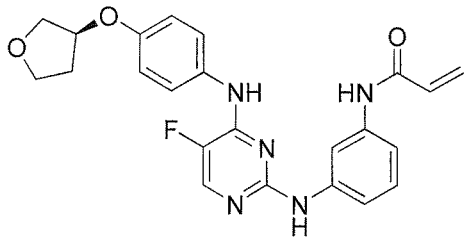
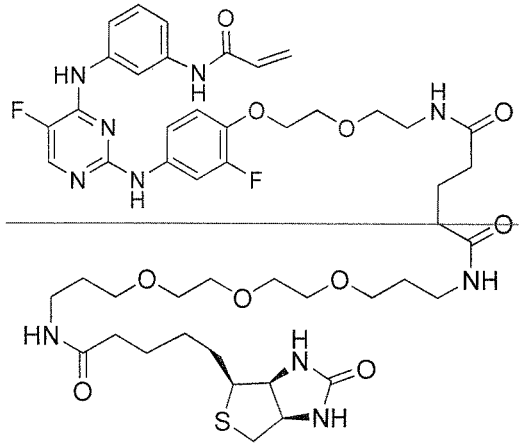
CLAIMS

We claim:

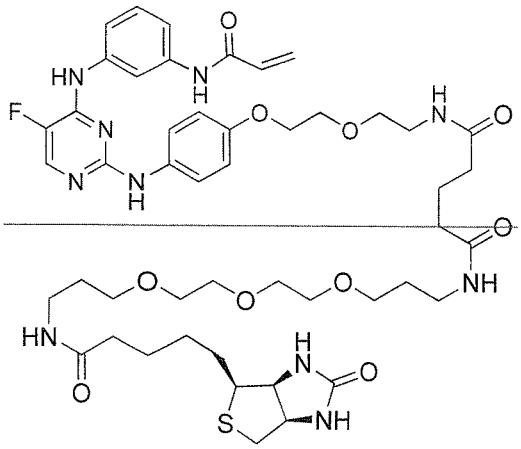
1. A compound selected from the group consisting of:



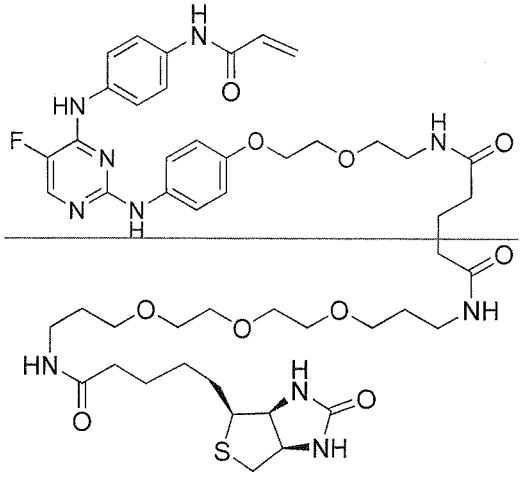
I-338



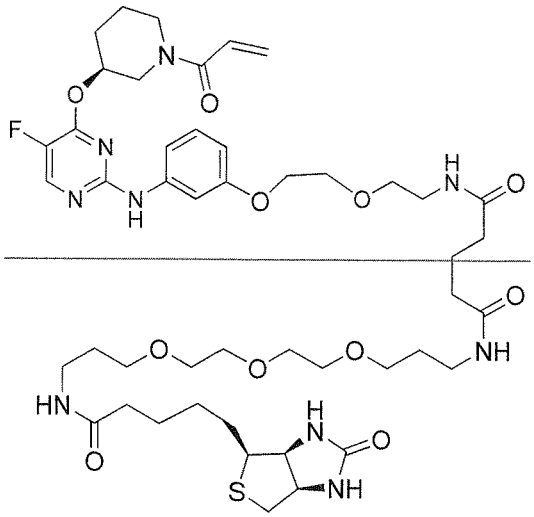
~~I-362~~



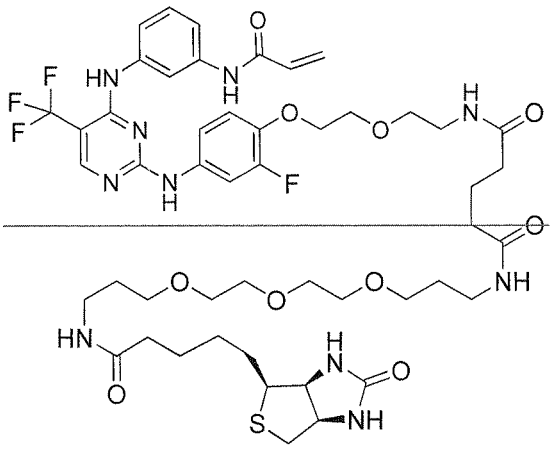
~~I-363~~

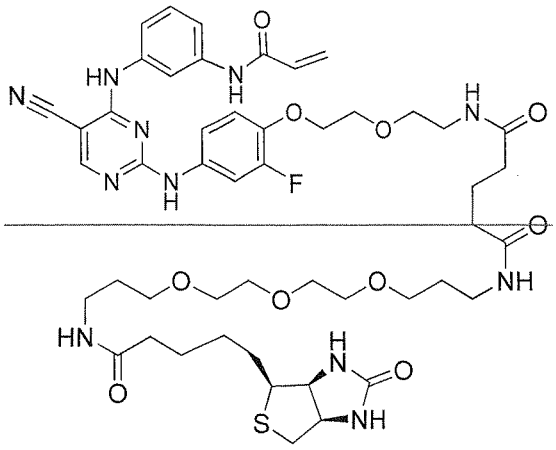


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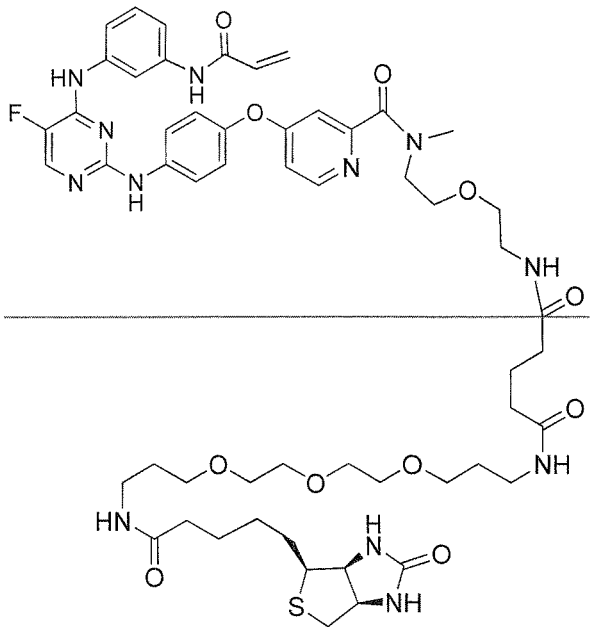


~~I-365~~

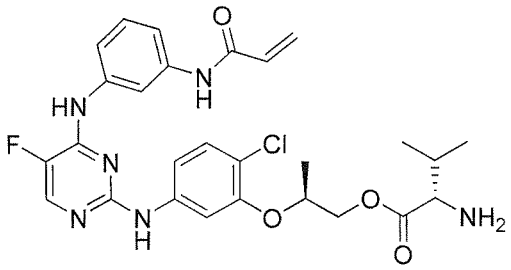




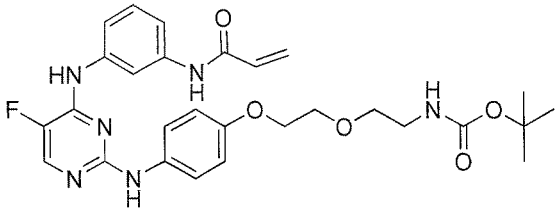
~~I-366~~ ~~I-367~~



~~I-368~~



I-369



I-370

2. A composition comprising a compound according to claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

3. The composition according to claim 2, in combination with an additional therapeutic agent.

4. The composition according to claim 3, wherein the additional therapeutic agent is a chemotherapeutic agent.

5. Use of a compound according to claim 1 in the manufacture of a medicament for inhibiting BTK, or a mutant thereof, in a biological sample~~activity~~, wherein said medicament is to be ~~administered to a patient or~~ contacted with ~~a~~ said biological sample.

6. The use according to claim 5, wherein the activity of BTK, or a mutant thereof, ~~activity~~ is inhibited irreversibly.

7. The use according to claim 6, wherein the activity of BTK, or a mutant thereof, ~~activity~~ is inhibited irreversibly by covalently modifying Cys 481 of BTK.

8. Use of a compound according to claim 1 in the manufacture of a medicament for treating a BTK-mediated disorder.

9. The use according to claim 8, wherein the disorder is an autoimmune disease, a heteroimmune disease, an inflammatory disease, a cancer, a disease of the bone and joints, or a thromboembolic disorder.

10. The use according to claim 9, wherein the disorder is selected from rheumatoid arthritis, multiple sclerosis, diabetes, B-cell chronic lymphocytic leukemia, acute lymphocytic leukemia, hairy cell leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, colorectal cancer, pancreatic cancer, bone cancer, bone metastasis, osteoporosis, diabetes, irritable bowel syndrome, Crohn's disease, systemic lupus erythematosis, or disorders associated with renal transplant.

~~leukemia, hairy cell leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, colorectal cancer, pancreatic cancer, bone cancer, bone metastasis, osteoporosis, diabetes, irritable bowel syndrome, Crohn's disease, systemic lupus erythematosis, or disorders associated with renal transplant.~~

11. Use of a compound according to claim 1 in the manufacture of a medicament for inhibiting one or more TEC- kinases, or a mutant thereof, in a biological sample~~activity~~, wherein said medicament is to be ~~administered to a patient or~~ contacted with ~~a~~ said biological sample.

12. The use according to claim 11, wherein the activity of the TEC-kinase, or a mutant thereof, ~~activity~~ is inhibited irreversibly.

13. The use according to claim 12 wherein the TEC-kinase is selected from one or more of TEC, ITK or BMX.

14. The use according to claim 13, where the one or more of TEC, ITK or BMX activity is inhibited irreversibly by ~~eolvalently~~ covalently modifying Cys 449 of TEC, Cys 442 of ITK or Cys 496 of BMX.

15. Use of a compound according to claim 1 in the manufacture of a medicament for treating a TEC-kinase-mediated disorder.

16. The use according to claim 15, wherein the disorder is an autoimmune disorder, an inflammatory disorder, a proliferative disorder, a hyperproliferative disease, an immunological-mediated diseases, a disease of the respiratory tract, a disease of the bone and joints, a skin disorder, a gastrointestinal disorder, a systemic disease, or allograft rejection.

17. Use of a compound according to claim 1 in the manufacture of a medicament for inhibiting one or more of ErbB1, ErbB2, ErbB3, ErbB4, or a mutant thereof, in a biological sample, wherein said medicament is to be contacted with said biological sample.

18. The use according to claim 17, wherein the activity of the one or more of ErbB1, ErbB2, or ErbB4, or a mutant thereof, is inhibited irreversibly.

~~compound according to claim 1 in the manufacture of a medicament for inhibiting one or more of ErbB1, ErbB2, ErbB3, ErbB4, or a mutant thereof, activity, wherein said medicament is to be administered to a patient or contacted with a biological sample.~~

~~18. The use according to claim 17, wherein the one or more of ErbB1, ErbB2, or ErbB4, or a mutant thereof, activity is inhibited irreversibly.~~

19. The use according to claim 18, wherein the activity of the one or more of ErbB1, ErbB2, or ErbB4~~, or a mutant thereof, activity~~ is inhibited irreversibly by covalently modifying Cys797 of ErbB1, Cys805 of ErbB2 or Cys803 of ErbB4.

20. Use of a compound according to claim 1 in the manufacture of a medicament for treating an ErB1-, ErbB2-, ErbB3-, or ErbB4-mediated disorder.

21. The use according to claim 20, wherein the disorder is a carcinoma selected from breast cancer, glioblastoma, lung cancer, cancer of the head and neck, colorectal cancer, bladder cancer, non-small cell lung cancer, squamous cell carcinoma, salivary gland carcinoma, ovarian carcinoma, colorectal cancer, or pancreatic cancer.

22. The use according to claim 21, wherein the disorder is selected from neurofibromatosis type I (NF1), neurofibromatosis type II (NF2) Schwann cell neoplasms (e.g. MPNST's), or a Schwannoma.

23. Use of a compound according to claim 1 in the manufacture of a medicament for inhibiting JAK3, or a mutant thereof, ~~activity~~in a biological sample, wherein said medicament is to be ~~administered to a patient or~~ contacted with ~~a~~ said biological sample.

24. The use according to claim 23, wherein the activity of JAK3, or a mutant thereof, ~~activity~~ is inhibited irreversibly.

25. The use according to claim 24, wherein the activity of JAK3, or a mutant thereof, ~~activity~~ is inhibited irreversibly by covalently modifying Cys 909 of JAK3.

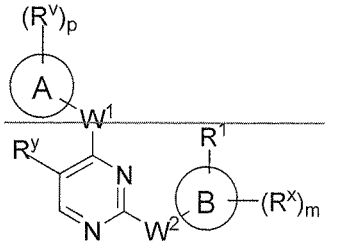
26. Use of a compound according to claim 1 in the manufacture of a medicament for treating a JAK3-mediated disorder in a patient.

~~26. A Use of a compound according to claim 1 in the manufacture of a medicament for treating a JAK3-mediated disorder in a patient.~~

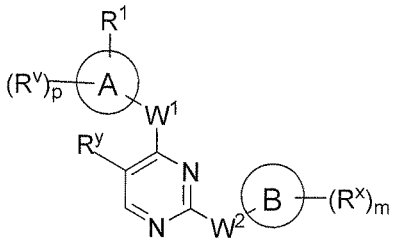
27. The use according to claim 26, wherein the disorder is selected from an autoimmune disorder, an inflammatory disorder, a neurodegenerative disorder, or a solid or hematologic malignancy.

28. The use according to claim 26, wherein the disorder is diabetes.

29. Use of a compound of formula ~~I-a or~~ **I-b** as shown below, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a BTK-mediated disorder,



~~I-a~~



I-b

wherein:

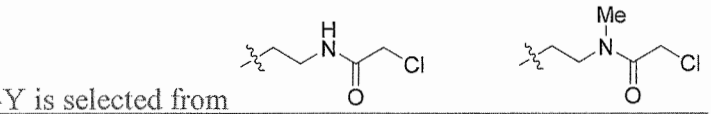
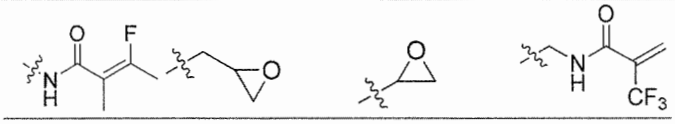
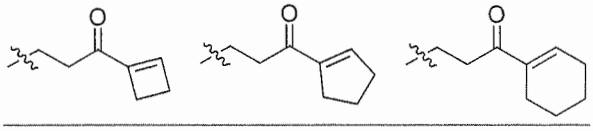
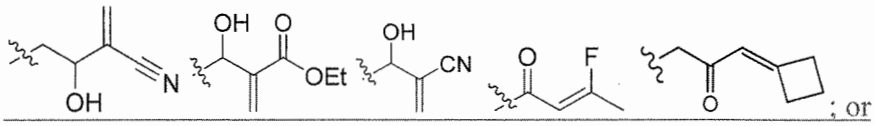
Ring A is ~~an optionally substituted group selected from~~ phenyl~~, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur~~;

Ring B is ~~an optionally substituted group selected from~~ phenyl~~, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from~~

~~nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or~~

~~sulfur, or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur~~;

R^1 is a warhead group -L-Y, wherein R^1 is attached to Ring A at the meta- or para- position relative to W^1;

-L-Y is selected from    ; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and one or two methylene units of L are optionally and independently replaced by -NRC(O)-, -C(O)NR-, -N(R)SO_2-, -SO_2N(R)-, –S-, -S(O)-, -SO_2-, -OC(O)-, -C(O)O-, cyclopropylene, –O-, -N(R)-, or -C(O)-; and Y is C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, a 3-10 membered monocyclic or bicyclic saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, -SO_2N(R)-, –S-, -S(O)-, -SO_2-, -OC(O)-, or –C(O)O-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -C(O)-, and one additional methylene unit of L is optionally replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -OC(O)-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one alkylidenyl double bond and at least one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO_2-, -SO_2N(R)-, -S-, -S(O)-, -SO_2-, -OC(O)-, or –C(O)O-, and one or two additional methylene units of L are optionally and independently replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-; or

L is -NRC(O)CH=$CHCH_2N(CH_3)$- or -NRC(O)CH=$CHCH_2O$-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one triple bond and one or two methylene units of L are optionally and independently replaced by –C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO_2-,–S-, -S(O)-, -SO_2-, -OC(O)-, or -C(O)O-; and

Y is hydrogen, C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein one methylene unit of L is replaced by cyclopropylene and one or two additional methylene units of L are independently replaced by –C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO_2-, -SO_2N(R)-, –S-, -S(O)-, -SO_2-, -OC(O)-, or -C(O)O-; and

Y is C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

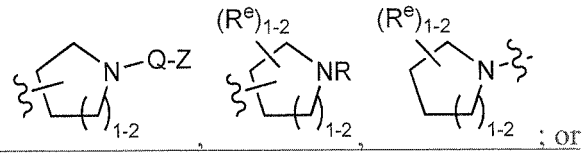
L is a covalent bond and Y is selected from:

(*ii*) C_{2-6} alkenyl substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

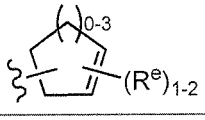
(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

(*vi*)  ; or

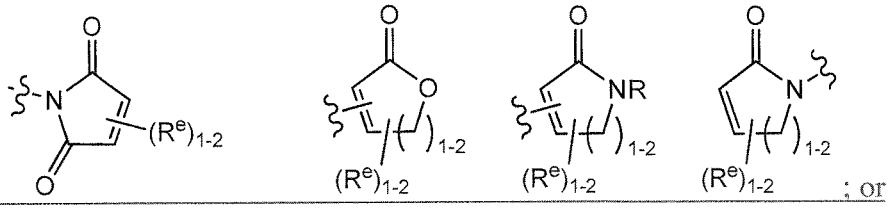
(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

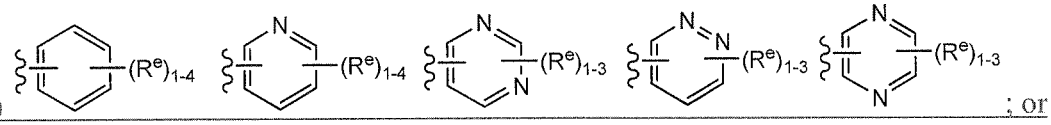
(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

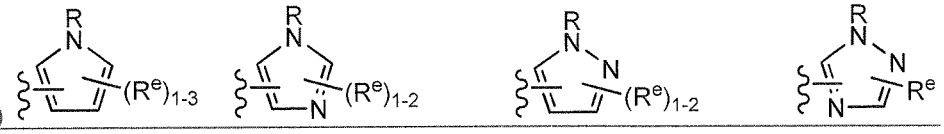
(*x*)  ; or

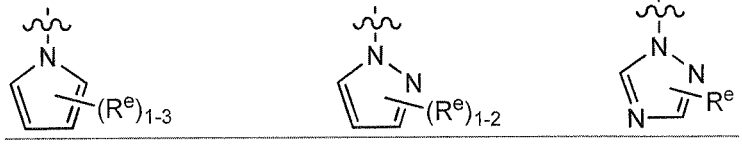
(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

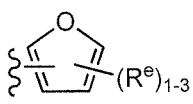
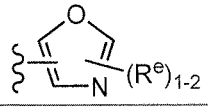
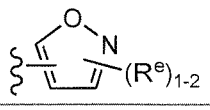
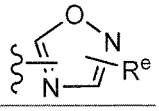
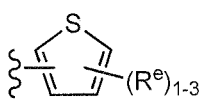
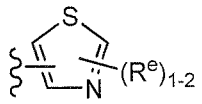
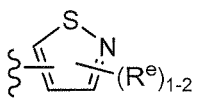
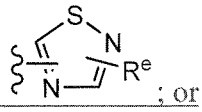
(*xii*)  ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xvi*) 



; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

L is –C(O)- and Y is selected from:

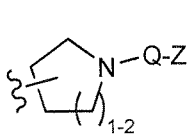
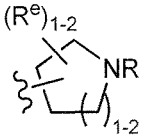
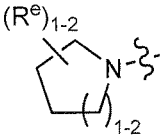
(*i*) C_{1-6} alkyl substituted with oxo, halogen, NO_2, or CN; or

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

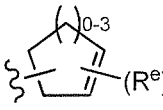
(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

(*vi*) , , ; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

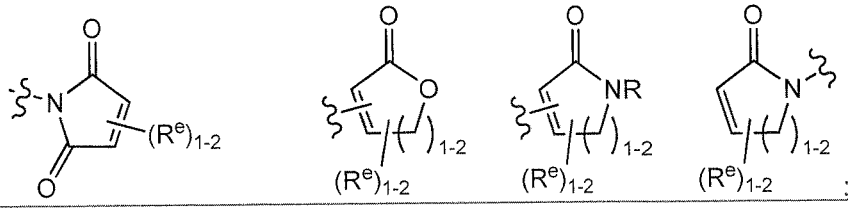
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

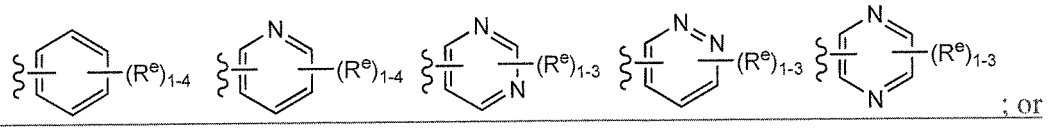
(*x*) ; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is

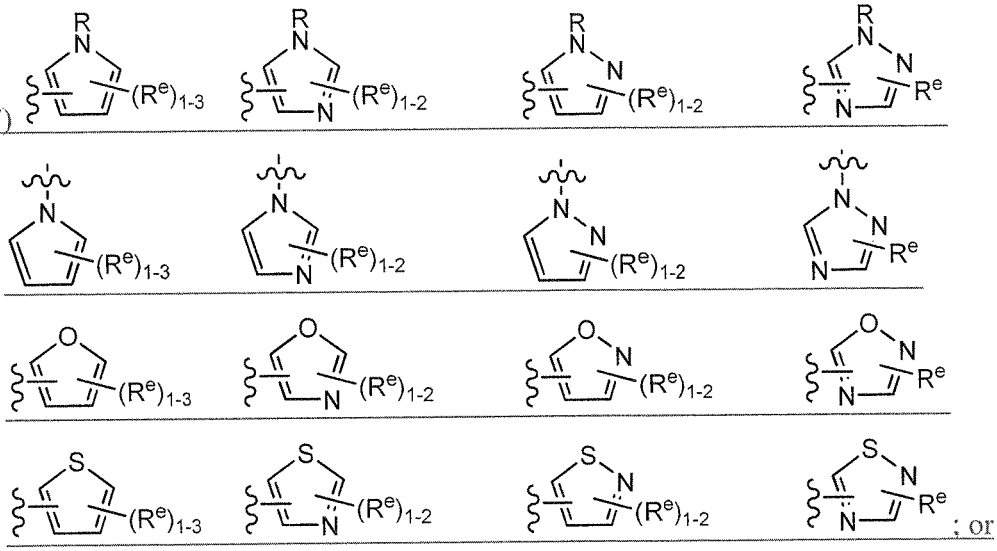
substituted with 1-4 R^e groups; or

(*xii*)  ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*)  ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

L is –N(R)C(O)- and Y is selected from:

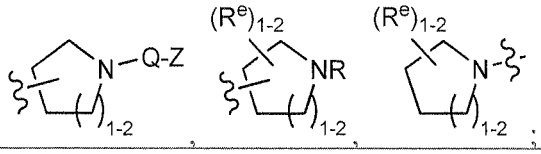
(*i*) C_{1-6} alkyl substituted with oxo, halogen, NO_2, or CN; or

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

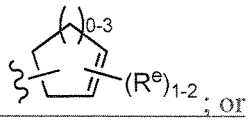
(*vi*) 

; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

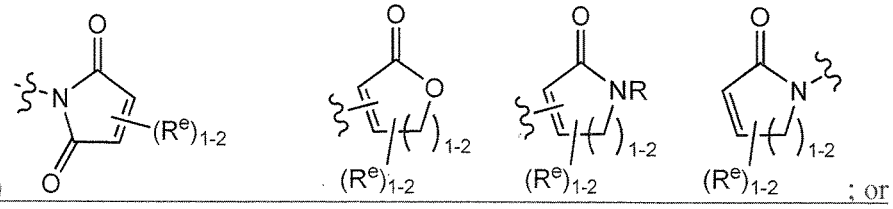
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*) 

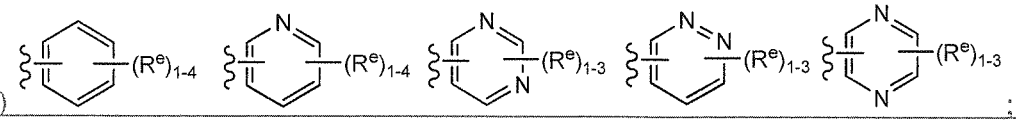
; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*) 

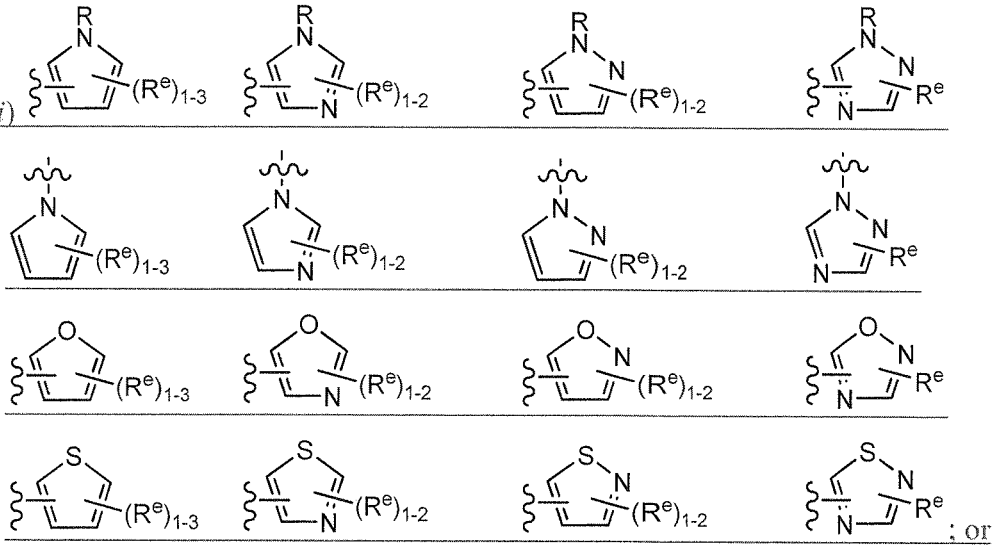
; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*) 

; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*) 

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

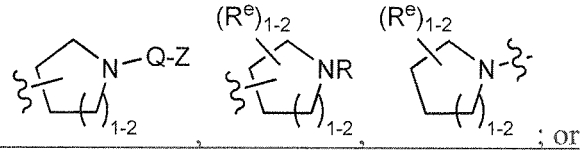
L is a bivalent C_{1-8} saturated or unsaturated, straight or branched, hydrocarbon chain; and Y is selected from:

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

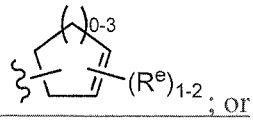
(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

(*vi*) 

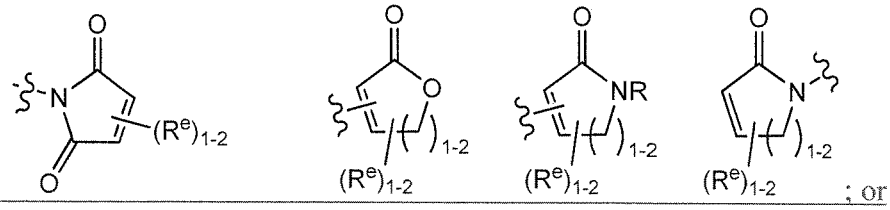
(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

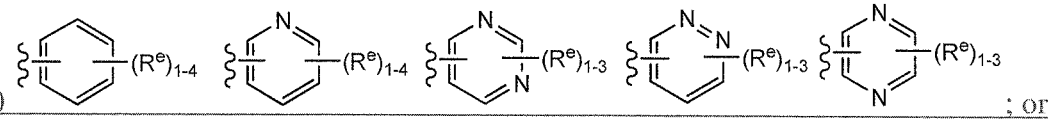
(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*) ; or

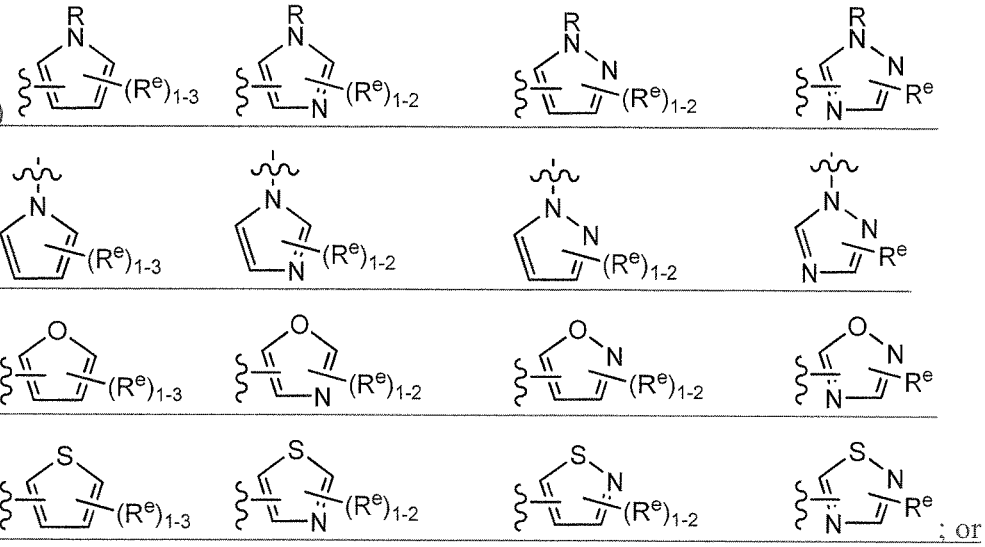
(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*) ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*) ; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*) ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

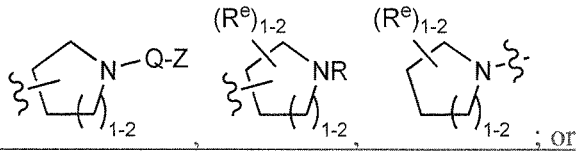
L is $-CH_2-$, -NH-, -C(O)-, $-CH_2NH-$, $-NHCH_2-$, $-NHC(O)-$, $-NHC(O)CH_2OC(O)-$, $-CH_2NHC(O)-$, $-NHSO_2CH_2-$, or $-SO_2NH-$; and Y is selected from:

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

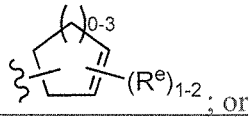
(*vi*) 

; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

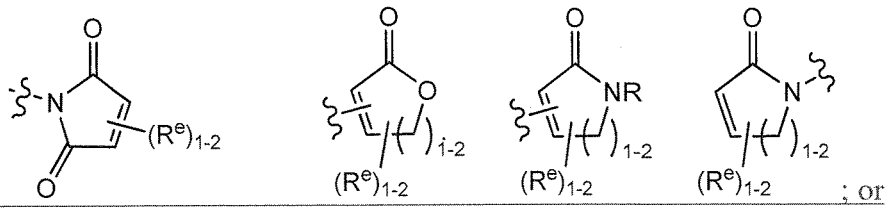
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

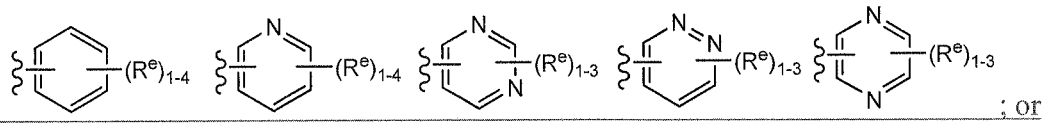
(*x*) 

; or

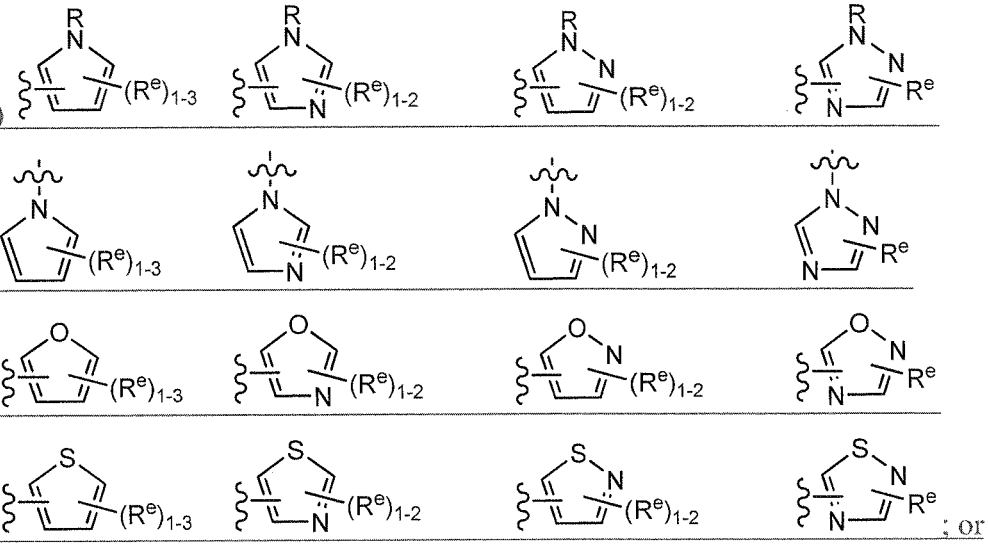
(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*)  ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*)  ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups;

each R^e is independently selected from –Q-Z, oxo, NO_2, halogen, CN, a suitable leaving group, or C_{1-6} aliphatic substituted with halogen, NO_2, or CN, wherein:

Q is a bivalent C_{2-6} unsaturated straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by –N(R)-, -S-, -O-, -C(O)-, -SO-, or -SO_2-, -N(R)C(O)-, -C(O)N(R)-; and

Z is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN;

R^y is ~~hydrogen,~~ halogen, -CN, $-CF_3$, C_{1-4} aliphatic, C_{1-4} haloaliphatic, -OR, -C(O)R, or $-C(O)N(R)_2$;

each R group is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered heterocylic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

W^1 and W^2 are each ~~independently a covalent bond or a bivalent C_{1-3} alkylene chain wherein one methylene unit of W^1 or W^2 is optionally replaced by~~ $-NR^2-$, ~~$-N(R^2)C(O)-$, $-C(O)N(R^2)-$, $-N(R^2)SO_2-$, $-SO_2N(R^2)-$, $-O-$, $-C(O)-$, $-OC(O)-$, $-C(O)O-$, $-S-$, $-SO-$ or $-SO_2-$~~;

R^2 is hydrogen, optionally substituted C_{1-6} aliphatic, or $-C(O)R$~~, or:~~

~~R^2 and a substituent on Ring A are taken together with their intervening atoms to form a 4-6 membered partially unsaturated or aromatic fused ring; or~~

~~R^2 and R^y are taken together with their intervening atoms to form a 4-6 membered saturated, partially unsaturated, or aromatic fused ring~~;

m and p are independently 0-4; and

each instance of Rx is independently selected from -R, halogen, –OR, or $-O(CH_2)_qOR$, wherein q is 1-4;

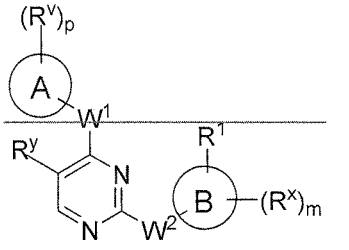
each instance of ~~R^x and~~ R^v ~~are~~ is independently selected from -R, halogen, –OR, $-O(CH_2)_qOR$, –CN, $-NO_2$, $-SO_2R$, $-SO_2N(R)_2$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, -NRC(O)N(R)$_2$, $-NRSO_2R$, or $-N(R)_2$, wherein q is 1-4; ~~or:~~

~~R^x and R^1 when concurrently present on Ring B are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with a warhead group and 0-3 groups independently selected from oxo, halogen, CN, or C_{1-6} aliphatic; or~~

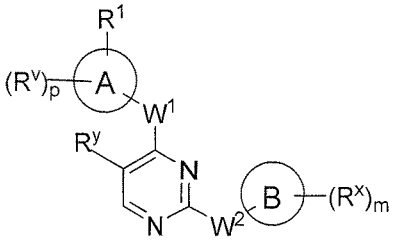
~~R^v and R^1 when concurrently present on Ring A are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with a warhead group and 0-3 groups independently selected from oxo, halogen, CN, or C_{1-6} aliphatic;~~

wherein the BTK-mediated disorder is pancreatic cancer.

30. Use of a compound of formula ~~I-a or~~ **I-b** as shown below, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a BTK-mediated disorder,



~~I-a~~



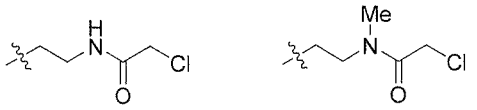
I-b

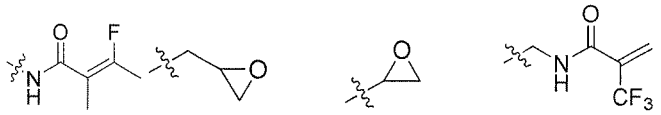
wherein:

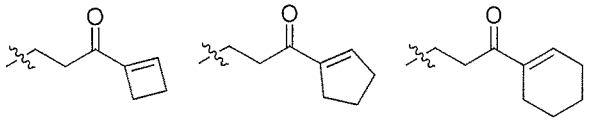
Ring A is ~~an optionally substituted group selected from~~ phenyl~~, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur~~;

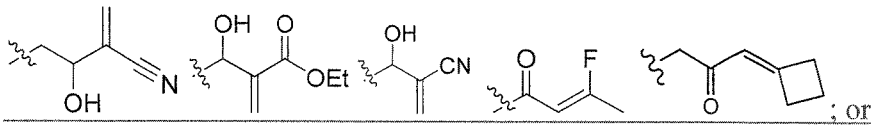
Ring B is ~~an optionally substituted group selected from~~ phenyl~~, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur~~;

R^1 is a warhead group -L-Y, wherein R^1 is attached to Ring A at the meta- or para- position relative to W^1;

-L-Y is selected from 







; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and one or two methylene units of L are optionally and independently replaced by -NRC(O)-, -C(O)NR-, $-N(R)SO_2-$, $-SO_2N(R)-$, –S-, -S(O)-, $-SO_2-$, -OC(O)-, -C(O)O-, cyclopropylene, –O-, -N(R)-, or -C(O)-; and Y is C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, a 3-10 membered monocyclic or bicyclic saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, $-SO_2N(R)-$, –S-, -S(O)-, $-SO_2-$, -OC(O)-, or –C(O)O-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -C(O)-, and one additional methylene unit of L is optionally replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -OC(O)-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one alkylidenyl double bond and at least one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, $-N(R)SO_2-$, $-SO_2N(R)-$, -S-, -S(O)-, $-SO_2-$, -OC(O)-, or –C(O)O-, and one or two additional methylene units of L are optionally and independently replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-; or

L is -NRC(O)CH=CHCH$_2$N(CH$_3$)- or -NRC(O)CH=CHCH$_2$O-; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one triple bond and one or two methylene units of L are optionally and independently replaced by –C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO$_2$-,–S-, -S(O)-, -SO$_2$-, -OC(O)-, or -C(O)O-; and

Y is hydrogen, C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein one methylene unit of L is replaced by cyclopropylene and one or two additional methylene units of L are independently replaced by –C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO$_2$-, -SO$_2$N(R)-, –S-, -S(O)-, -SO$_2$-, -OC(O)-, or -C(O)O-; and

Y is C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; or

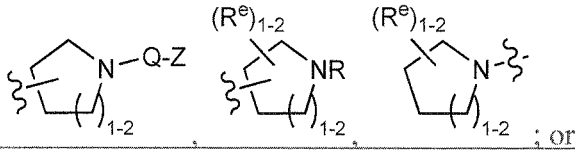
L is a covalent bond and Y is selected from:

(*ii*) C_{2-6} alkenyl substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

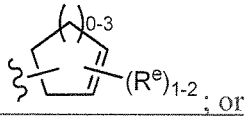
(*vi*) 

; or

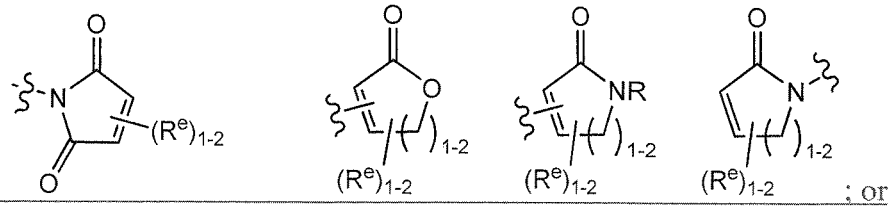
(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

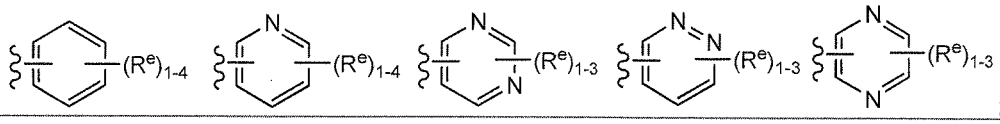
(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

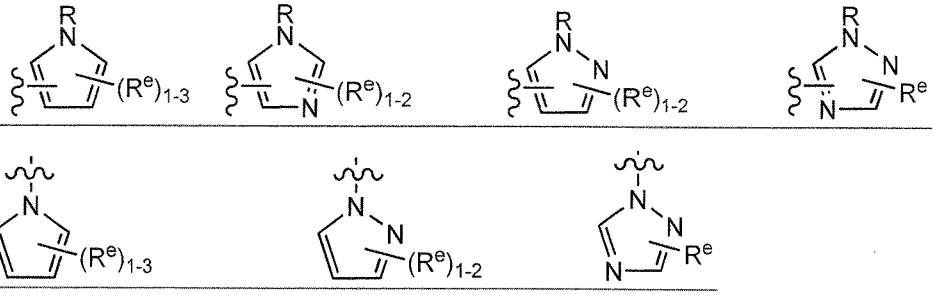
(*x*)  ; or

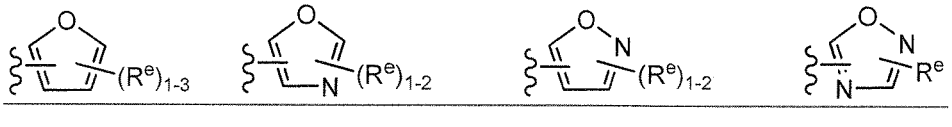
(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

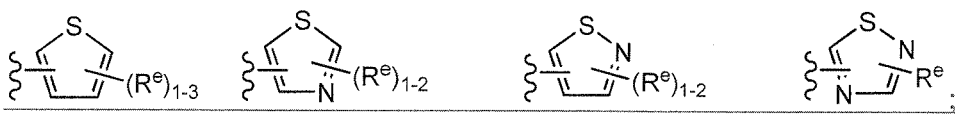
(*xii*)  ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xvi*) 



 ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

L is –C(O)- and Y is selected from:

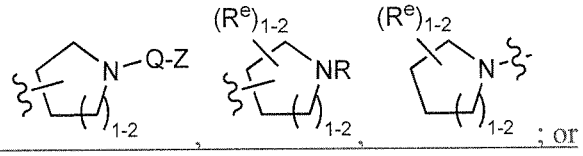
(*i*) C_{1-6} alkyl substituted with oxo, halogen, NO_2, or CN; or

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

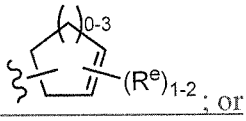
(*vi*) 

; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

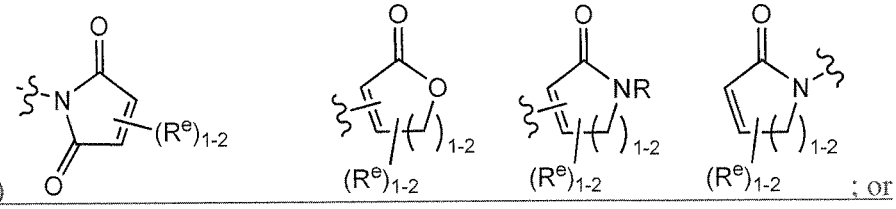
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*) 

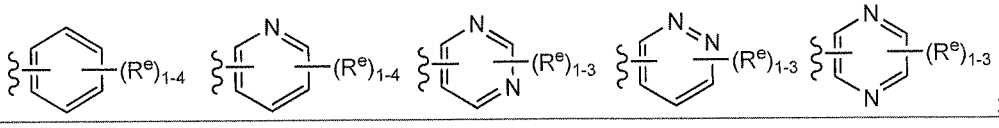
; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*) 

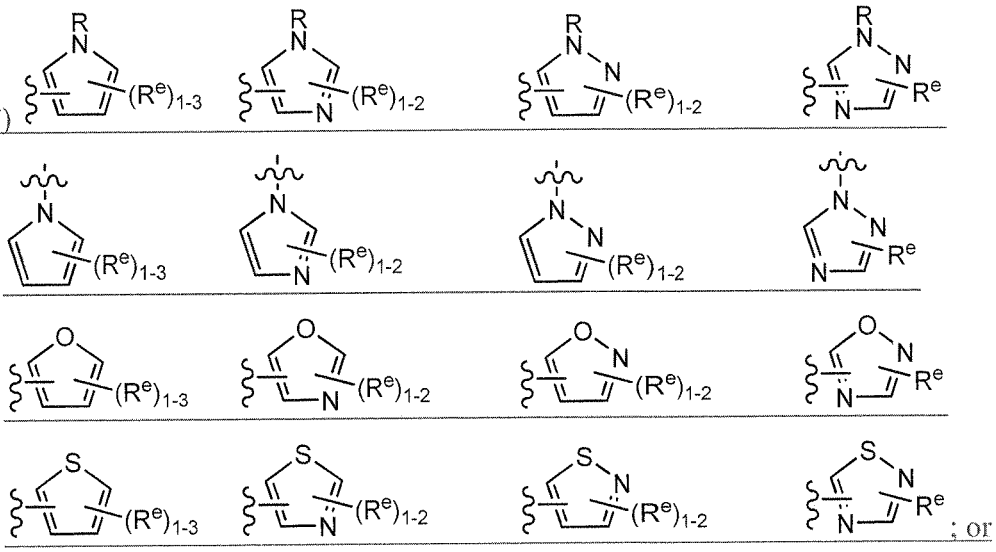
; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*) 

; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*) 

; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

L is –N(R)C(O)- and Y is selected from:

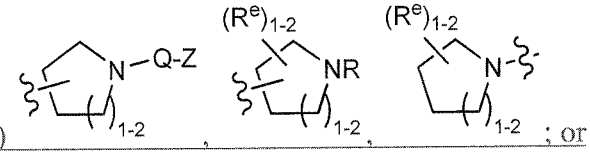
(*i*) C_{1-6} alkyl substituted with oxo, halogen, NO_2, or CN; or

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

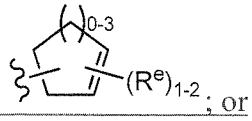
(*vi*) 

; or

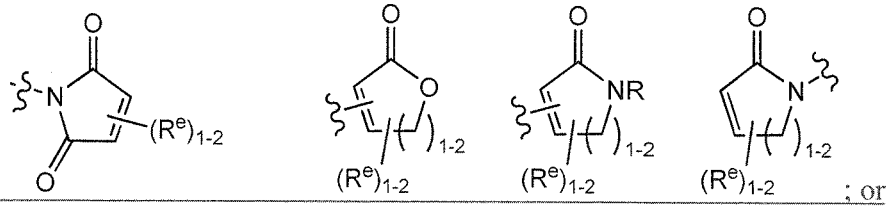
(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

