165	
166	
167	

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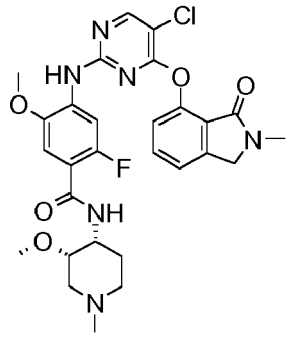
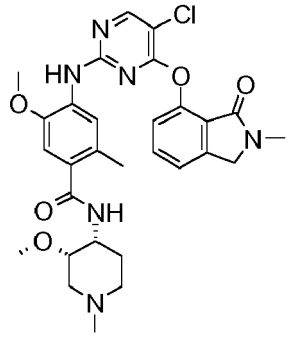
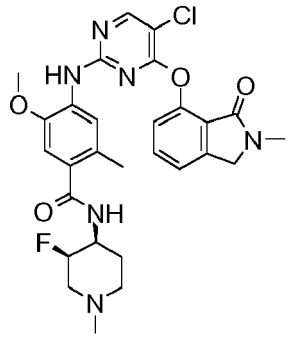
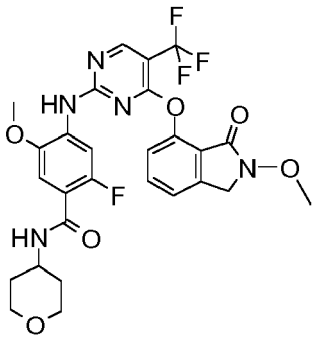
168	
169	
170	
171	

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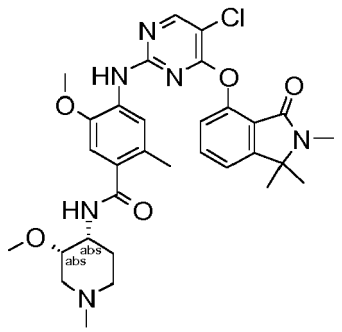
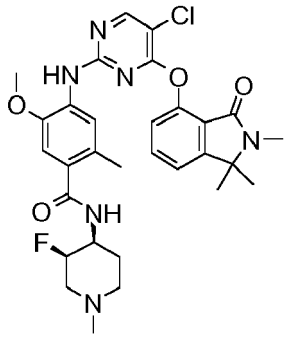
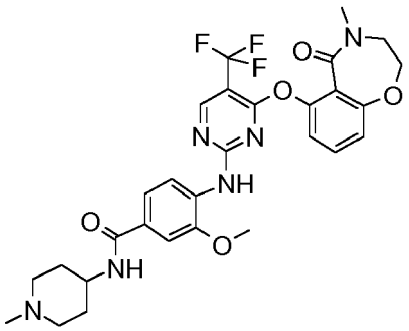
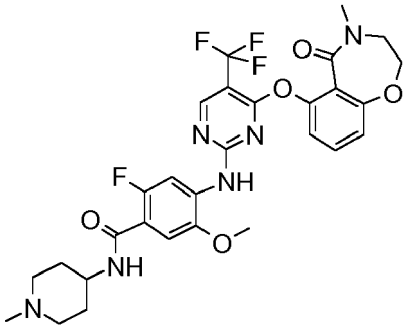
172	 Chiral
173	
174	
175	

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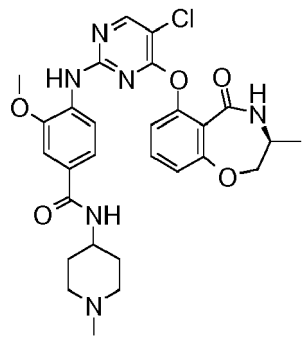
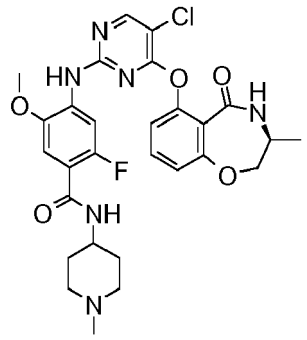
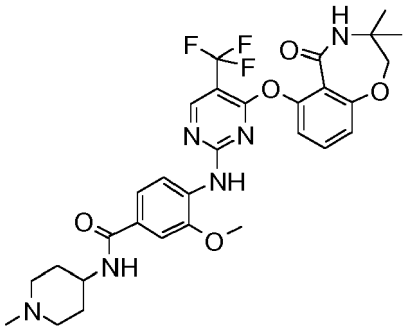
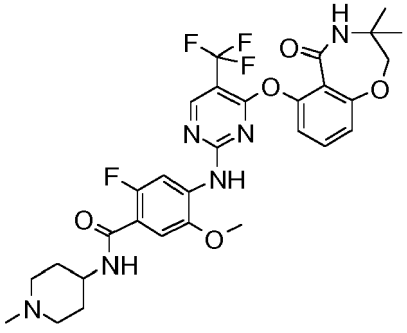
176	
177	
178	
179	

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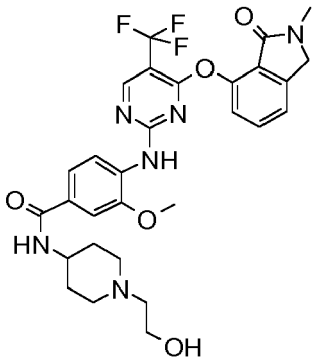
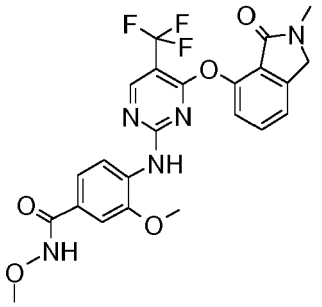
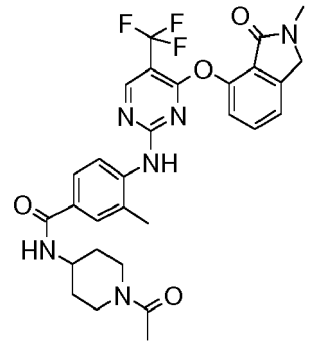
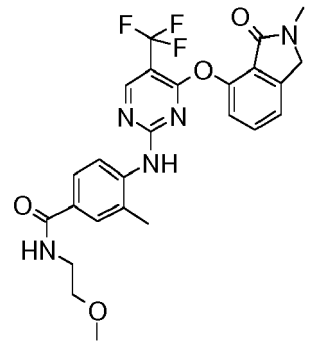
180	
181	
182	
183	

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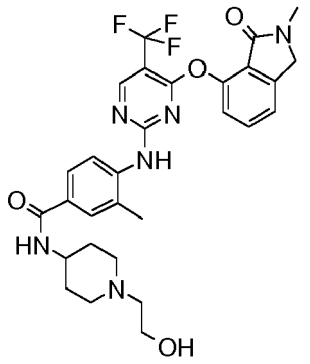
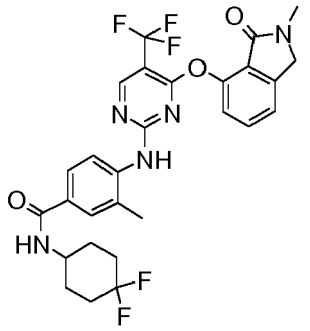
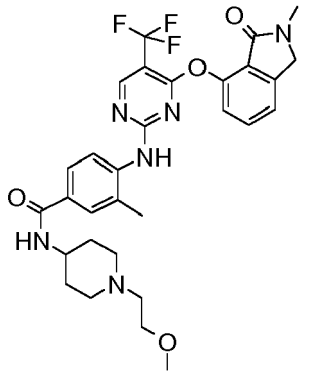
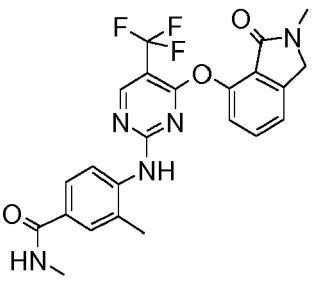
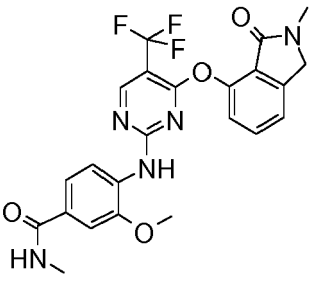
184	
185	
186	
187	
188	