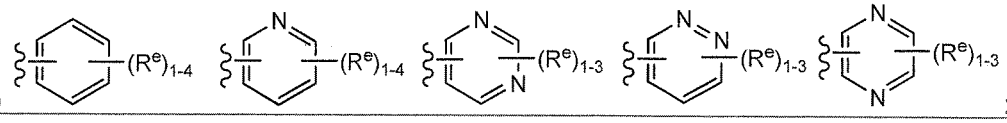
(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*)  ; or

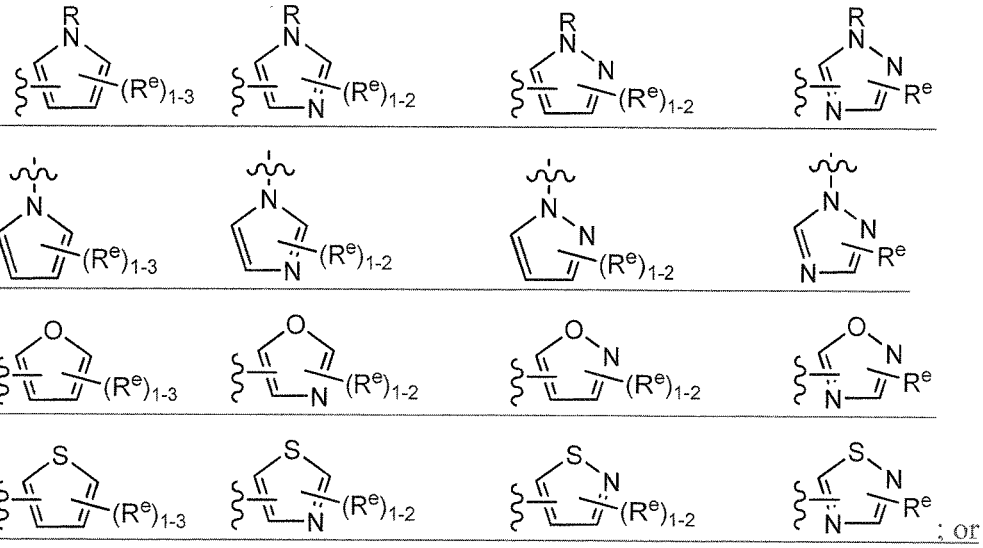
(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*)  ; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*)  ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

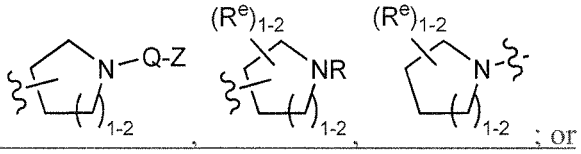
L is a bivalent C_{1-8} saturated or unsaturated, straight or branched, hydrocarbon chain; and Y is selected from:

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

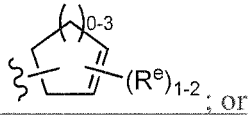
(*vi*) 

; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

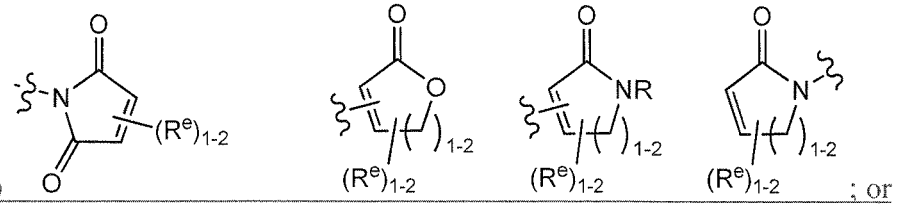
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*) 

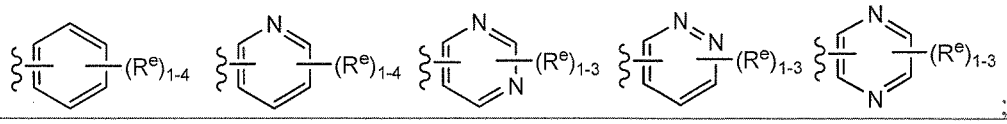
; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

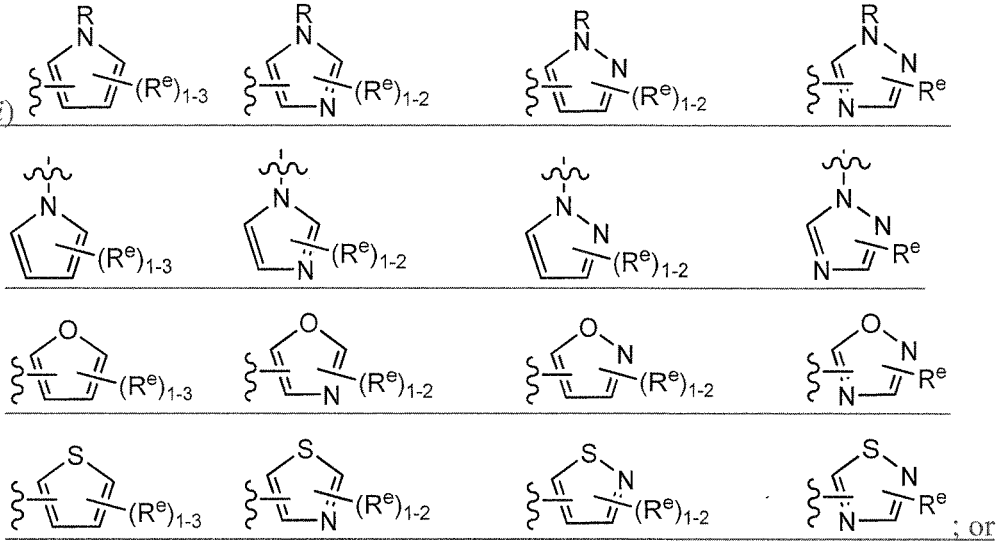
(*xii*) 

; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*)  ; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*)  ; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

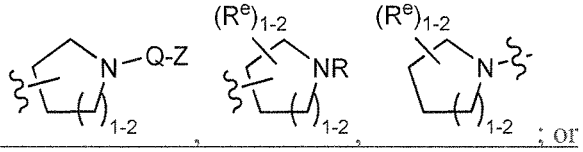
L is $-CH_2-$, -NH-, -C(O)-, $-CH_2NH-$, $-NHCH_2-$, –NHC(O)-, $-NHC(O)CH_2OC(O)-$, $-CH_2NHC(O)-$, $-NHSO_2CH_2-$, or $-SO_2NH-$; and Y is selected from:

(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

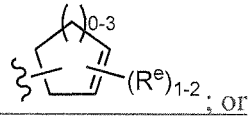
(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

(*vi*)  ; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

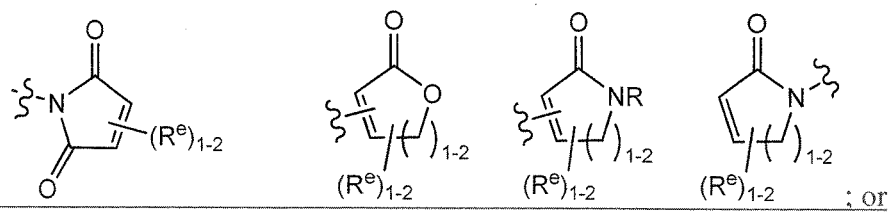
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

(*x*) 

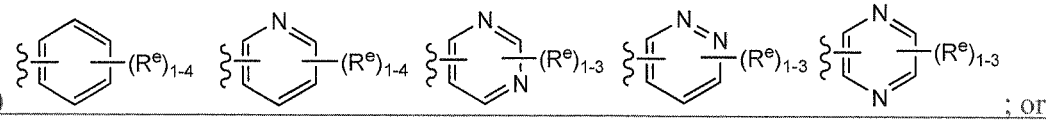
; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*) 

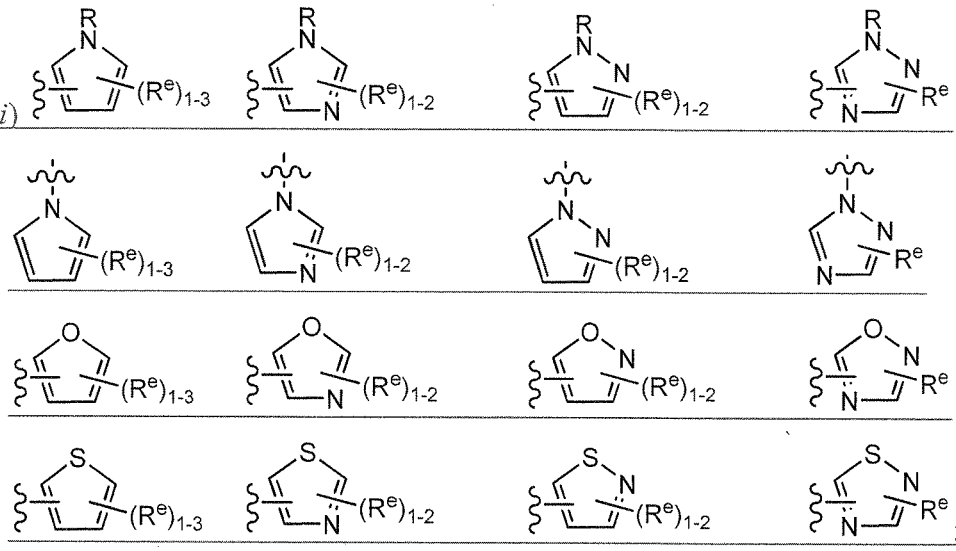
; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*) 

; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*) 

; or

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups;

each R^e is independently selected from –Q-Z, oxo, NO_2, halogen, CN, a suitable leaving group, or C_{1-6} aliphatic substituted with halogen, NO_2, or CN, wherein:

Q is a bivalent C_{2-6} unsaturated straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by –N(R)-, -S-, -O-, -C(O)-, -SO-, or -SO_2-, -N(R)C(O)-, -C(O)N(R)-; and

Z is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN;

R^y is ~~hydrogen,~~ halogen, -CN, $-CF_3$, C_{1-4} aliphatic, C_{1-4} haloaliphatic, -OR, -C(O)R, or $-C(O)N(R)_2$;

each R group is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered heterocylic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

W^1 and W^2 are each ~~independently a covalent bond or a bivalent C_{1-3} alkylene chain wherein one methylene unit of W^1 or W^2 is optionally replaced by $-NR^2-$, $-N(R^2)C(O)-$, $-C(O)N(R^2)-$, $-N(R^2)SO_2-$, $-SO_2N(R^2)-$, $-O-$, $-C(O)-$, $-OC(O)-$, $-C(O)O-$, $-S-$, $-SO-$ or $-SO_2-$~~;

R^2 is hydrogen, optionally substituted C_{1-6} aliphatic, or $-C(O)R$~~, or:~~

~~R^2 and a substituent on Ring A are taken together with their intervening atoms to form a 4-6 membered partially unsaturated or aromatic fused ring; or~~

~~R^2 and R^y are taken together with their intervening atoms to form a 4-6 membered saturated, partially unsaturated, or aromatic fused ring~~;

m and p are independently 0-4; and

each instance of Rx is independently selected from -R, halogen, –OR, or $-O(CH_2)_qOR$, wherein q is 1-4;

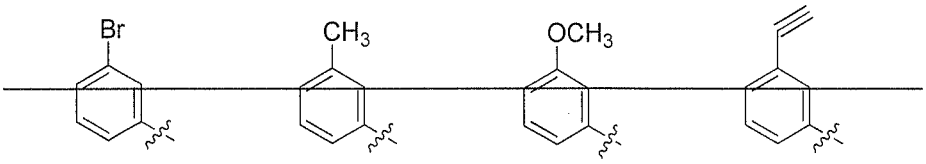
each instance of ~~R^x and~~ R^v ~~are~~ is independently selected from -R, halogen, –OR, $-O(CH_2)_qOR$, –CN, $-NO_2$, $-SO_2R$, $-SO_2N(R)_2$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $-N(R)_2$, wherein q is 1-4~~; or:~~

~~R^x and R^1 when concurrently present on Ring B are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with a warhead group and 0-3 groups independently selected from oxo, halogen, CN, or C_{1-6} aliphatic; or~~

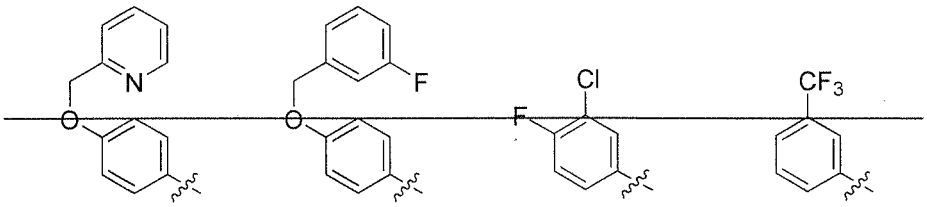
~~R^v and R^1 when concurrently present on Ring A are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with a warhead group and 0-3 groups independently selected from oxo, halogen, CN, or C_{1-6} aliphatic~~;

wherein the BTK-mediated disorder is colorectal cancer.

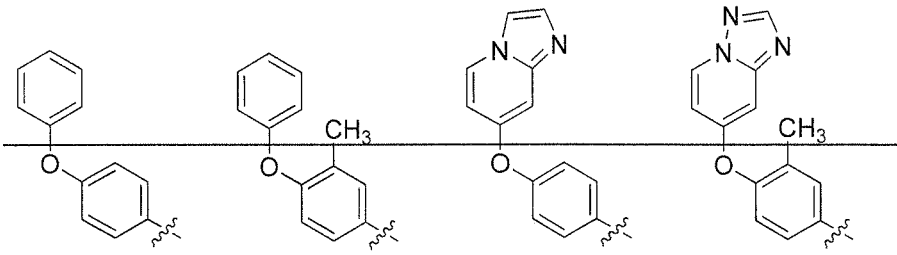
31. The use according to claim 29 or 30, wherein Ring A is selected from:



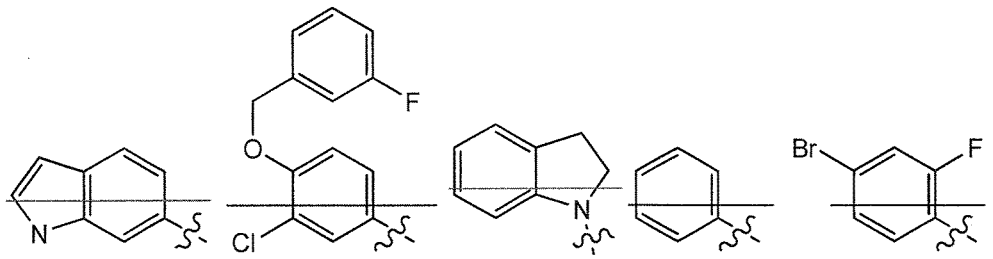
i *ii* *iii* *iv*



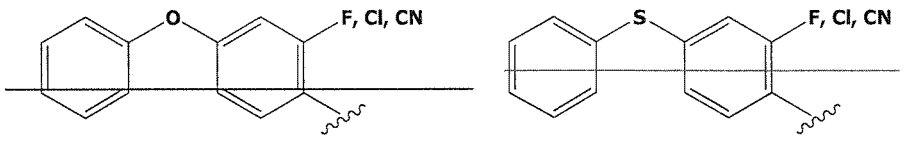
v *vi* *vii* *viii*



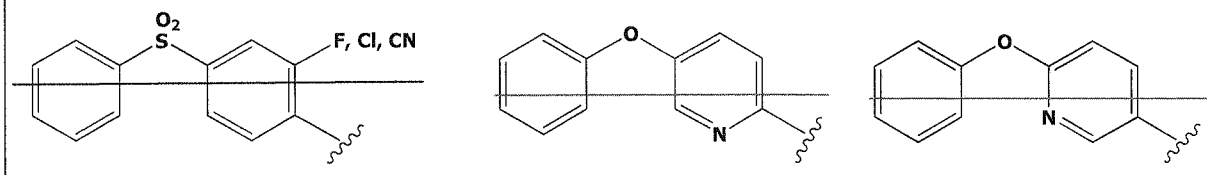
ix *x* *xi* *xii*



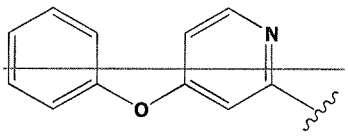
xiii *xiv* *xv* *xvi* *xvii*



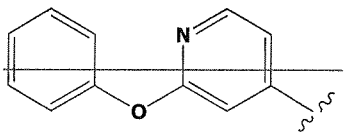
xviii *xix*



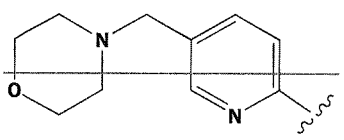
xx *xxi* *xxii*



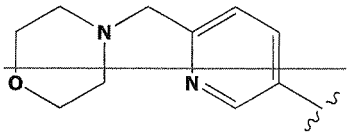
xxiii



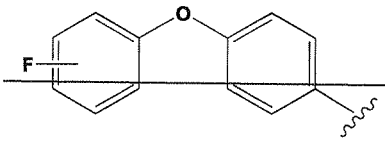
xxiv



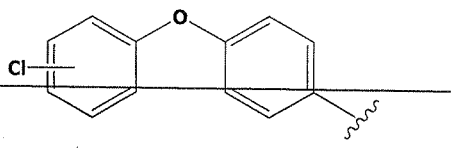
xxv



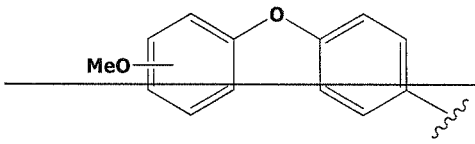
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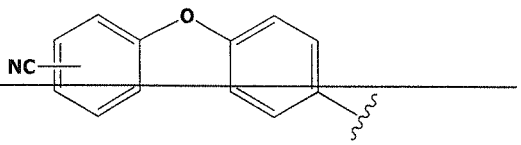
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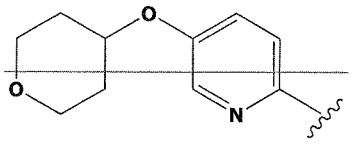
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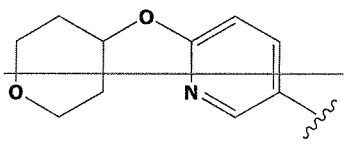
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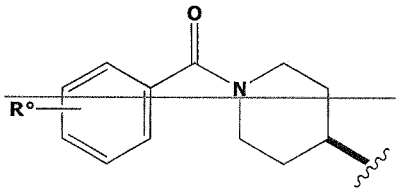
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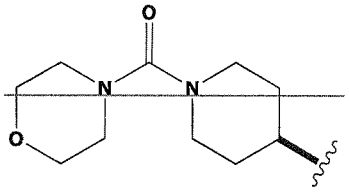
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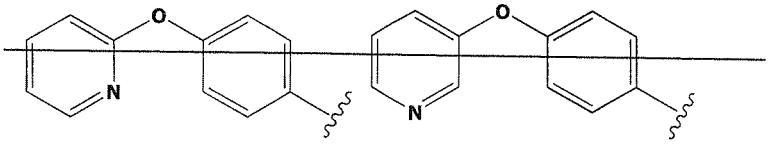
xxxii



xxxiii

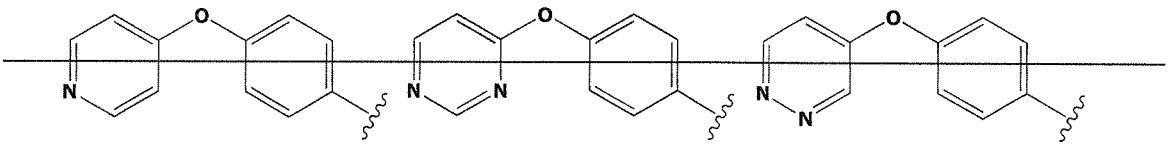


xxxiv



xxxv

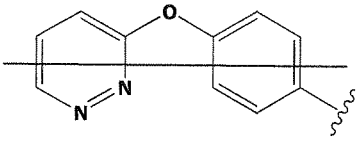
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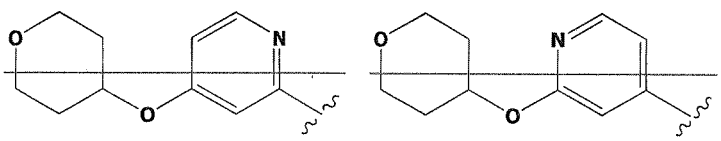
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xxxviii