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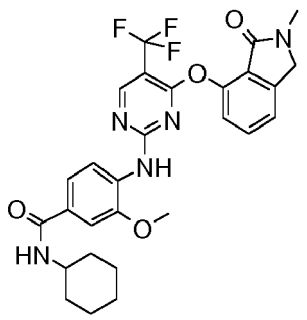
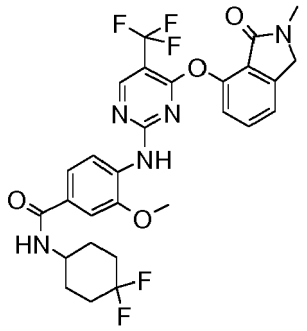
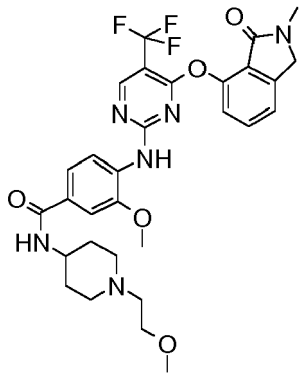
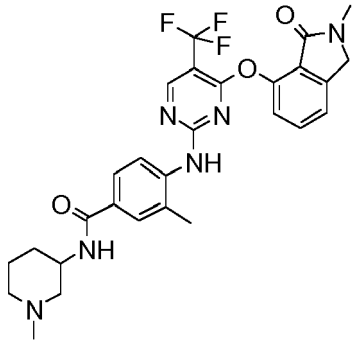
189	
190	
191	
192	

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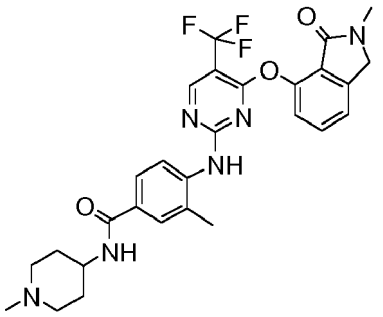
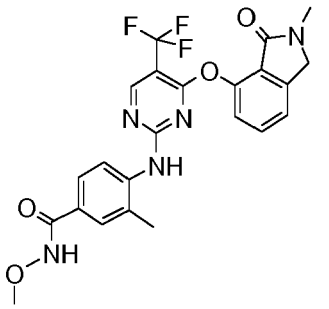
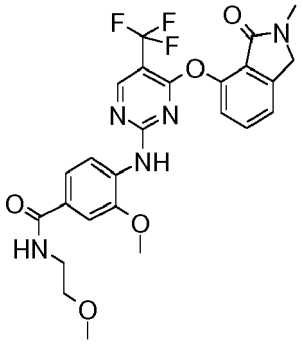
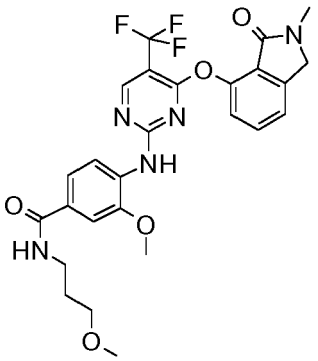
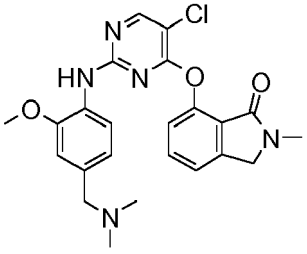
193	
194	
195	
196	
197	

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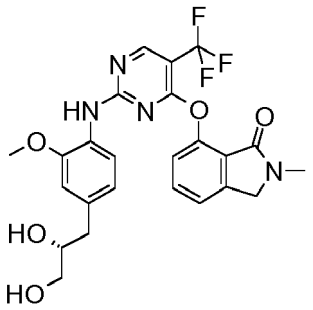
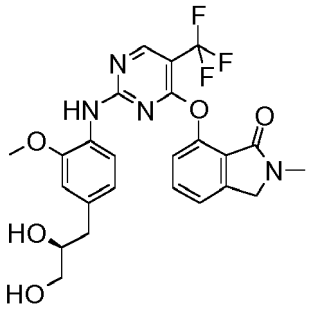
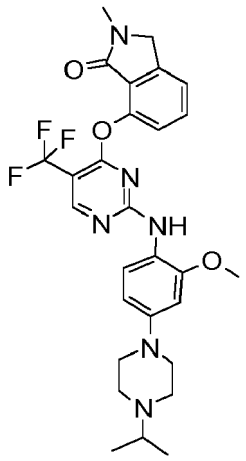
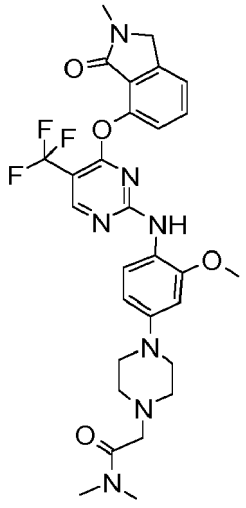
198	
199	
200	
201	

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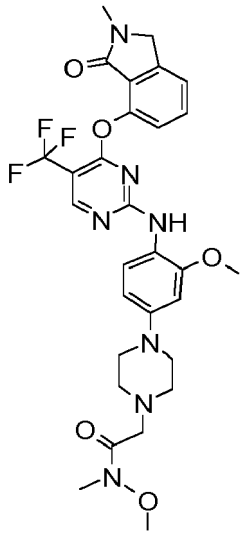
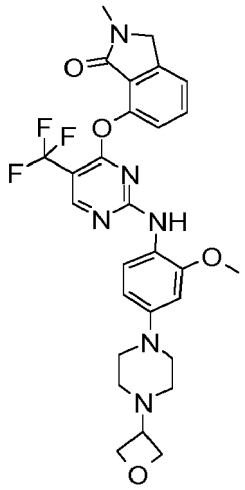
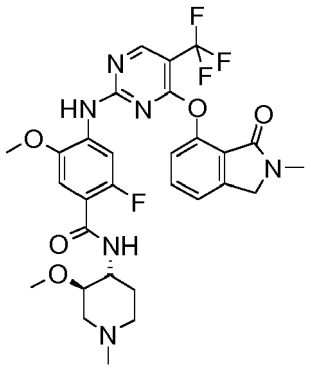
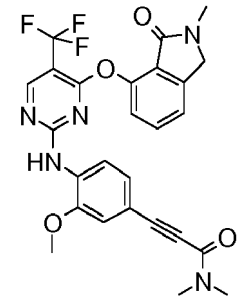
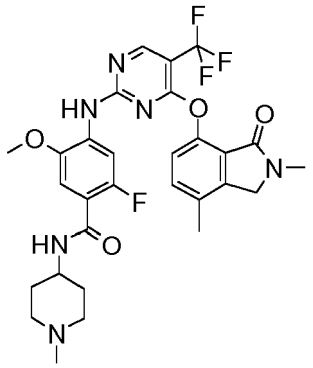
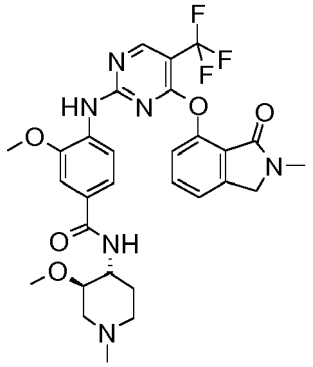
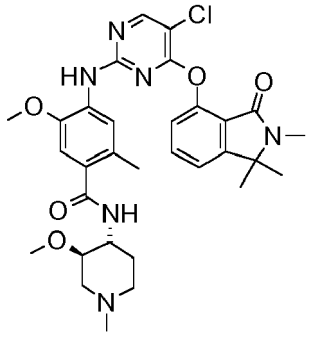
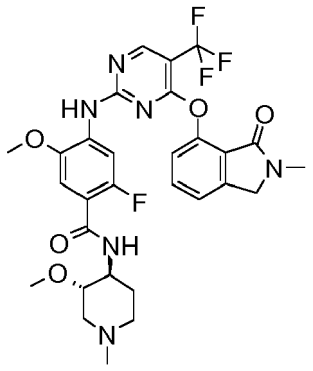
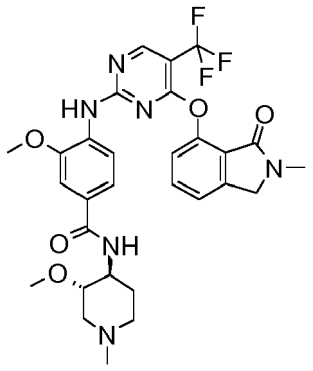
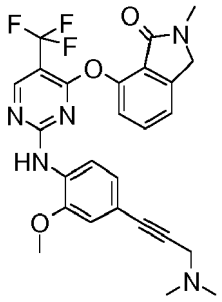
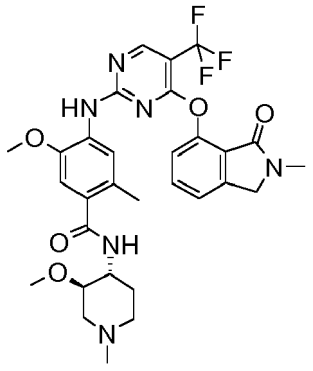
202	
203	
204	