xxxix

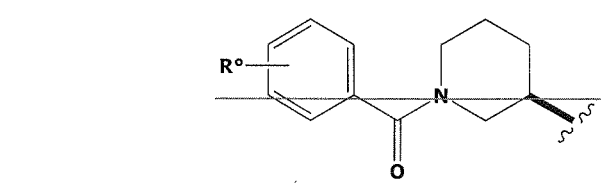


xl

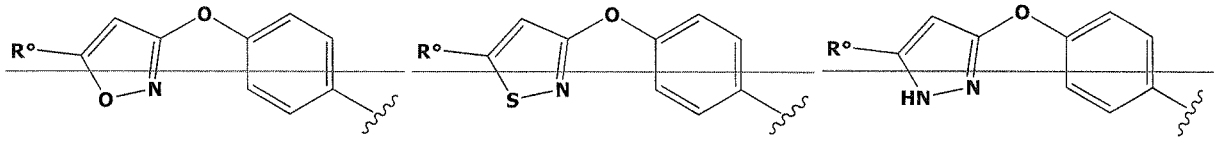


xli

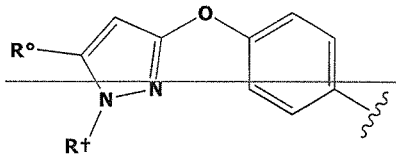
xlii



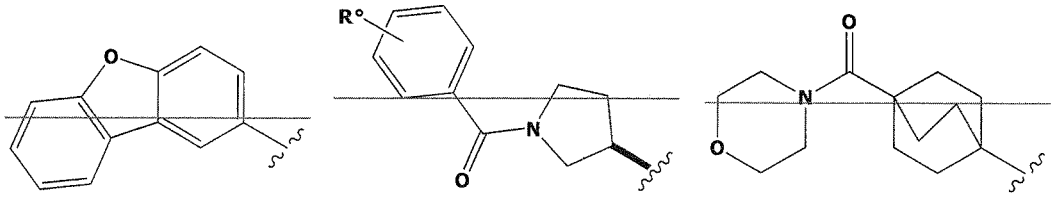
xliii *xliv*



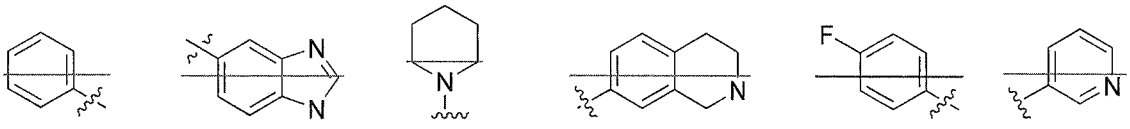
xlv *xlvi* *xlvii*



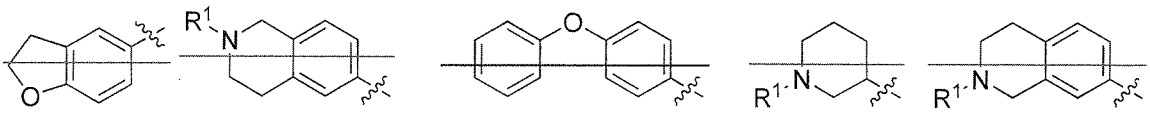
xlviii



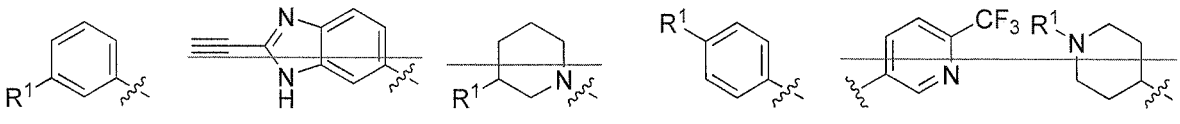
xlix *l* *li*



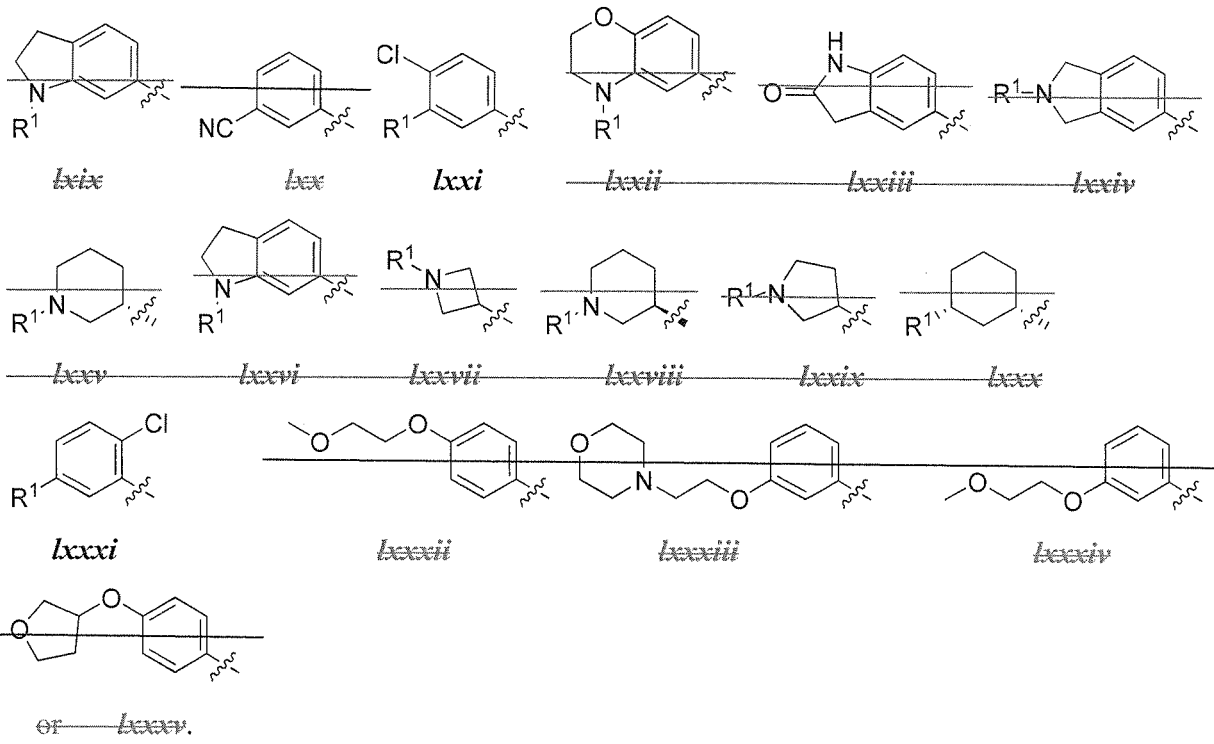
lii *liii* *liv* *lv* *lvi* *lvii*



lviii *lix* *lx* *lxi* *lxii*



lxiii *lxiv* *lxv* *lxvi* *lxvii* *lxviii*



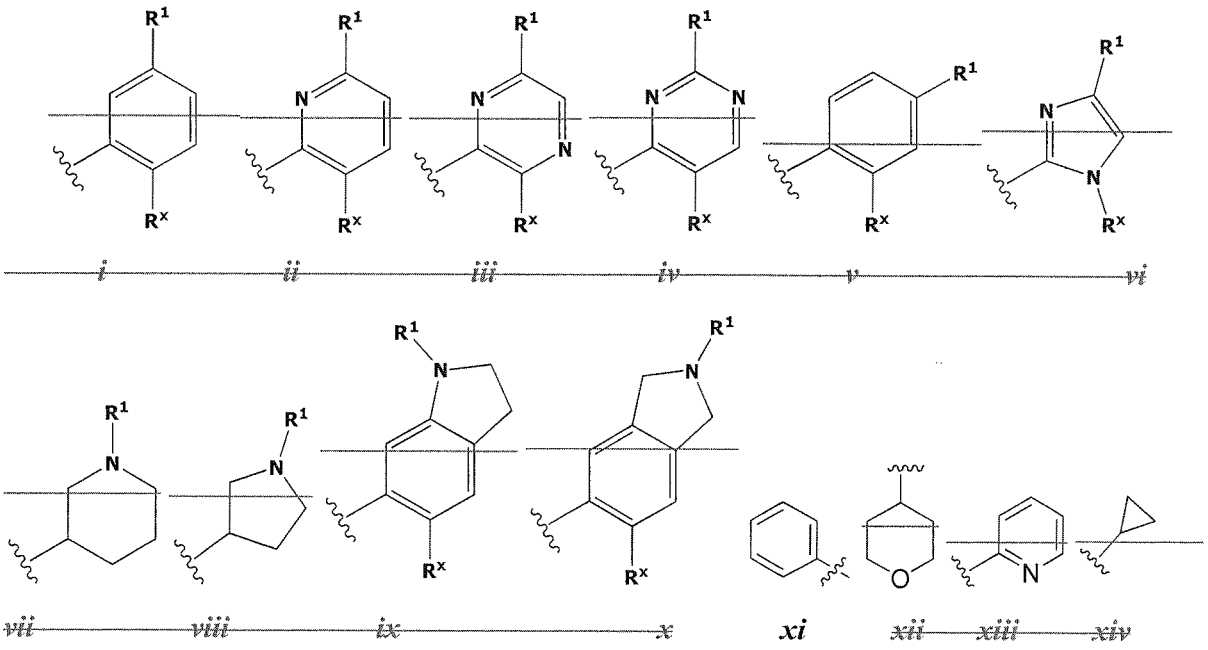
~~lxxix~~ ~~lxxx~~ ***lxxxi*** ~~lxxxii~~ ~~lxxxiii~~ ~~lxxxiv~~ ~~lxxxv~~ ~~lxxxvi~~ ~~lxxxvii~~ ~~lxxxviii~~ ~~lxxxix~~ ~~lxxxx~~

lxxxi ~~lxxxii~~ ~~lxxxiii~~ ~~lxxxiv~~

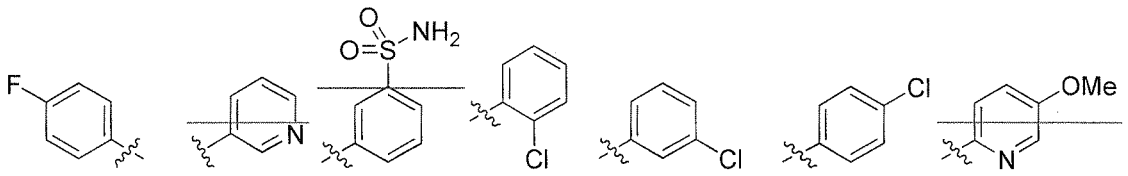
~~or lxxxv~~.

32. The use according to claim ~~29 or 30~~31, wherein Ring A is selected from ~~*i, ii, iv, v, vi, vii, ix, xiv, xvi, lii, lxiii,*~~ ***lxxi***~~*, lxxiv, lxxvi, lxxviii,*~~ and ***lxxxi***.

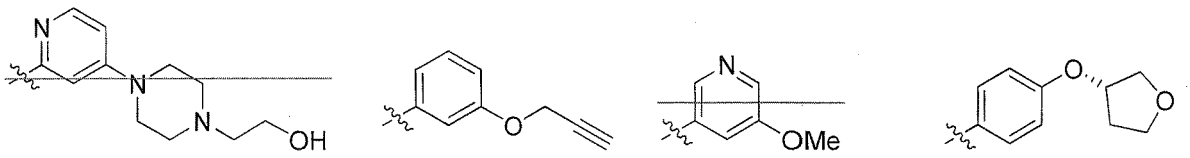
33. The use according to claim 29 or 30, wherein Ring B is selected from:



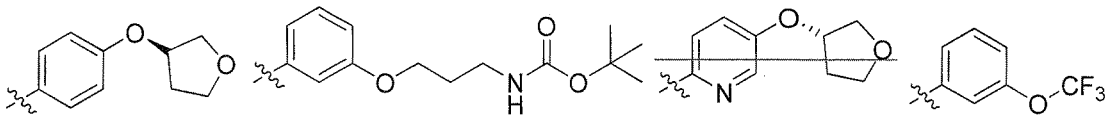
~~*i*~~ ~~*ii*~~ ~~*iii*~~ ~~*iv*~~ ~~*v*~~ ~~*vi*~~ ~~*vii*~~ ~~*viii*~~ ~~*ix*~~ ~~*x*~~ ***xi*** ~~*xii*~~ ~~*xiii*~~ ~~*xiv*~~



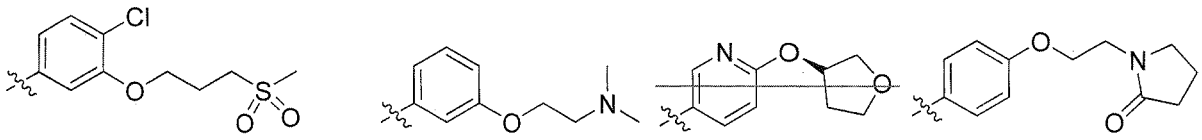
xv *~~xvi~~* *~~xvii~~* *xviii* *xix* *xx* *~~xxi~~*



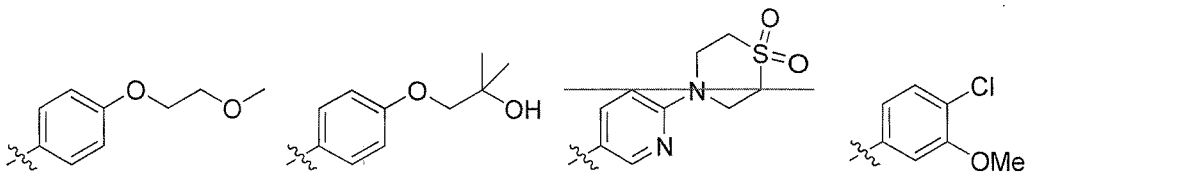
~~xxii~~ *xxiii* *~~xxiv~~* *xxv*



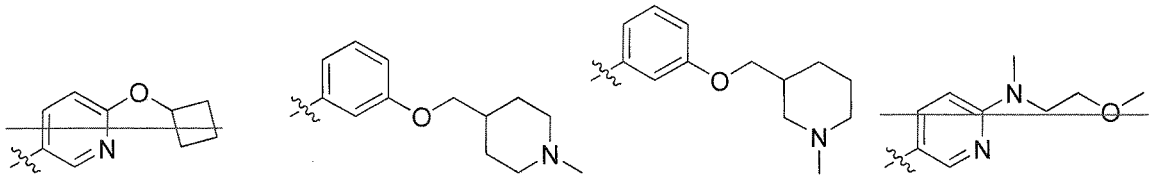
xxvi *xxvii* *~~xxviii~~* *xxix*



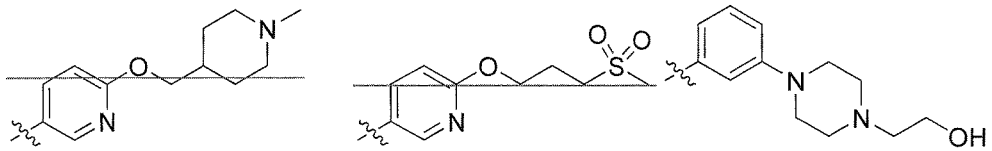
xxx *xxxi* *~~xxxii~~* *xxxiii*



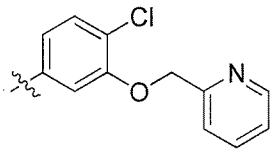
xxxiv *xxxv* *~~xxxvi~~* *xxxvii*



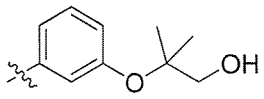
~~xxxviii~~ *xxxix* *xl* *~~xli~~*



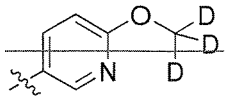
~~xlii~~ *~~xliii~~* *xliv*



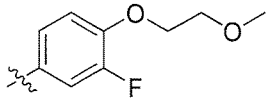
xlv



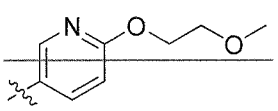
xlvi



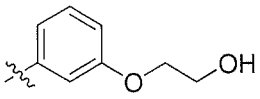
~~*xlvii*~~



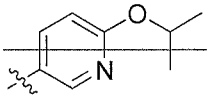
xlviii



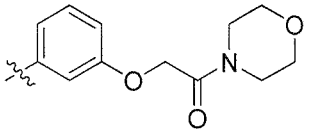
~~*xlix*~~



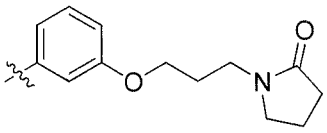
l



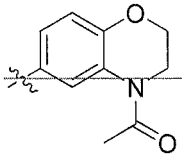
~~*li*~~



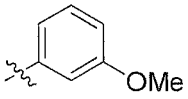
lii



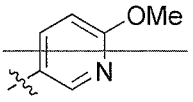
liii



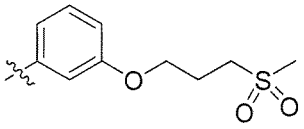
~~*liv*~~



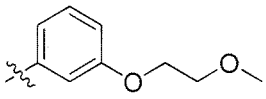
lv



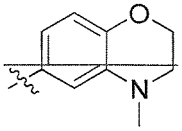
~~*lvi*~~



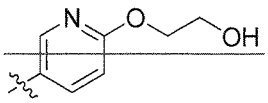
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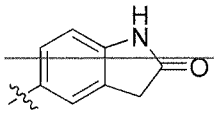
lviii



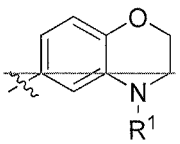
~~*lix*~~



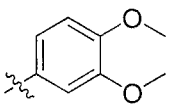
~~*lx*~~



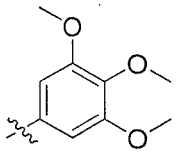
~~*lxi*~~



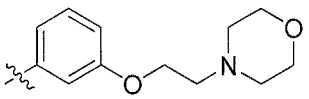
~~*lxii*~~



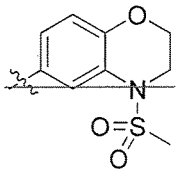
lxiii



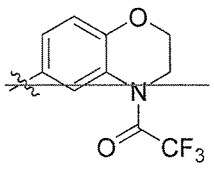
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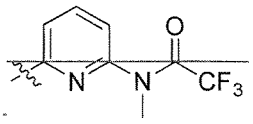
lxv



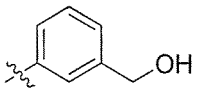
~~*lxvi*~~



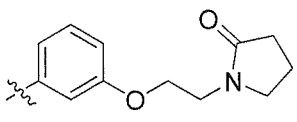
~~*lxvii*~~



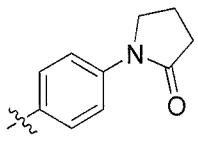
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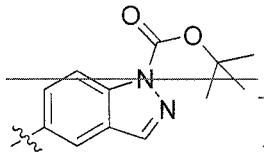
lxix



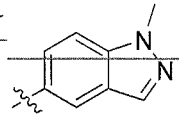
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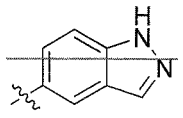
lxxi



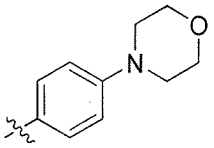
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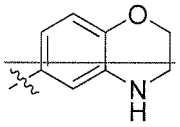
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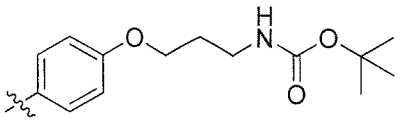
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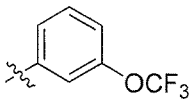
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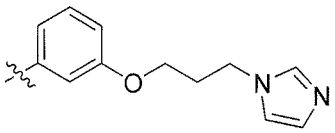
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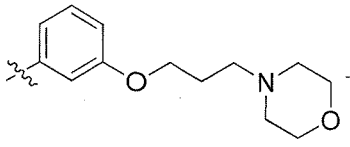
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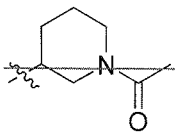
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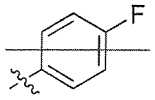
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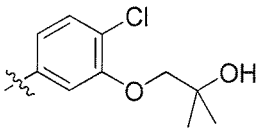
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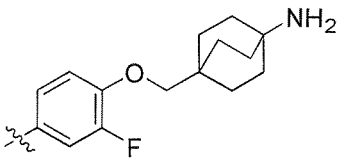
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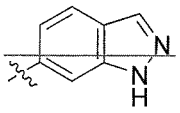
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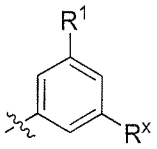
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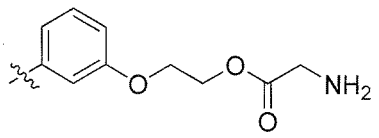
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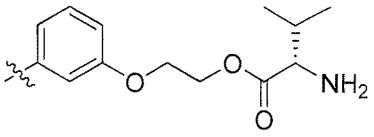
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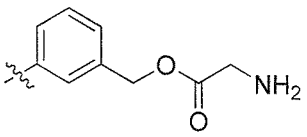
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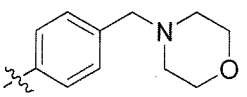
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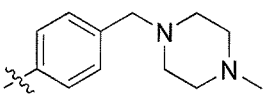
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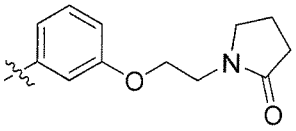
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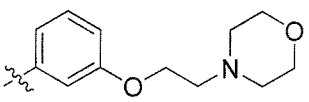
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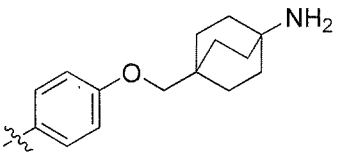
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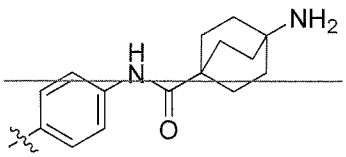
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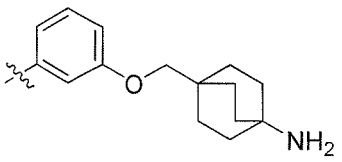
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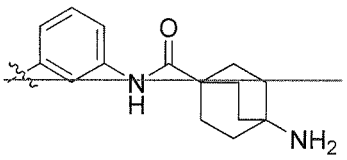
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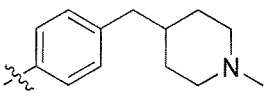
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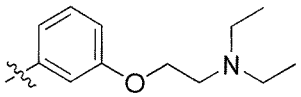
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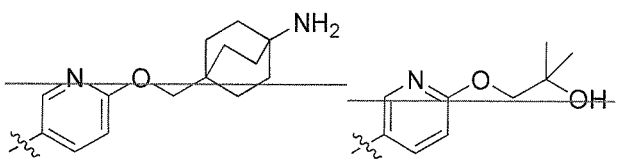
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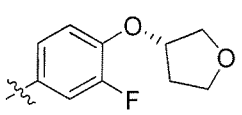
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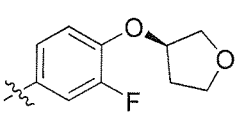
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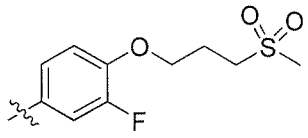
~~e~~ ~~ei~~



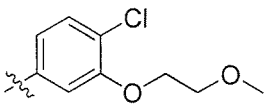
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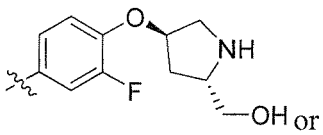
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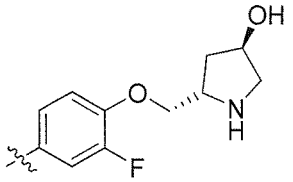
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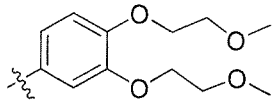
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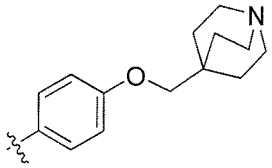
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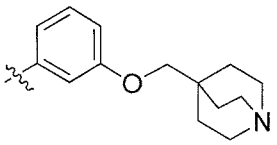
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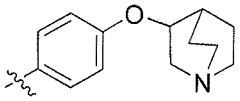
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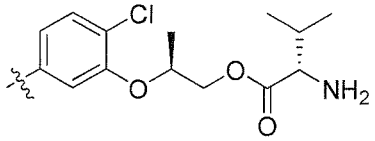
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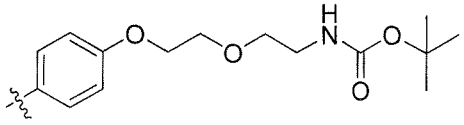
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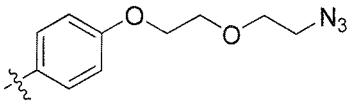
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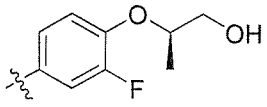
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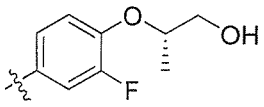
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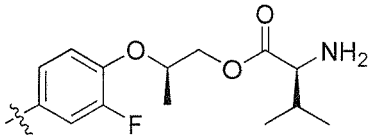
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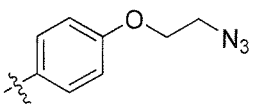
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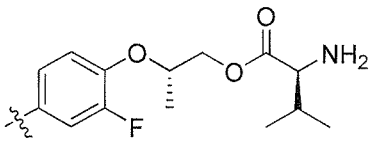
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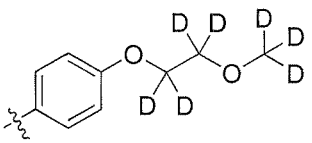
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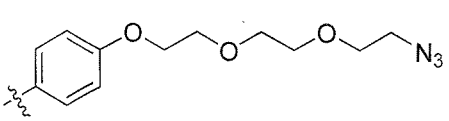
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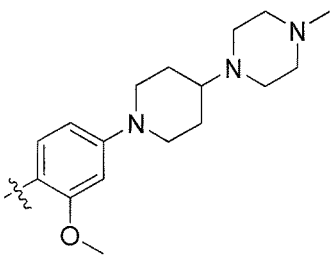
cxxix



cxx



cxxi



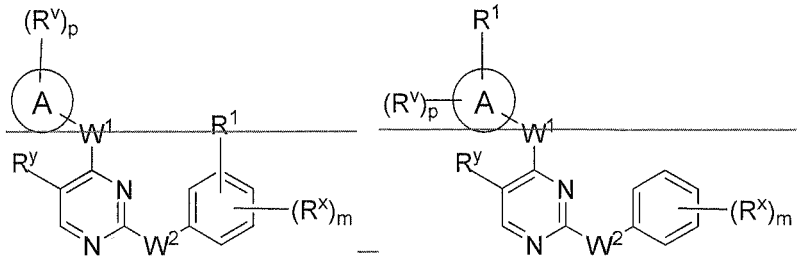
or *cxxii*.

34. The use according to claim ~~29 or 30~~33, wherein Ring B is selected from ~~*i, ii, iii, iv, v, ix, x,*~~ ***xi***, ~~*xiii, xvi, xvii,*~~ ***xix***, ***xx***, ***xxv***, ***xxvi***, ~~*xxxii,*~~ ***xxxiv***, ***xxxv***, ~~*xxxviii, xlii,*~~ ***xlvi***, ***xlviii***, ***l***, ***lviii***, ***lxiv***, ***lxxviii***, ***lxxxiii***, ***lxxxvi***, ***xciv***, ~~*c, ci,*~~ ***cii***, ***ciii***, ***civ***, and ***cv***.