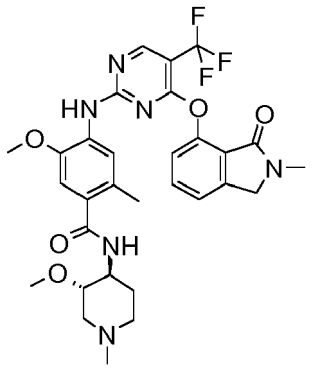
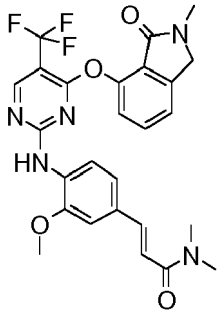
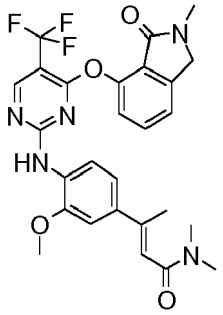
(suite)

205	
206	
207	
208	

(suite)

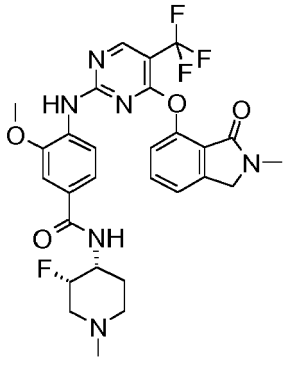
209	
210	
211	
212	

(suite)

213	
214	
215	

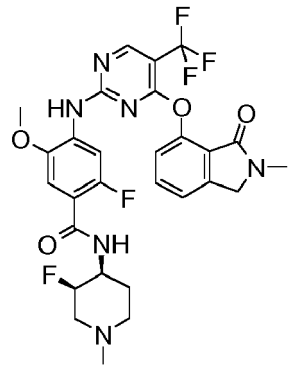
ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

8. Composé selon la revendication 7 répondant à la formule

64	

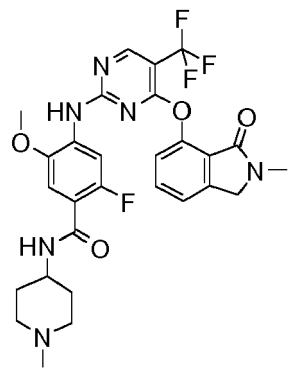
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

9. Composé selon la revendication 7 répondant à la formule

65	

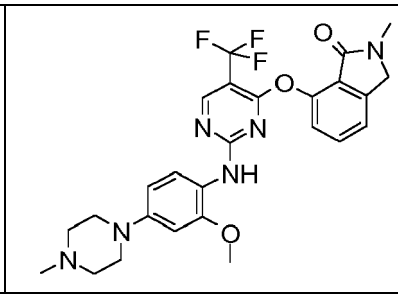
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

10. Composé selon la revendication 7 répondant à la formule

69	

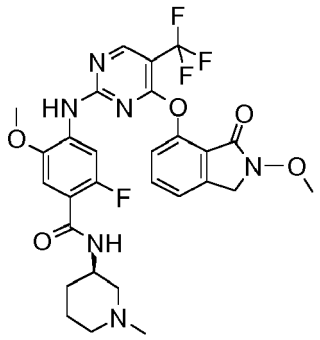
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

11. Composé selon la revendication 7 répondant à la formule

101	

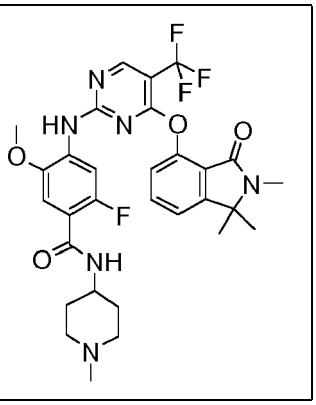
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

12. Composé selon la revendication 7 répondant à la formule

116	

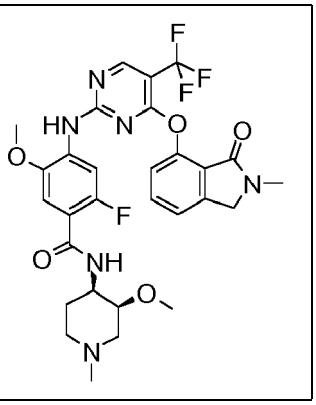
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

13. Composé selon la revendication 7 répondant à la formule

118	

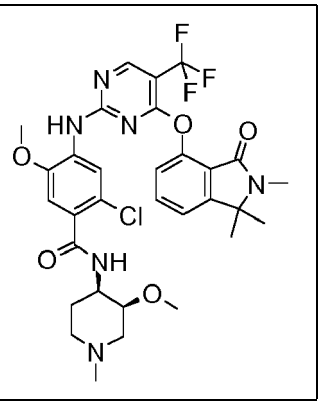
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

14. Composé selon la revendication 7 répondant à la formule

119	

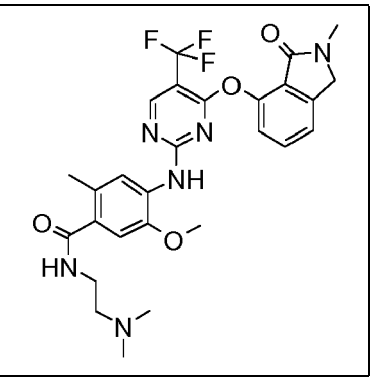
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

15. Composé selon la revendication 7 répondant à la formule

121	

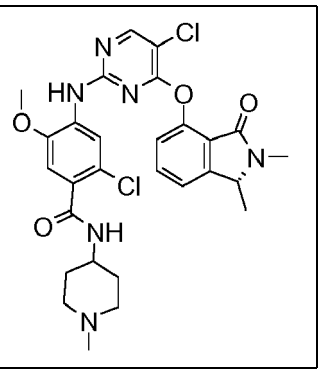
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