~~35. The use according to claim 29 or 30, wherein W^1 and W^2 are each a bivalent C_{1-3} alkylene chain wherein one methylene unit of W^1 or W^2 is optionally replaced by $-NR^2-$, $-N(R^2)C(O)-$, $-C(O)N(R^2)-$, $-N(R^2)SO_2-$, $-SO_2N(R^2)-$, $-O-$, $-C(O)-$, $-OC(O)-$, $-C(O)O-$, $-S-$, $-SO-$ or $-SO_2-$.~~

~~36. The use according to claim 29 or 30, wherein W^1 and W^2 are each independently $-C(=O)-$, $-NR^2-$, $-S-$, or $-O-$.~~

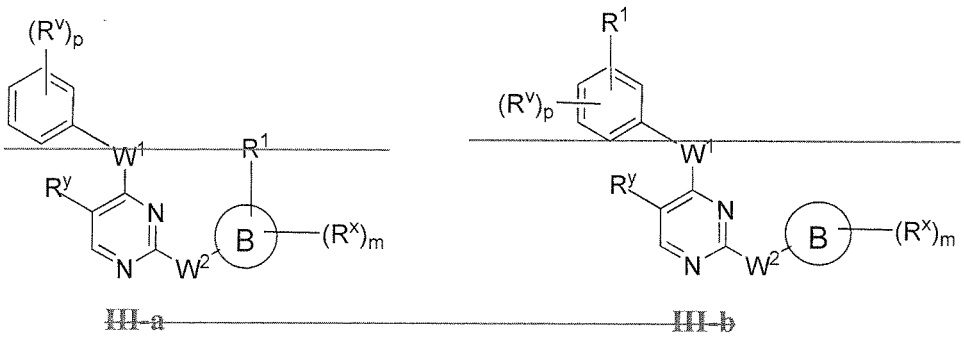
~~37. The use according to claim 29 or 30, wherein said compound is of formula II-a or II-b:~~



~~II-a II-b~~

~~or a pharmaceutically acceptable salt thereof.~~

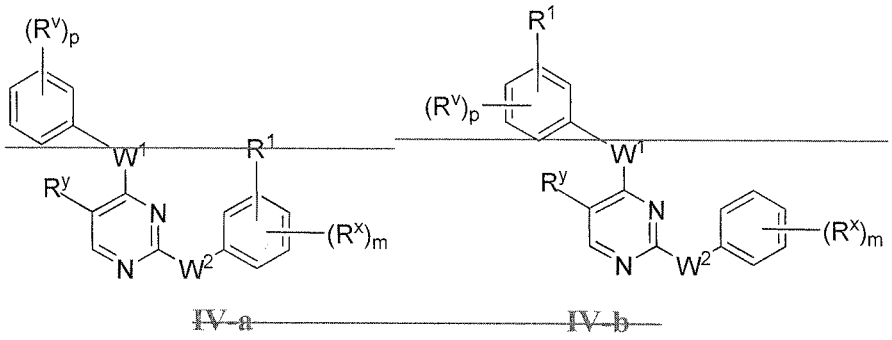
~~38. The use according to claim 29 or 30, wherein said compound is of formula III-a or III-b:~~



~~III-a~~ ~~III-b~~

~~or a pharmaceutically acceptable salt thereof.~~

~~39. The use according to claim 29 or 30, wherein said compound is of formula IV-a or IV-b:~~



~~IV-a~~ ~~IV-b~~

~~or a pharmaceutically acceptable salt thereof.~~

4035. The use according to claim 29 or 30, wherein R^1 is –L-Y, wherein:

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and one or two ~~additional~~ methylene units of L are optionally and independently replaced by -NRC(O)-, -C(O)NR-, -N(R)SO_2-, -SO_2N(R)-, –S-, -S(O)-, -SO_2-, -OC(O)-, -C(O)O-, cyclopropylene, –O-, -N(R)-, or -C(O)-; and

Y is ~~hydrogen,~~ C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups.~~; and~~

~~each R^e is independently selected from Q-Z, oxo, NO_2, halogen, CN, a suitable leaving group, or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, wherein:~~

~~Q is a covalent bond or a bivalent C_{1-6} saturated or unsaturated, straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by N(R), S, O, C(O), OC(O), C(O)O, SO, or SO_2, N(R)C(O), C(O)N(R), $N(R)SO_2$, or $SO_2N(R)$; and~~

~~Z is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN.~~

~~41~~36. The use according to claim ~~40~~29 or 30, wherein:

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and ~~at least~~ one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, ~~$N(R)SO_2$-~~, $-SO_2N(R)-$, –S-, -S(O)-, $-SO_2-$, -OC(O)-, or –C(O)O-~~, and one or two additional methylene units of L are optionally and independently replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-~~; and

Y is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN.

~~42~~37. The use according to claim ~~41~~36, wherein L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -C(O)-, and one ~~or two~~ additional methylene ~~units~~ unit of L ~~are~~ is optionally ~~and independently~~ replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-.

~~43~~38. The use according to claim ~~41~~36, wherein L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein L has at least one double bond and at least one methylene unit of L is replaced by -OC(O)-.

~~44~~39. The use according to claim ~~41~~29 or 30, wherein L is -NRC(O)CH=CH-, $-NRC(O)CH=CHCH_2N(CH_3)-$, $-NRC(O)CH=CHCH_2O-$, $-CH_2NRC(O)CH=CH-$, ~~$-NRSO_2CH=CH-$~~, $-NRSO_2CH=CHCH_2-$, ~~$-NRC(O)(C=N_2)$, $-NRC(O)(C=N_2)C(O)-$, $-NRC(O)CH=CHCH_2N(CH_3)-$, $-NRSO_2CH=CH-$, $-NRSO_2CH=CHCH_2-$, $-NRC(O)CH=CHCH_2O-$~~, or $-NRC(O)C(=CH_2)CH_2-$~~, $-CH_2NRC(O)-$, $-CH_2NRC(O)CH=CH-$, $-CH_2CH_2NRC(O)-$, or $-CH_2NRC(O)$cyclopropylene~~; wherein R is H or optionally substituted C_{1-6} aliphatic; and Y is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN.

4540. The use according to claim 4439, wherein L is -NHC(O)CH=CH-, -NHC(O)CH=CHCH$_2$N(CH$_3$)-, -NHC(O)CH=CHCH$_2$O-, -CH$_2$NHC(O)CH=CH-, ~~-NHSO$_2$CH=CH-,~~ -NHSO$_2$CH=CHCH$_2$-, ~~-NHC(O)(C=N$_2$)-, -NHC(O)(C=N$_2$)C(O)-, -NHC(O)CH=CHCH$_2$N(CH$_3$)-, -NHSO$_2$CH=CH-, -NHSO$_2$CH=CHCH$_2$-, -NHC(O)CH=CHCH$_2$O-,~~or -NHC(O)C(=CH$_2$)CH$_2$-~~, -CH$_2$NHC(O)-, -CH$_2$NHC(O)CH=CH-, -CH$_2$CH$_2$NHC(O)-, or -CH$_2$NHC(O)cyclopropylene-~~.

4641. The use according to claim 4129 or 30, wherein L is a bivalent C$_{2-8}$ straight or branched, hydrocarbon chain wherein L has at least one alkylidenyl double bond and at least one methylene unit of L is replaced by -C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO$_2$-, -SO$_2$N(R)-, -S-, -S(O)-, -SO$_2$-, -OC(O)-, or –C(O)O-, and one or two additional methylene units of L are optionally and independently replaced by cyclopropylene, –O-, -N(R)-, or -C(O)-.

4742. The use according to claim 29 or 30, wherein R^1 is –L-Y, wherein:

L is a bivalent C$_{2-8}$ straight or branched, hydrocarbon chain wherein L has at least one triple bond and one or two ~~additional~~ methylene units of L are optionally and independently replaced by -C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO$_2$-, ~~-SO$_2$N(R)-,~~ -S-, -S(O)-, -SO$_2$-, -OC(O)-, or -C(O)O-~~;~~

~~Y is hydrogen, C$_{1-6}$ aliphatic optionally substituted with oxo, halogen, NO$_2$, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups; and~~

~~each R^e is independently selected from –Q-Z, oxo, NO$_2$, halogen, CN, a suitable leaving group, or C$_{1-6}$ aliphatic optionally substituted with oxo, halogen, NO$_2$, or CN, wherein:~~

~~Q is a covalent bond or a bivalent C$_{1-6}$ saturated or unsaturated, straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by –N(R)-, -S-, -O-, -C(O)-, -OC(O)-, -C(O)O-, -SO-, or -SO$_2$-, -N(R)C(O)-, -C(O)N(R)-, -N(R)SO$_2$-, or -SO$_2$N(R)-; and~~

~~Z is hydrogen or C$_{1-6}$ aliphatic optionally substituted with oxo, halogen, NO$_2$, or CN~~.

~~48~~43. The use according to claim ~~47~~42, wherein Y is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN.

~~49~~44. The use according to claim ~~48~~43, wherein L is -C≡C-, ~~-C≡CCH$_2$N(isopropyl)-,~~ -NHC(O)C≡CCH$_2$CH$_2$-, -CH$_2$-C≡C-CH$_2$-, ~~-C≡CCH$_2$O-,~~ -CH$_2$C(O)C≡C-, -C(O)C≡C-, or -CH$_2$OC(=O)C≡C-.

~~50~~45. The use according to claim 29 or 30, wherein R^1 is –L-Y, wherein:

L is a bivalent C_{2-8} straight or branched, hydrocarbon chain wherein one methylene unit of L is replaced by cyclopropylene and one or two additional methylene units of L are independently replaced by -C(O)-, -NRC(O)-, -C(O)NR-, -N(R)SO$_2$-, -SO$_2$N(R)-, –S-, -S(O)-, -SO$_2$-, -OC(O)-, or -C(O)O-; and

Y is ~~hydrogen~~, C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, or a 3-10 membered monocyclic or bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and wherein said ring is substituted with 1-4 R^e groups~~; and~~

~~each R^e is independently selected from –Q-Z, oxo, NO_2, halogen, CN, a suitable leaving group, or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, wherein:~~

~~Q is a covalent bond or a bivalent C_{1-6} saturated or unsaturated, straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by –N(R)-, -S-, -O-, -C(O)-, -OC(O)-, -C(O)O-, -SO-, or -SO$_2$-, -N(R)C(O)-, -C(O)N(R)-, -N(R)SO$_2$-, or -SO$_2$N(R)-; and~~

~~Z is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN~~.

~~51~~46. The use according to claim ~~50~~45, wherein Y is ~~hydrogen or~~ C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN.

~~52~~47. The use according to claim 29 or 30, wherein R^1 is –L-Y, wherein:

L is ~~a covalent bond,~~ -C(O)-, -N(R)C(O)-, or a bivalent C_{1-8} saturated or unsaturated, straight or branched, hydrocarbon chain; and

Y is selected from ~~the following (*i*) through (*xvii*)~~:

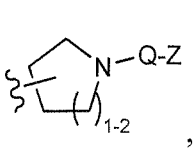
(*i*) C_{1-6} alkyl substituted with oxo, halogen, NO_2, or CN; or

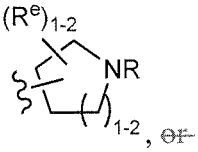
(*ii*) C_{2-6} alkenyl optionally substituted with oxo, halogen, NO_2, or CN; or

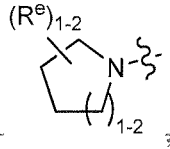
(*iii*) C_{2-6} alkynyl optionally substituted with oxo, halogen, NO_2, or CN; or

(*iv*) a saturated 3-4 membered heterocyclic ring having 1 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-2 R^e groups; or

(*v*) a saturated 5-6 membered heterocyclic ring having 1-2 heteroatom selected from oxygen or nitrogen wherein said ring is substituted with 1-4 R^e groups; or

(*vi*) 

, 

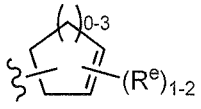
, ~~or~~ 

~~, wherein each R, Q, Z~~; or

(*vii*) a saturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups; or

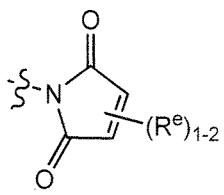
(*viii*) a partially unsaturated 3-6 membered monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

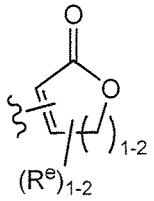
(*ix*) a partially unsaturated 3-6 membered carbocyclic ring, wherein said ring is substituted with 1-4 R^e groups;

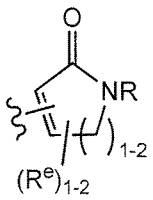
(*x*) 

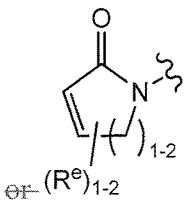
; or

(*xi*) a partially unsaturated 4-6 membered heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups; or

(*xii*) 

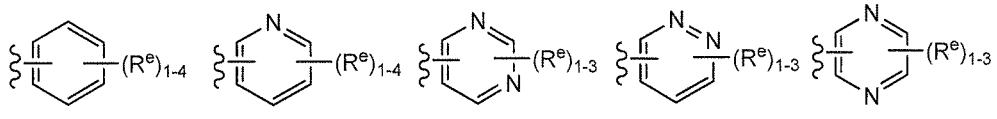






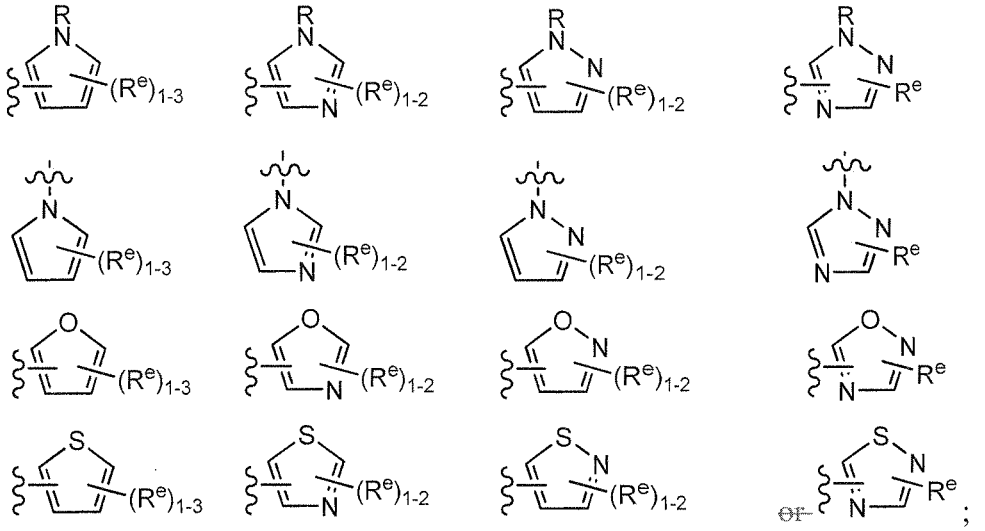
; or

(*xiii*) a 6-membered aromatic ring having 0-2 nitrogens wherein said ring is substituted with 1-4 R^e groups; or

(*xiv*) 

~~wherein each R^e is as defined above and described herein~~; or

(*xv*) a 5-membered heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-3 R^e groups; or

(*xvi*) 

(*xvii*) an 8-10 membered bicyclic, saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is substituted with 1-4 R^e groups;

~~wherein:~~

~~each R group is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered heterocylic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;~~

~~each R^e is independently selected from -Q-Z, oxo, NO_2, halogen, CN, a suitable leaving group, or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN, wherein:~~

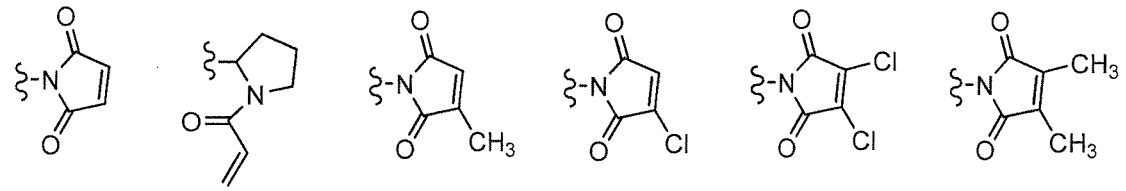
~~Q is a covalent bond or a bivalent C_{1-6} saturated or unsaturated, straight or branched, hydrocarbon chain, wherein one or two methylene units of Q are optionally and independently replaced by -N(R)-, -S-, -O-, -C(O)-, -OC(O)-, -C(O)O-, -SO-, or $-SO_2$-, -N(R)C(O)-, -C(O)N(R)-, $-N(R)SO_2$-, or $-SO_2N(R)$-; and~~

~~Z is hydrogen or C_{1-6} aliphatic optionally substituted with oxo, halogen, NO_2, or CN~~.

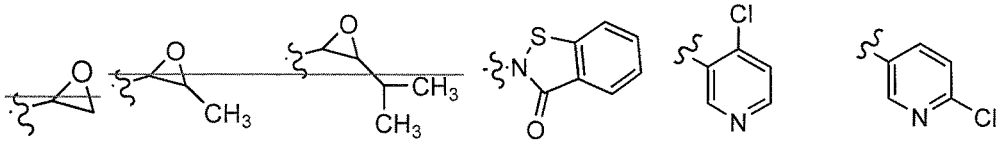
~~53~~48. The use according to claim ~~52~~29 or 30, wherein L is a covalent bond, $–CH_2$-, -NH-, -C(O)-, $-CH_2NH$-, $-NHCH_2$-, –NHC(O)-, $-NHC(O)CH_2OC(O)$-, $-CH_2NHC(O)$-, ~~$-NHSO_2-$~~, $-NHSO_2CH_2$-, ~~$-NHC(O)CH_2OC(O)-$~~, or $-SO_2NH$-.

~~54~~49. The use according to claim ~~53~~48, wherein L is a covalent bond.

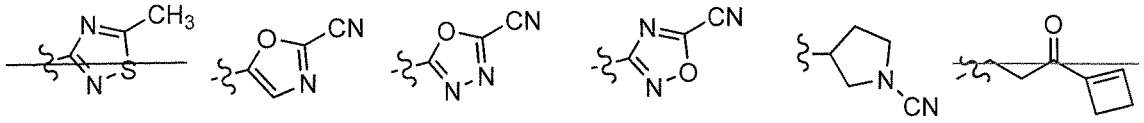
~~55~~50. The use according to claim ~~52~~47, wherein Y is selected from:



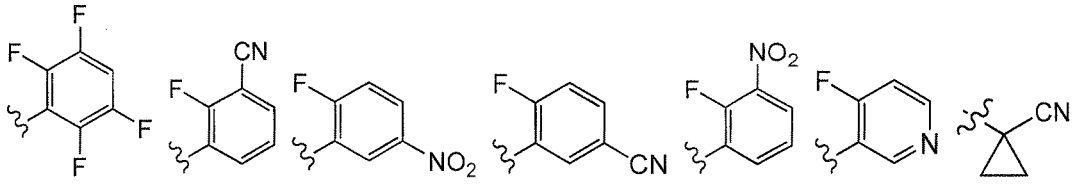
a ***b*** ***c*** ***d*** ***e*** ***f***



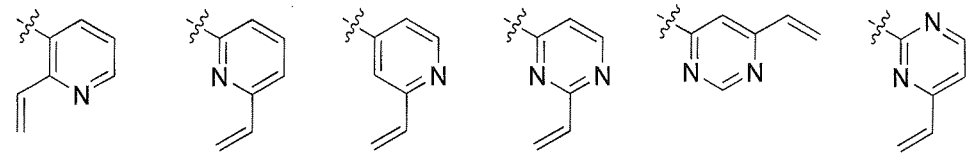
~~*g*~~ ~~*h*~~ ~~*i*~~ ***j*** ***k*** ***l***



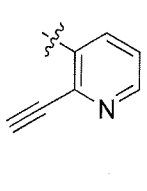
~~*m*~~ ***n*** ***o*** ***p*** ***q*** ~~*r*~~



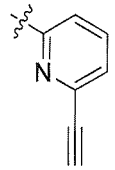
s ***t*** ***u*** ***v*** ***w*** ***x*** ***y***



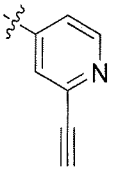
z ***aa*** ***bb*** ***cc*** ***dd*** ***ee***



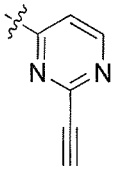
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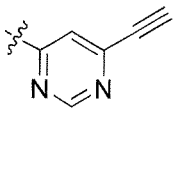
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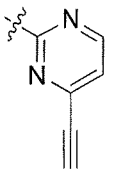
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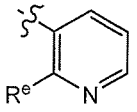
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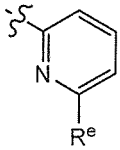
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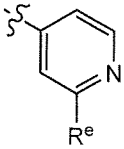
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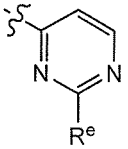
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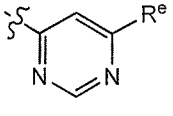
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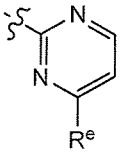
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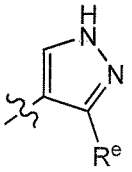
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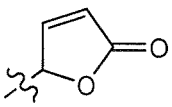
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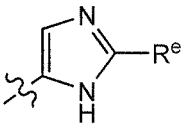
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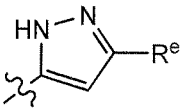
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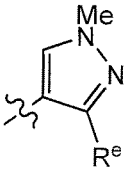
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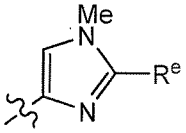
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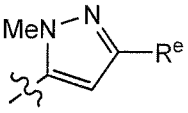
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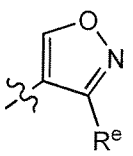
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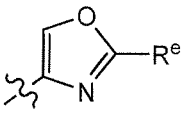
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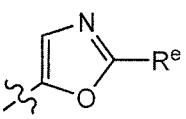
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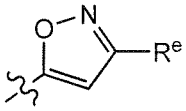
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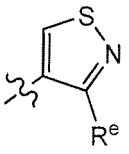
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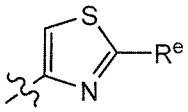
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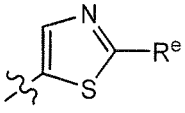
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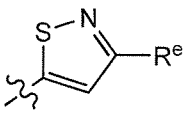
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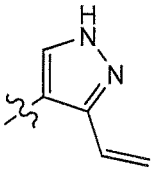
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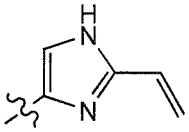
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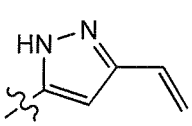
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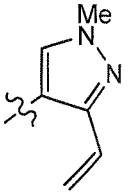
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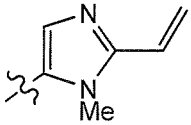
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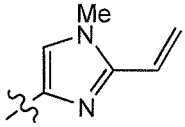
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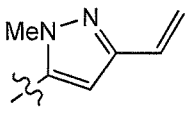
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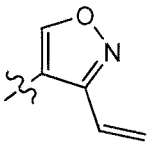
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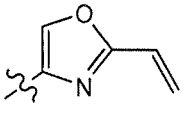
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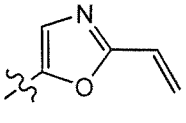
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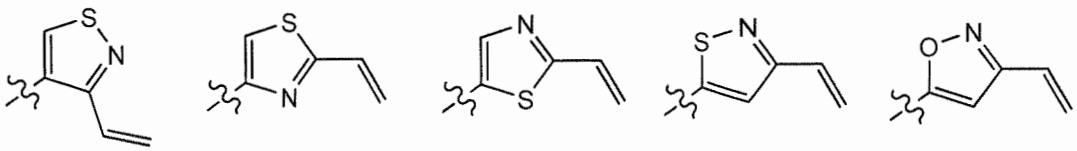
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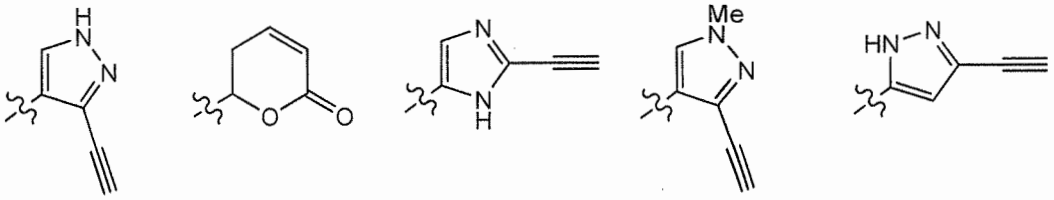
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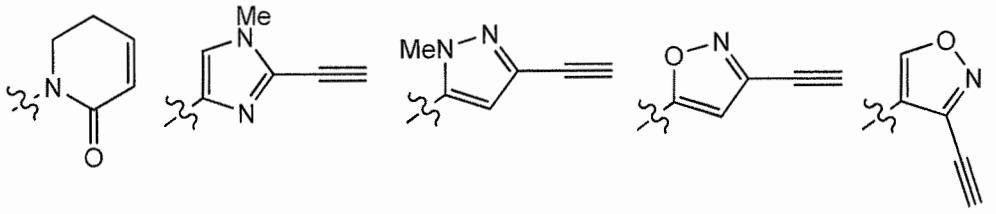
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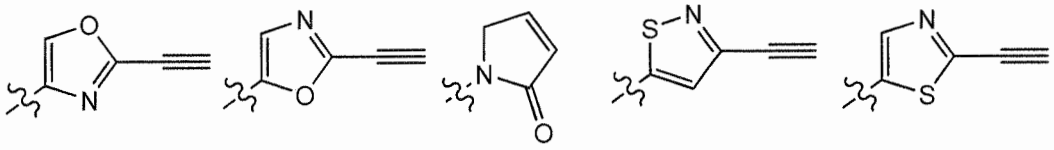
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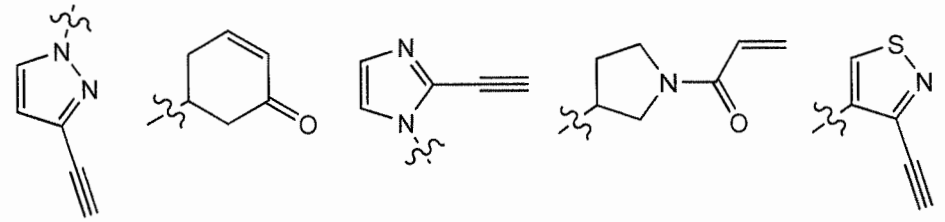
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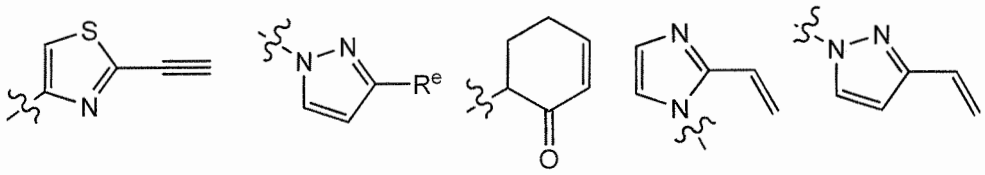
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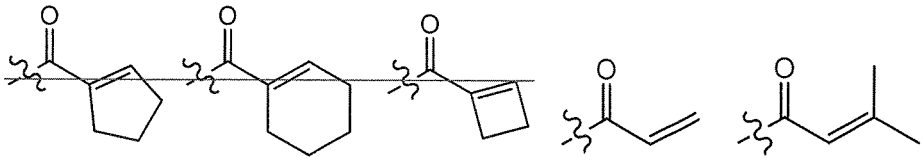
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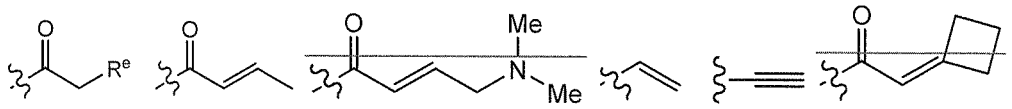
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oooo *pppp* *qqqq* *rrrr* *ssss*