16. Composé selon la revendication 7 répondant à la formule

139	

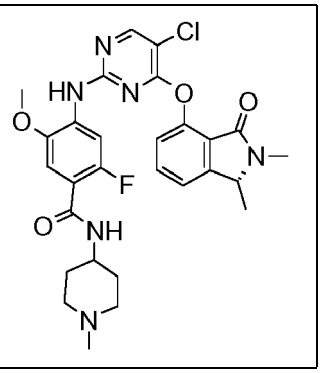
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

17. Composé selon la revendication 7 répondant à la formule

146	

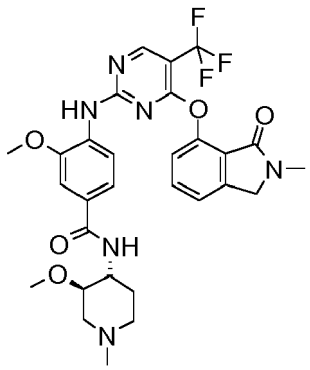
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

18. Composé selon la revendication 7 répondant à la formule

148	

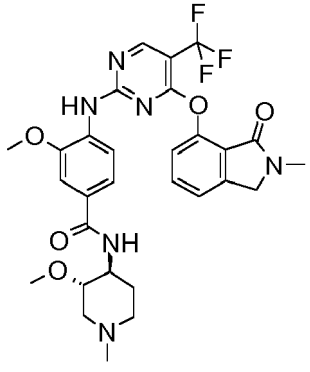
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

19. Composé selon la revendication 7 répondant à la formule

207	

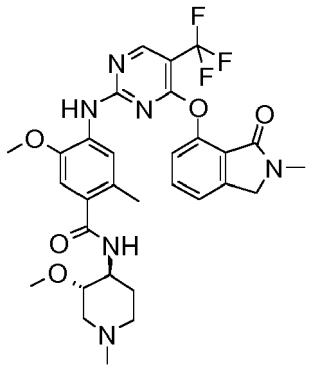
- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

20. Composé selon la revendication 7 répondant à la formule

210	

- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

21. Composé selon la revendication 7 répondant à la formule

213	

- ou un sel d'addition d'acide pharmacologiquement acceptable de celui-ci.

22. Composé - ou les sels pharmaceutiquement efficaces de celui-ci - selon l'une quelconque des revendications 1 à 21 pour une utilisation en tant que médicament.

23. Composé - ou les sels pharmaceutiquement efficaces de celui-ci - selon l'une quelconque des revendications 1 à 21 pour la préparation d'un médicament ayant une activité antiprolifératives et/ou pro-apoptotique.

24. Préparation pharmaceutique, contenant en tant que substance active un ou plusieurs composés de formules générales (Ia), (1b), (1c) ou (1d) selon l'une des revendications 1 à 21 ou les sels physiologiquement acceptables de ceux-ci, éventuellement en association avec des excipients et/ou vecteurs conventionnels.

25. Utilisation d'un composé de formule générale (Ia), (1b), (1c) ou (1d) selon l'une des revendications 1 à 21 pour la préparation d'une composition pharmaceutique pour le traitement et/ou la prévention du cancer, d'infections, d'inflammations et de maladies auto-immunes.

26. Préparation pharmaceutique comprenant un composé de formule générale (Ia), (1b), (1c) ou (1d) selon l'une des revendications 1 à 21 et au moins une autre substance active cytostatique ou cytotoxique différente de la formule (Ia), (1b), (1c) ou (1d), éventuellement sous la forme des tautomères, des racémates, des énantiomères, des diastéréomères et des mélanges de ceux-ci, ou des sels d'addition d'acide pharmacologiquement acceptables de ceux-ci.

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

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- US 2008255172 A **[0003]**
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Non-patent literature cited in the description

- *J. Med. Chem.,* 1999, vol. 42 (12), 2087-2104 **[0076]**