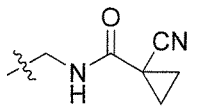
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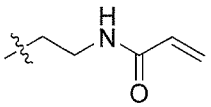
yyyy *zzzz* *aaaaa* *bbbbb* *ccccc* *ddddd*

wherein each R^e is ~~independently selected from~~ halogen.

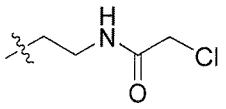
~~56~~51. The use according to claim 29 or 30, wherein R^1 is selected from:



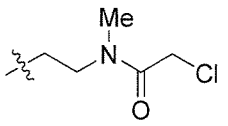
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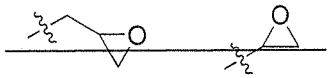
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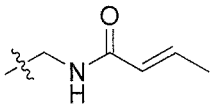
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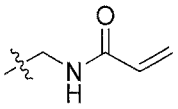
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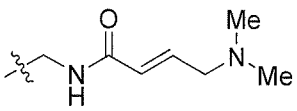
~~*e*~~ ~~*f*~~



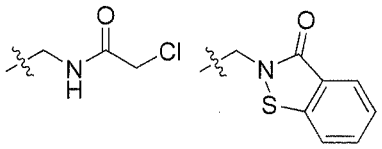
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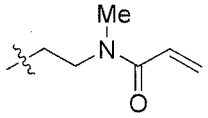
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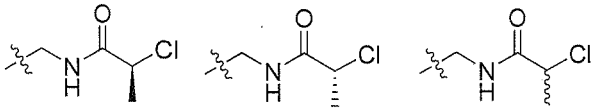
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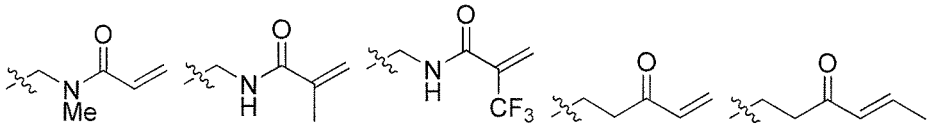
j *k*



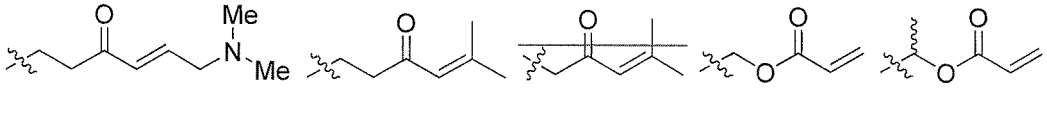
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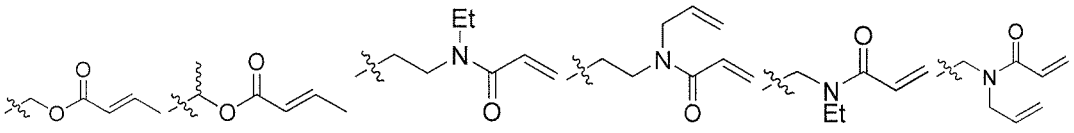
m *n* *o*



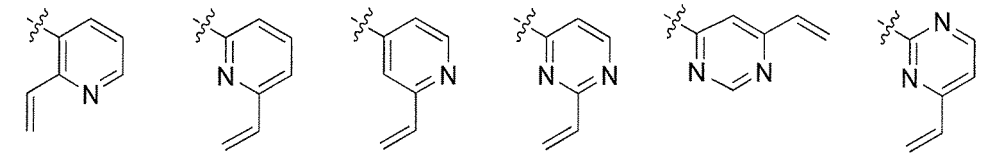
p *q* *r* *s* *t*



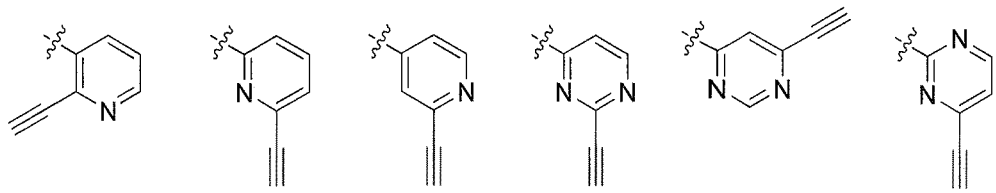
u *v* ~~*w*~~ *x* *y*



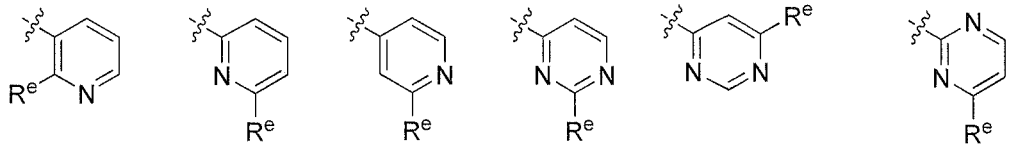
z *aa* *bb* *cc* *dd* *ee*



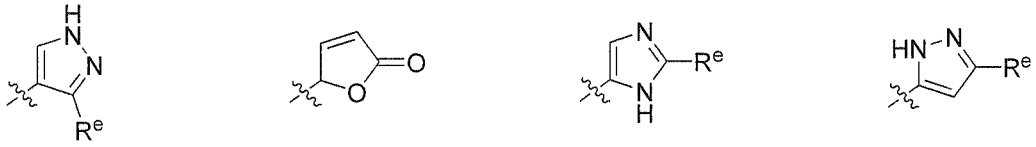
ff *gg* *hh* *ii* *jj* *kk*



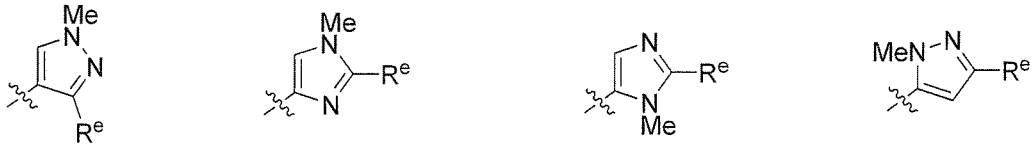
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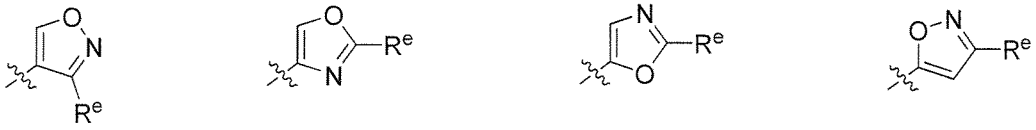
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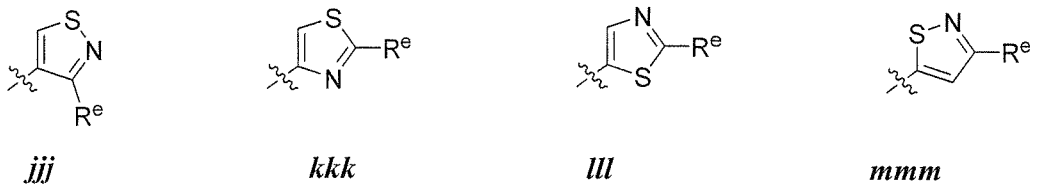
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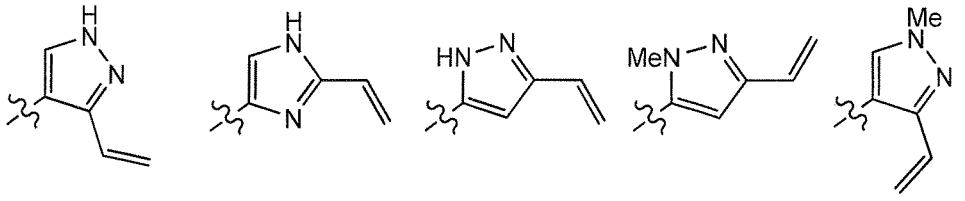
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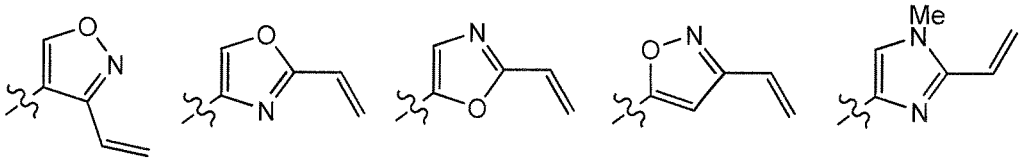
fff *ggg* *hhh* *iii*



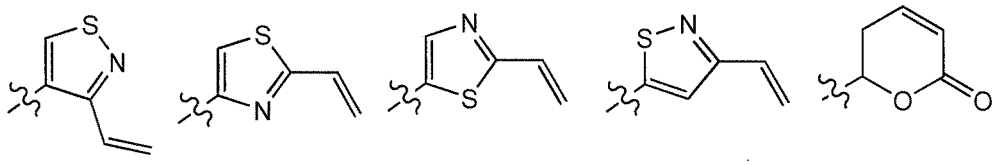
jjj *kkk* *lll* *mmm*



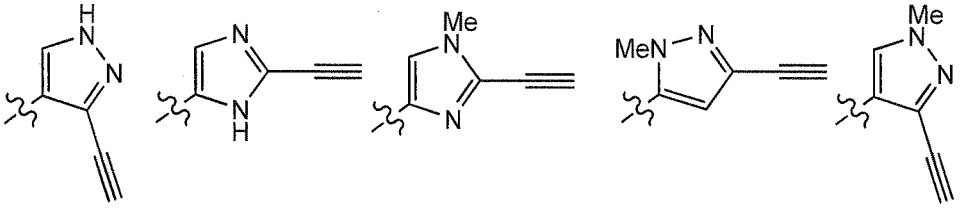
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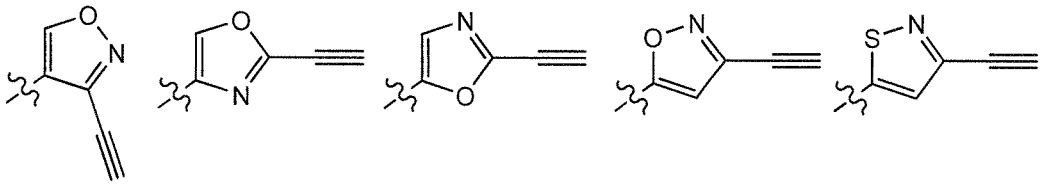
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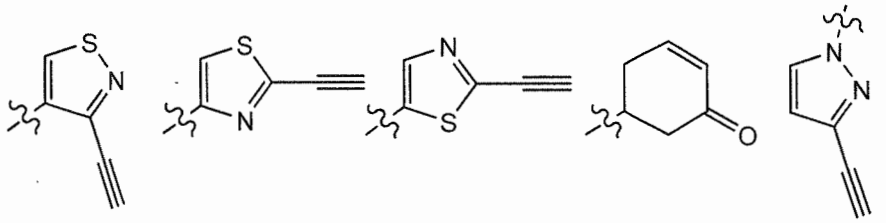
www *xxx* *yyy* *zzz* *aaaa*



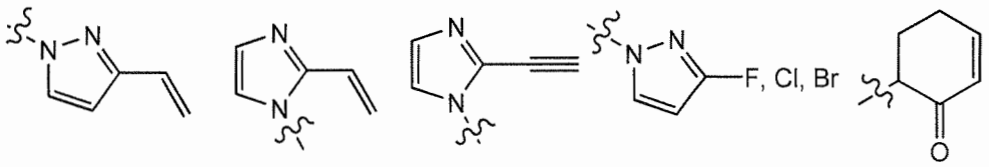
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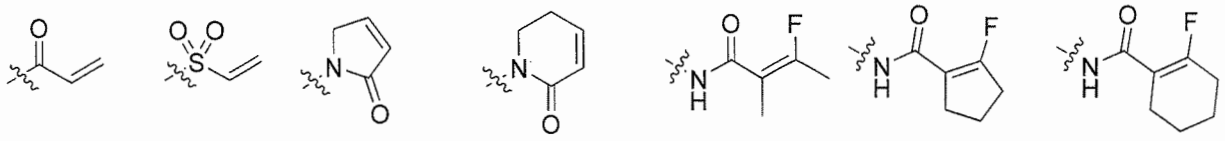
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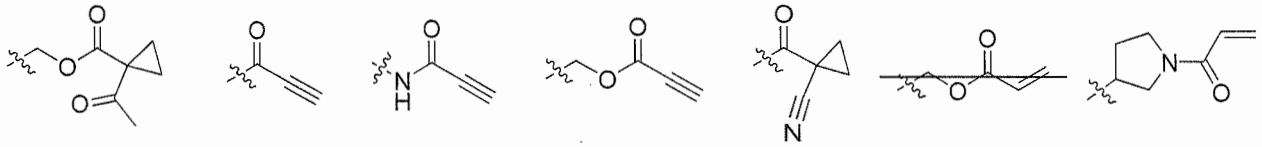
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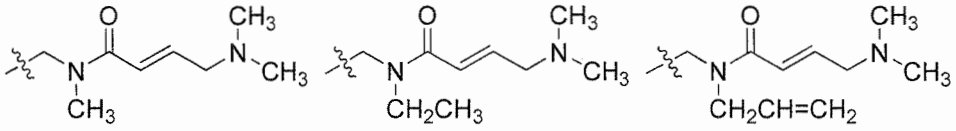
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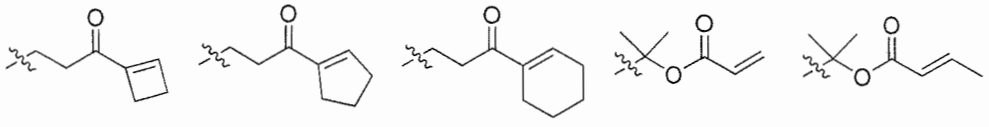
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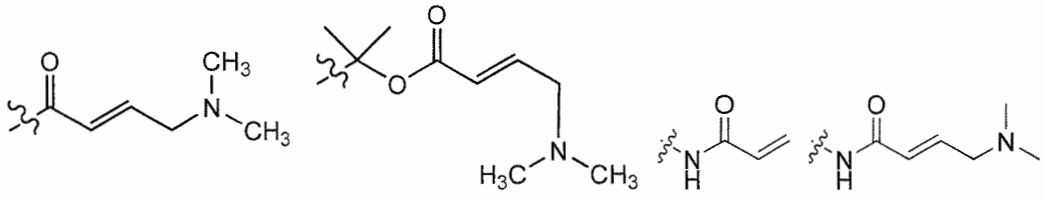
ccccc *ddddd* *eeeee* *fffff* *ggggg* ~~*hhhhh*~~ *iiiii*



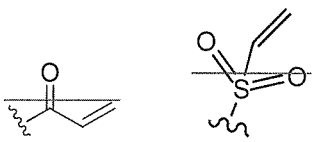
jjjjj *kkkkk* *lllll*



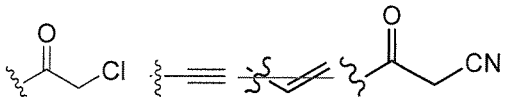
mmmmm *nnnnn* *ooooo* *ppppp* *qqqqq*



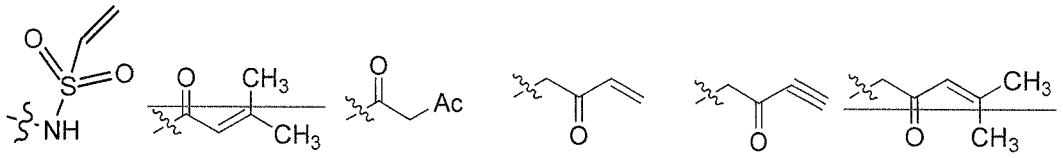
rrrrr *sssss* *ttttt* *uuuuu*



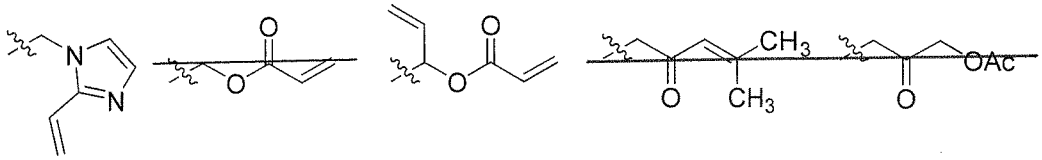
~~vvvvv~~ ~~wwwww~~



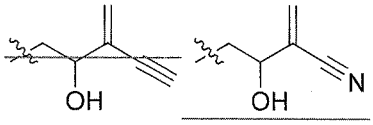
xxxxx *yyyyy* ~~*zzzzz*~~ *aaaaaa* *bbbbbbb*



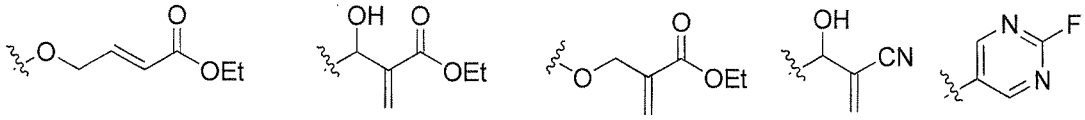
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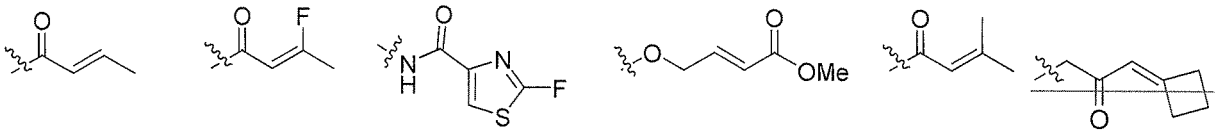
iiiiii ~~*jjjjjj*~~ *kkkkkk* ~~*llllll*~~ ~~*mmmmmmm*~~



nnnnnn



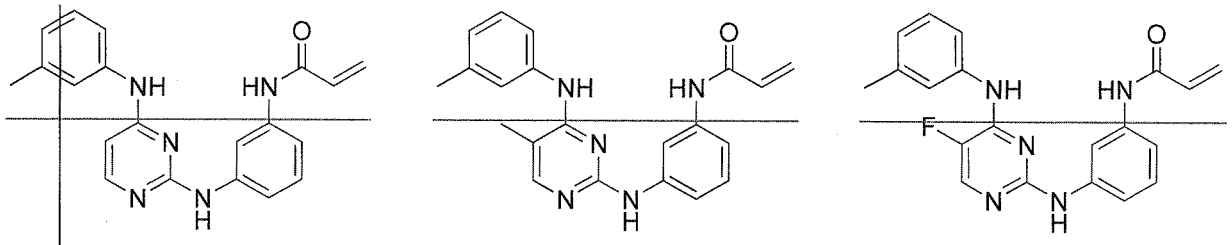
oooooo *pppppp* *qqqqqq* *rrrrrr* *ssssss*



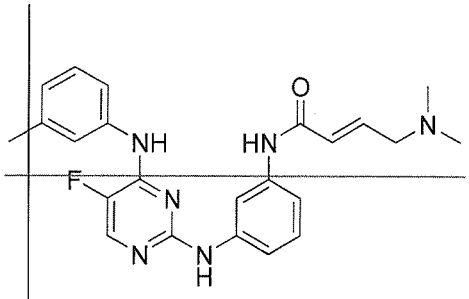
tttttt *uuuuuu* *vvvvvv* *wwwwww* or *xxxxxx* ~~or~~ ~~*yyyyyy*~~

wherein each R^e is independently a suitable leaving group, NO_2, CN, or oxo.

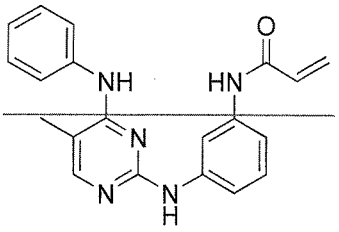
~~57~~52. The use according to claim 29 or 30 wherein the compound is selected from the group consisting of:



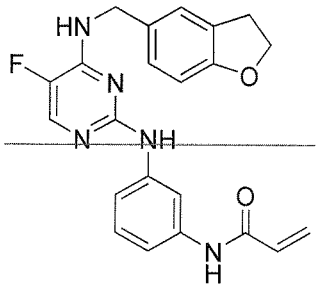
~~I-1~~ ~~I-2~~ ~~I-3~~



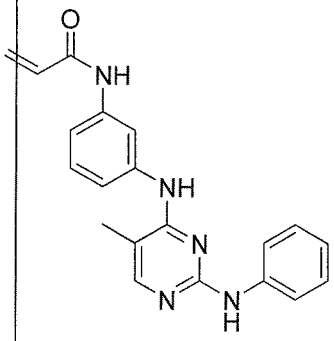
~~I-4~~



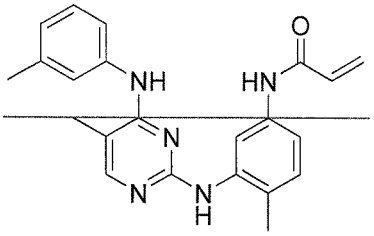
~~I-5~~



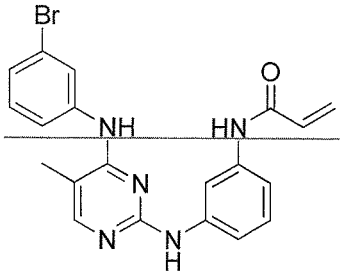
~~I-6~~



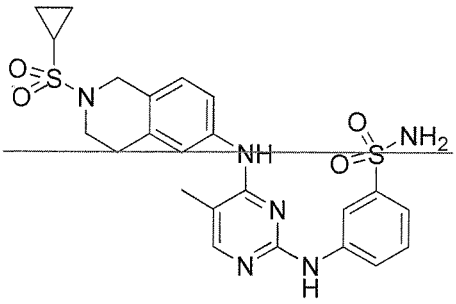
I-7



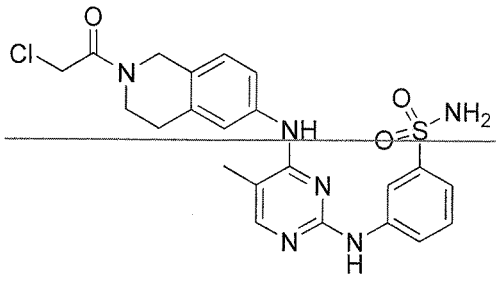
~~I-8~~



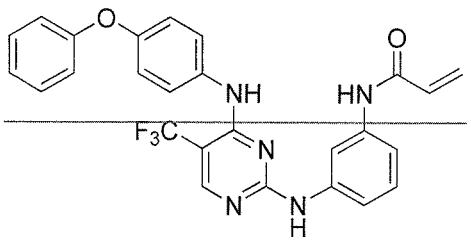
~~I-9~~



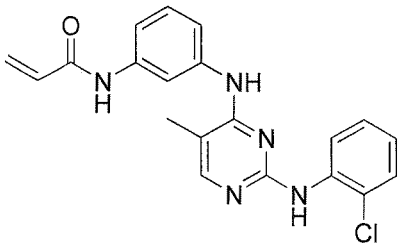
~~I-10~~



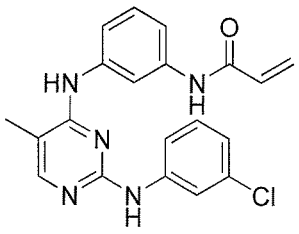
~~I-11~~



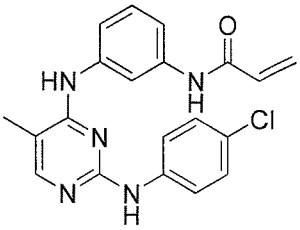
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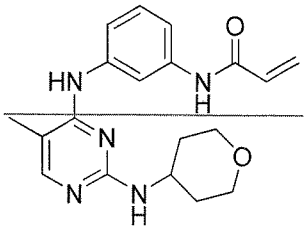
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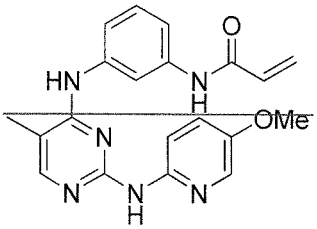
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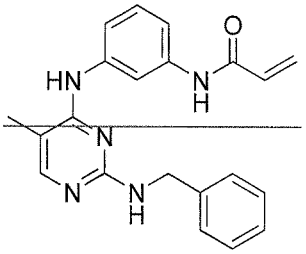
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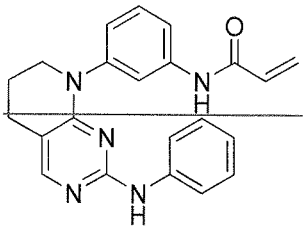
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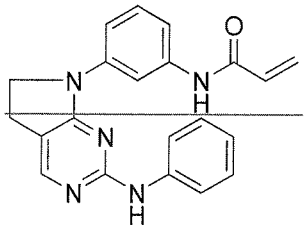
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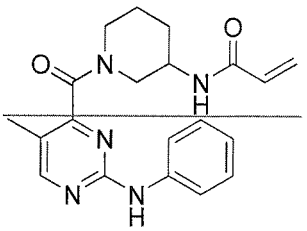
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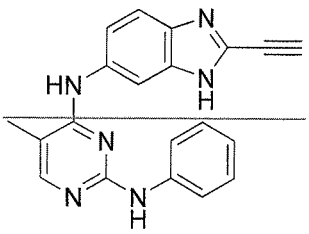
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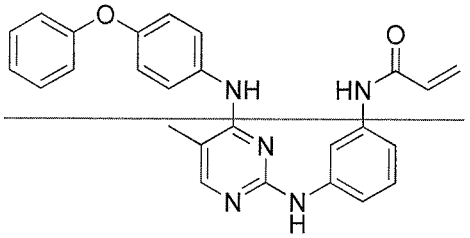
~~I-20~~



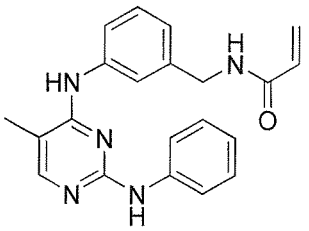
~~I-21~~



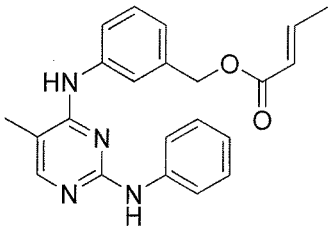
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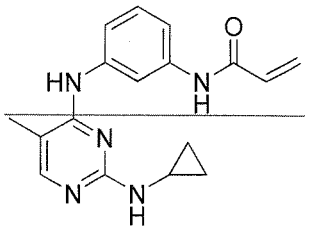
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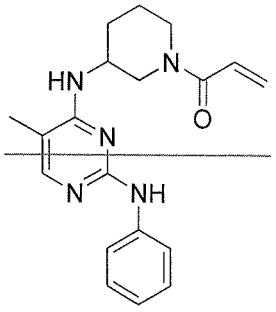
I-24



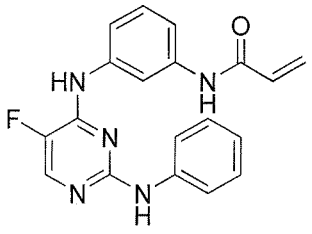
I-25



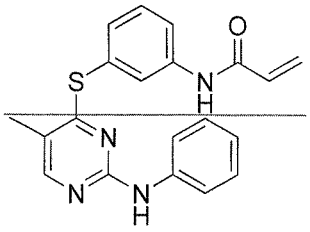
~~I-26~~



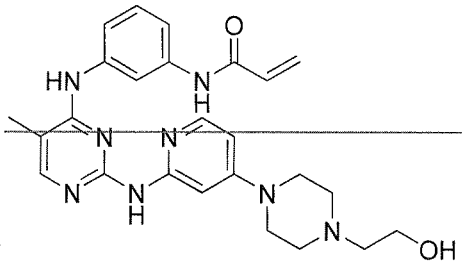
~~I-27~~



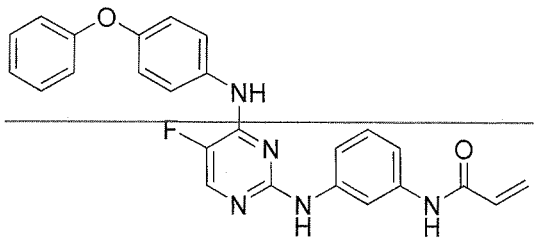
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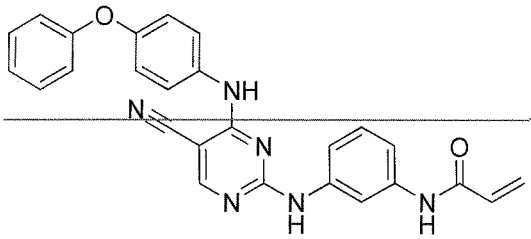
~~I-29~~



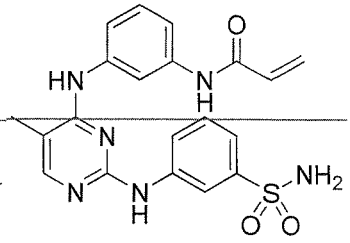
~~I-30~~



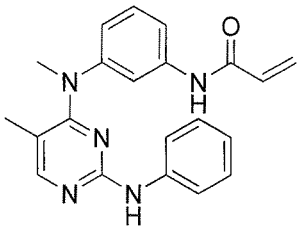
~~I-31~~



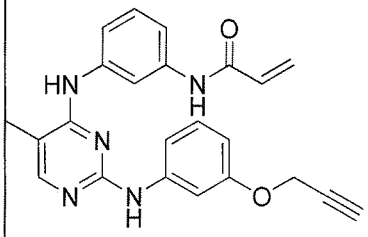
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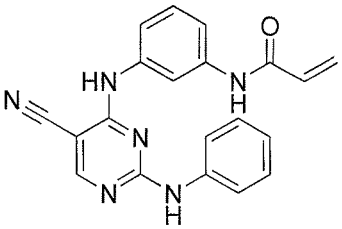
~~I-33~~



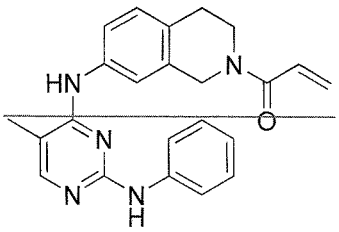
I-34



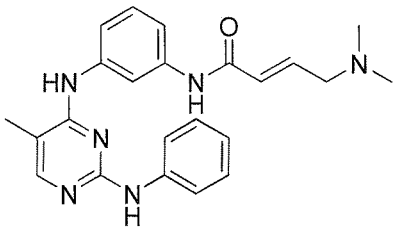
I-35



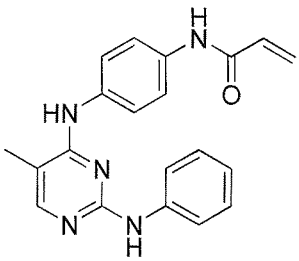
I-36



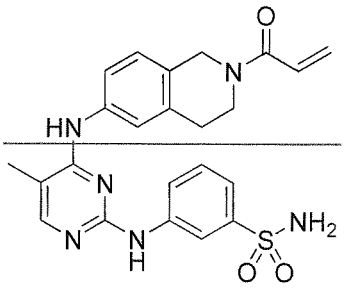
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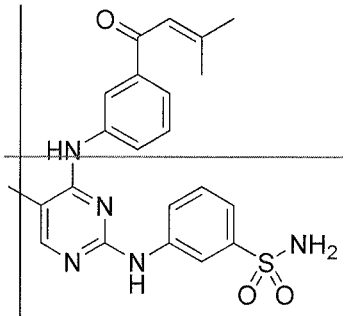
I-38



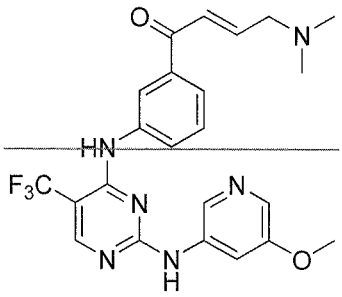
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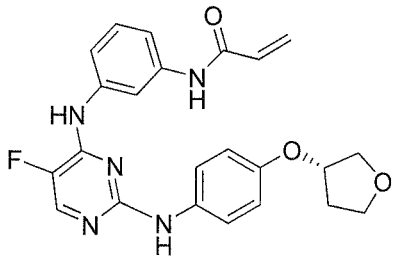
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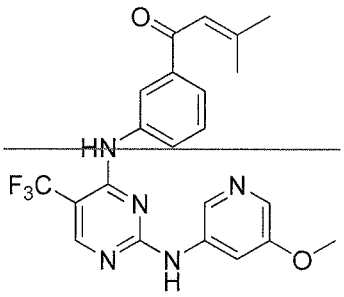
~~I-41~~



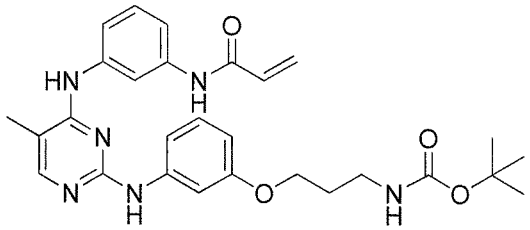
~~I-42~~



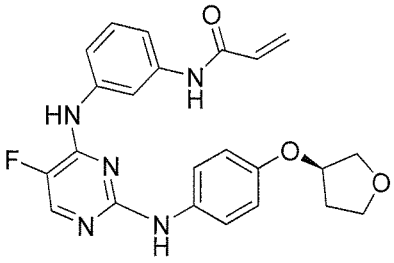
I-43



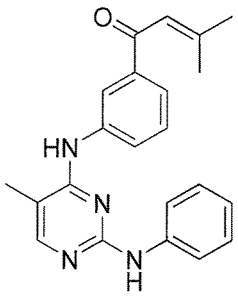
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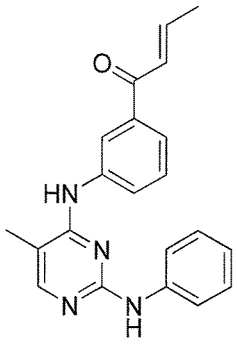
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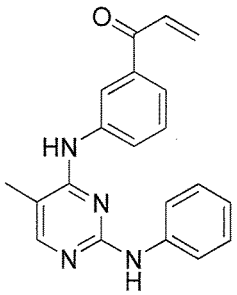
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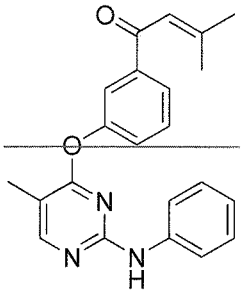
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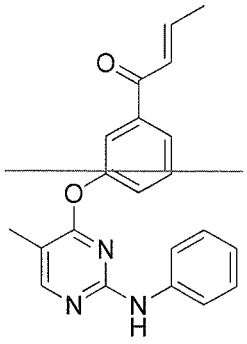
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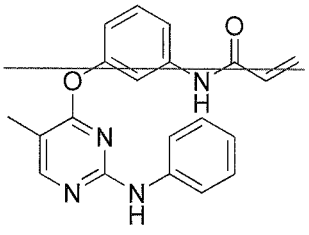
I-49



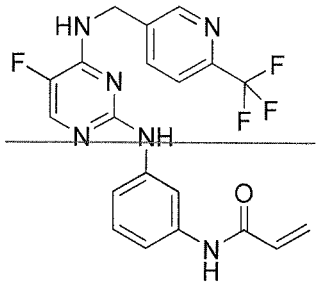
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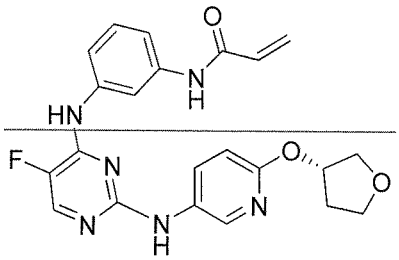
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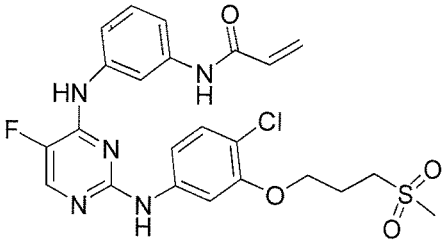
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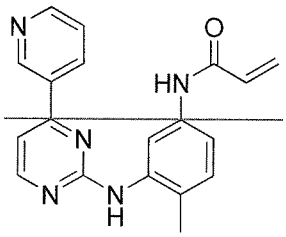
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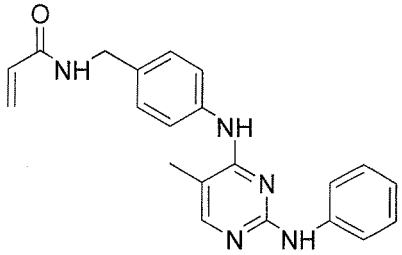
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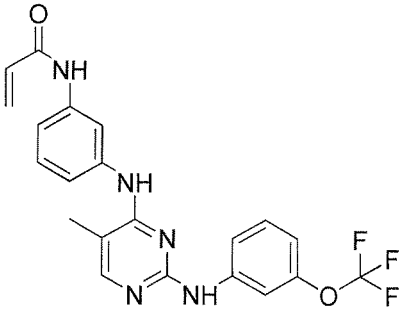
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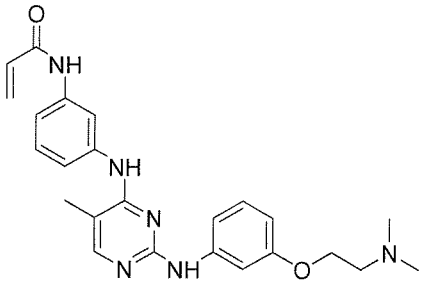
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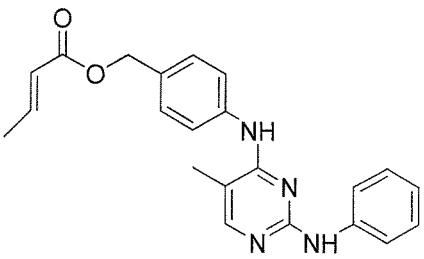
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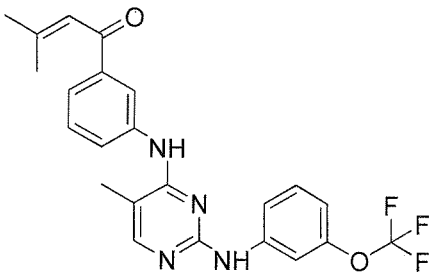
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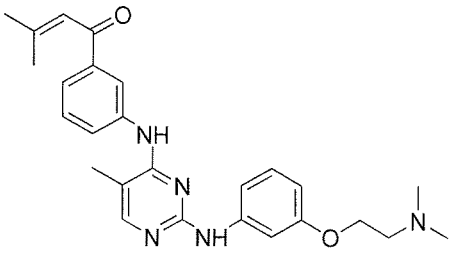
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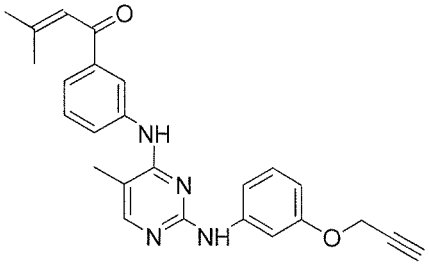
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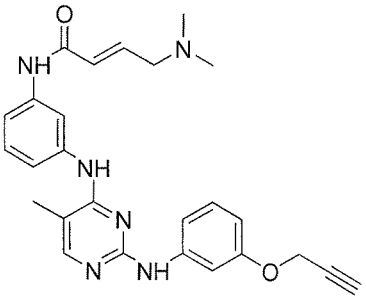
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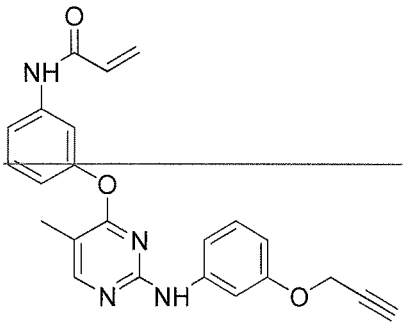
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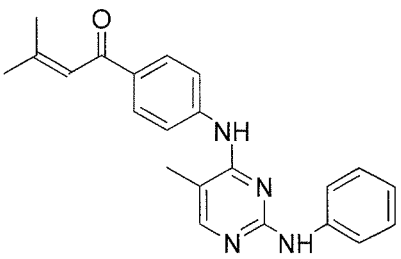
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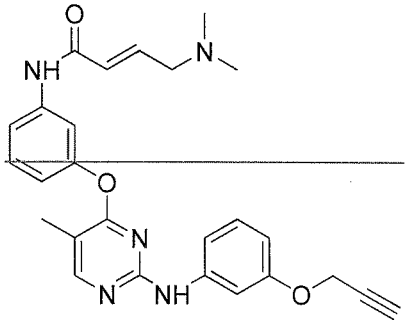
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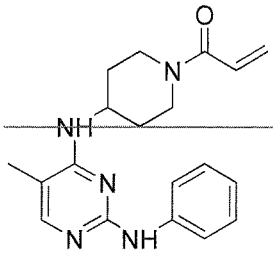
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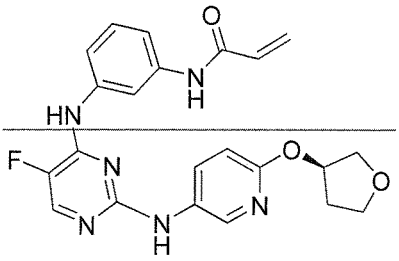
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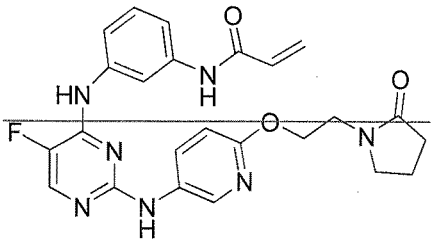
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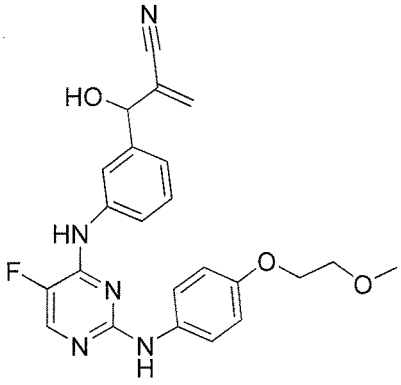
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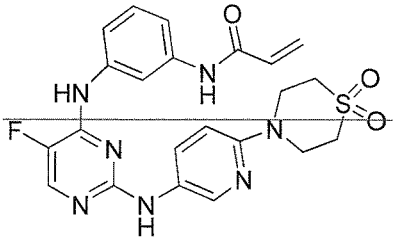
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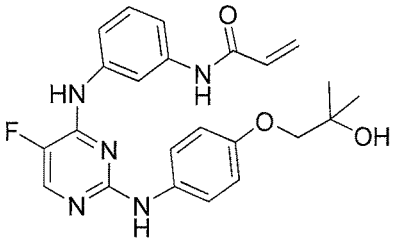
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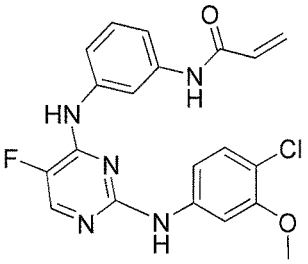
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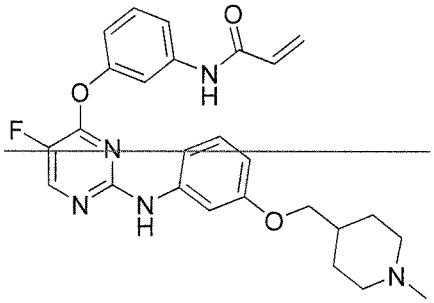
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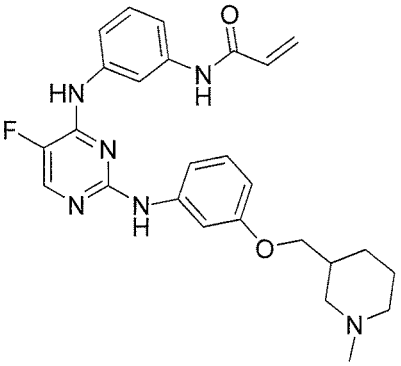
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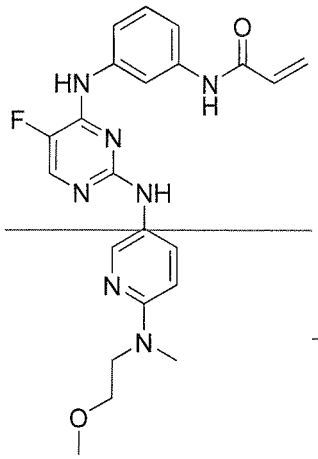
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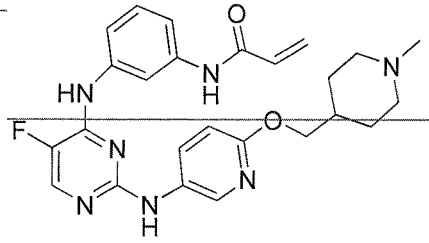
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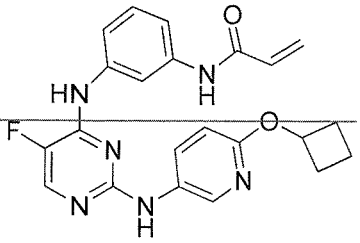
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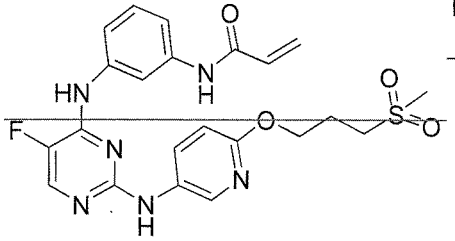
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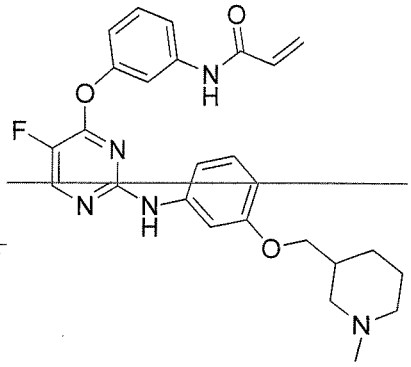
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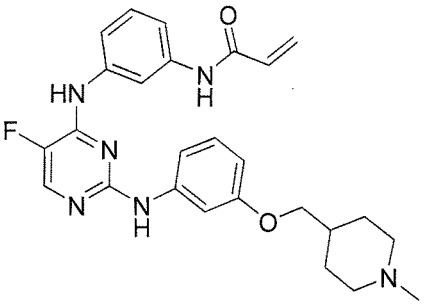
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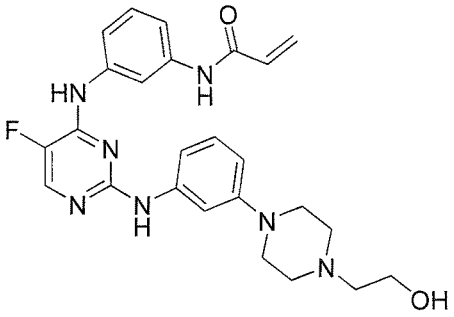
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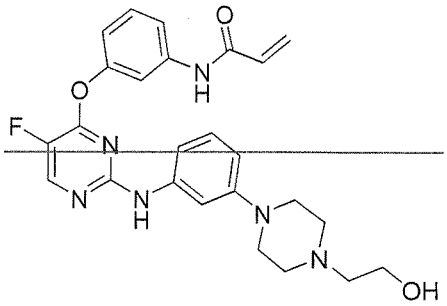
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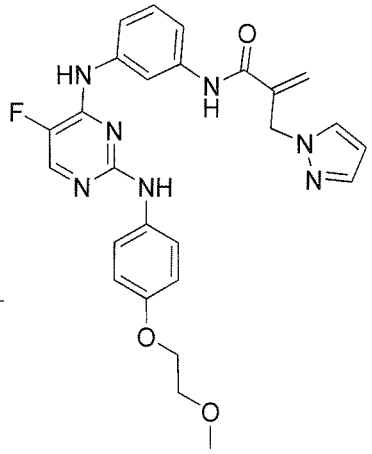
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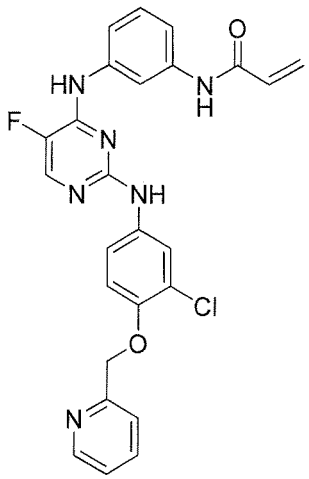
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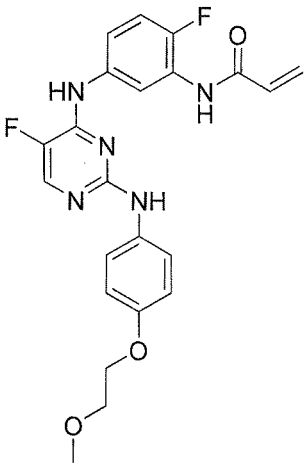
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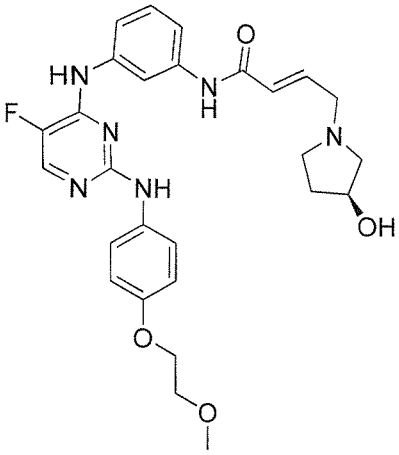
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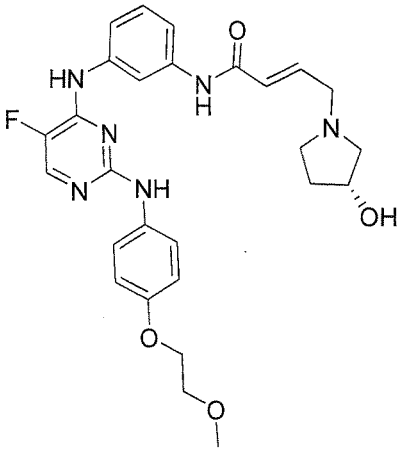
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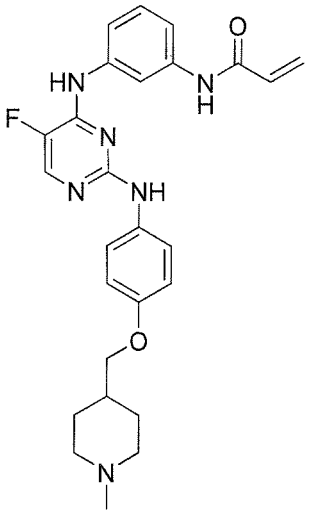
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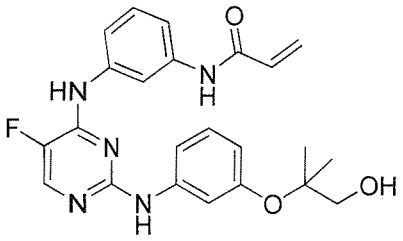
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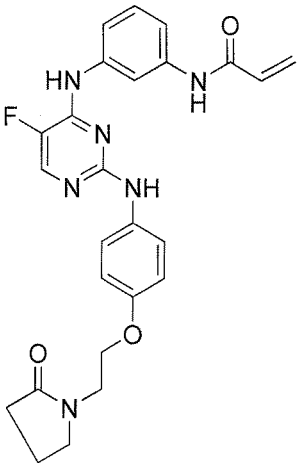
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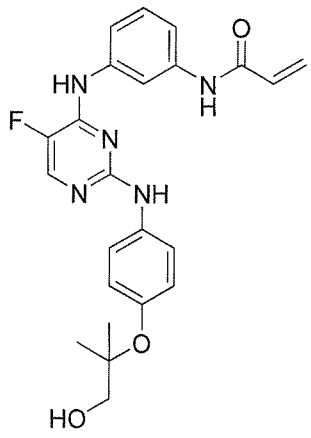
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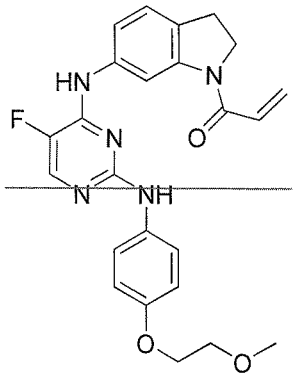
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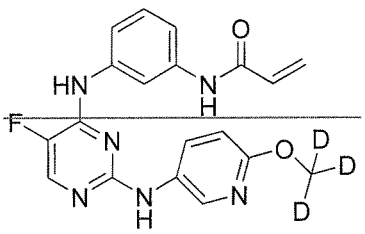
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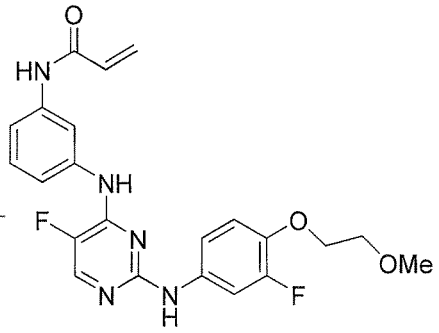
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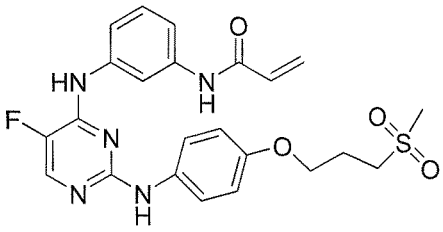
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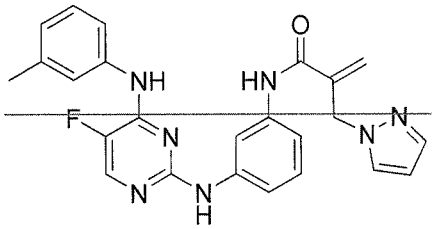
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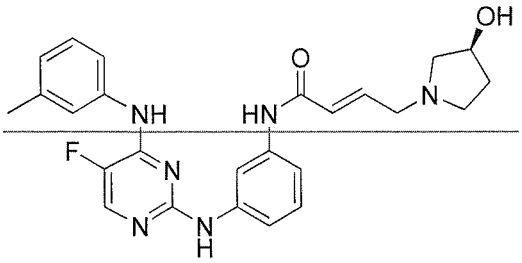
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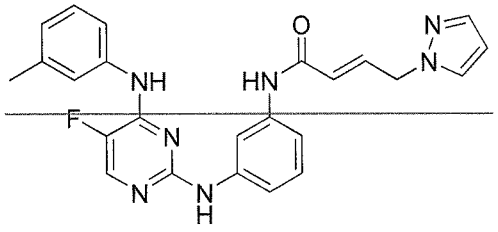
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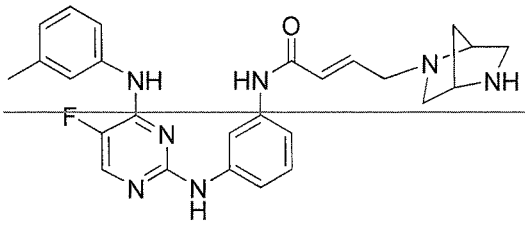
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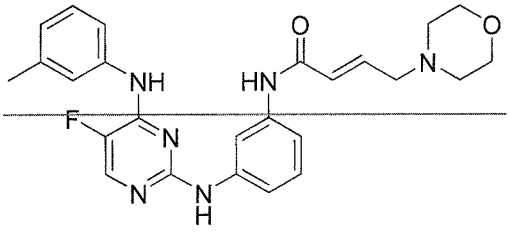
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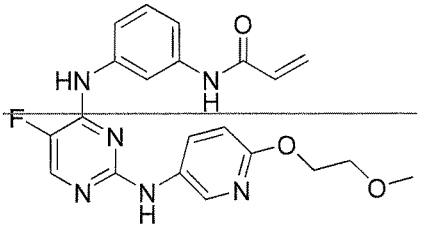
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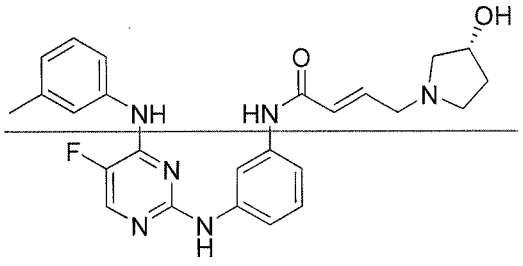
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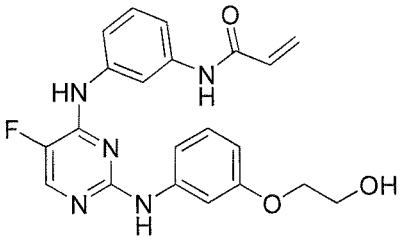
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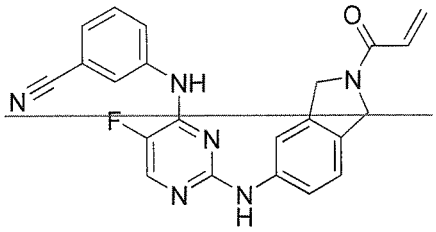
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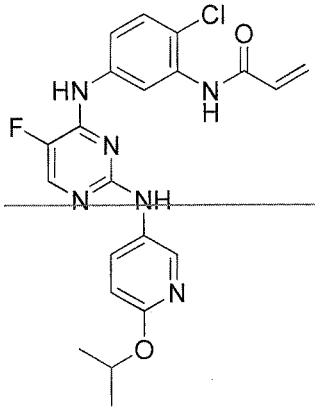
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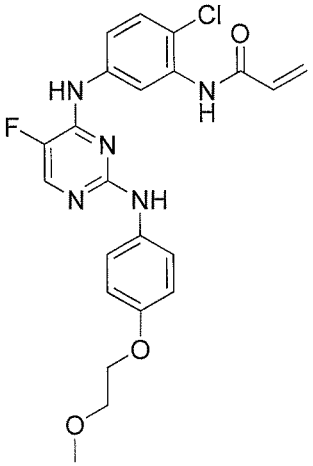
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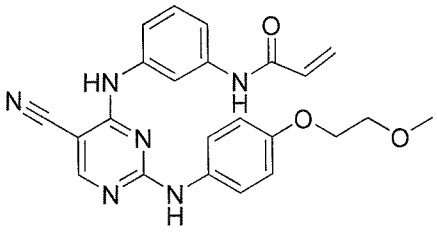
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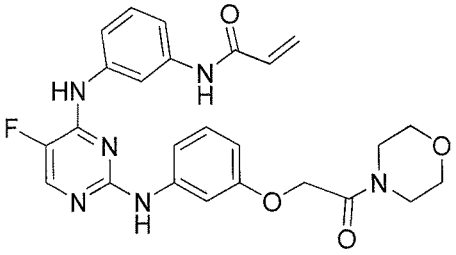
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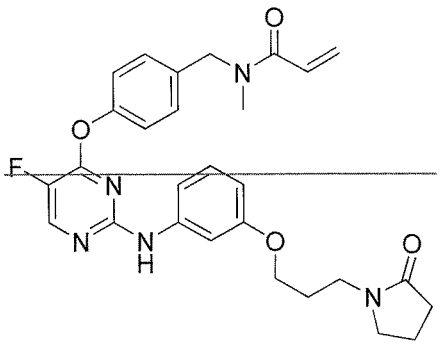
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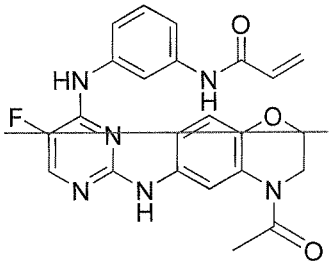
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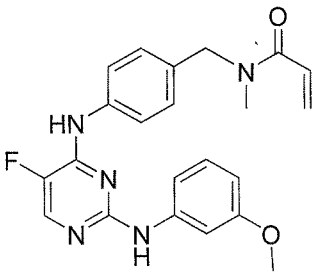
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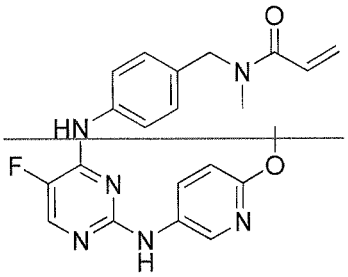
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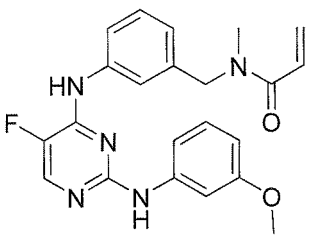
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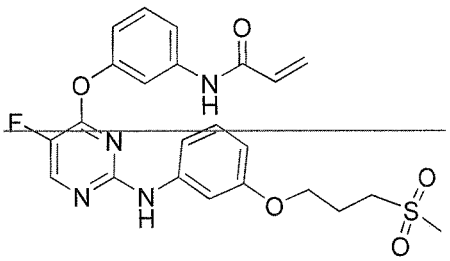
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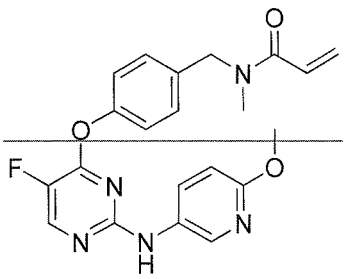
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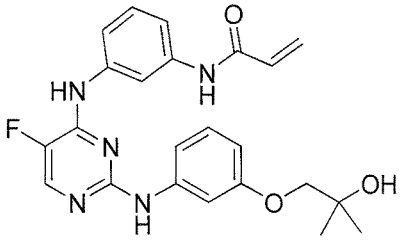
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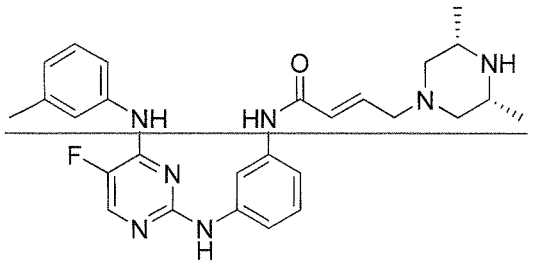
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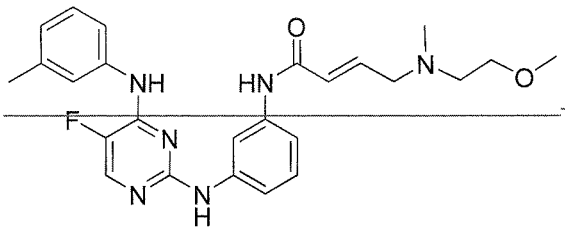
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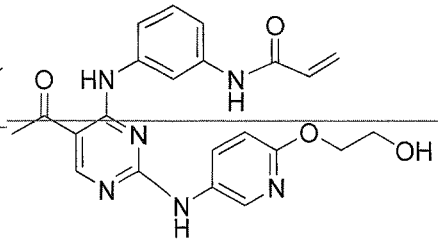
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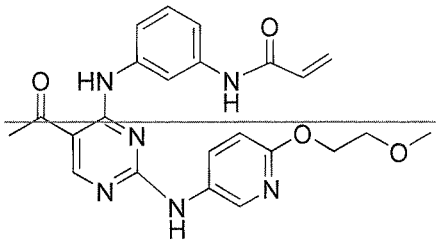
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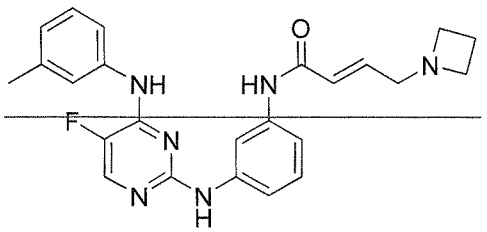
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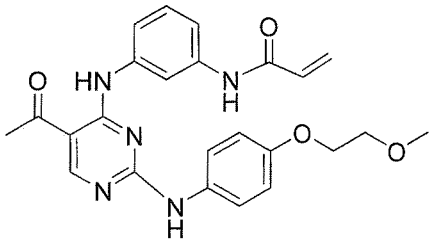
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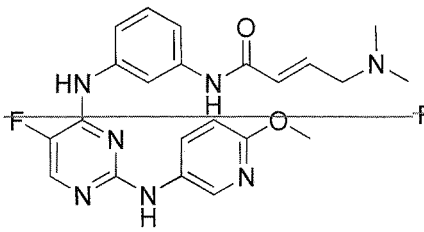
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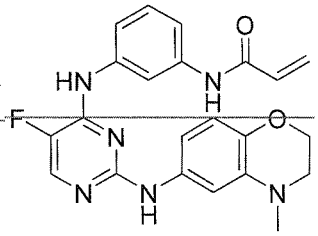
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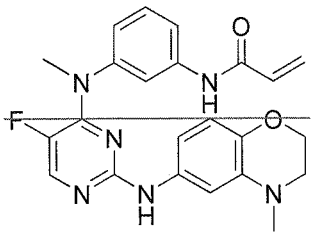
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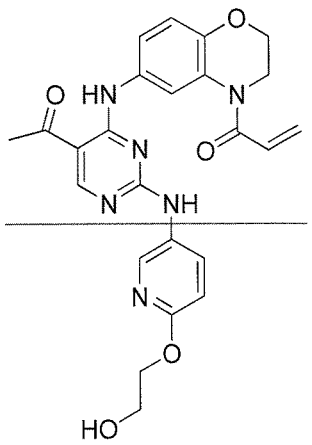
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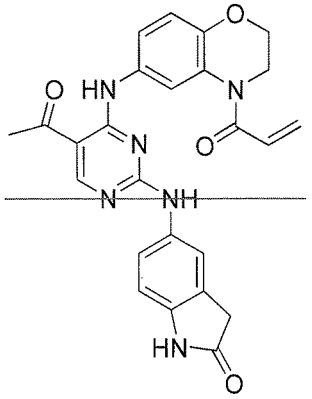
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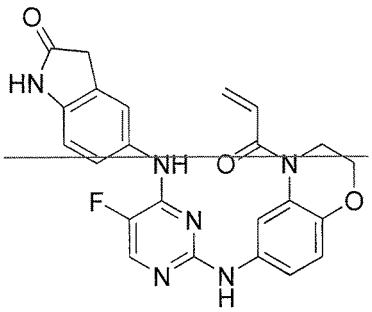
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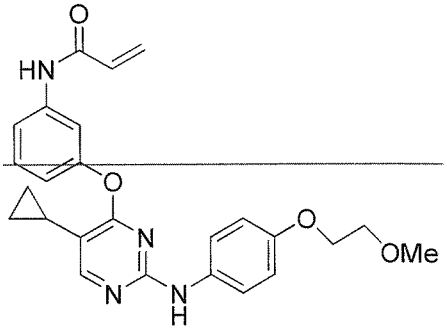
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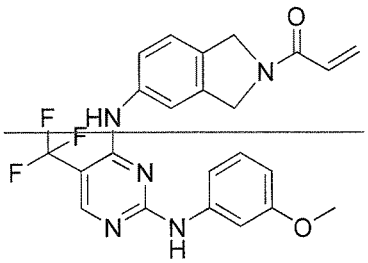
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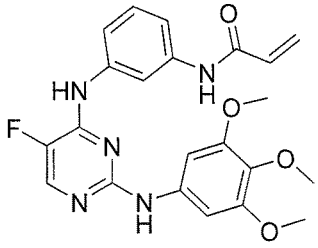
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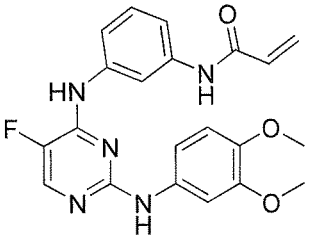
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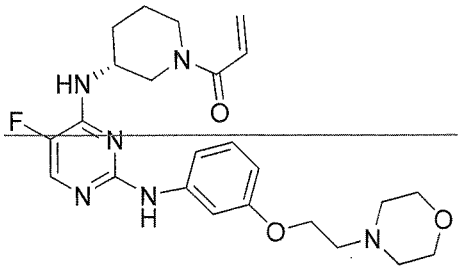
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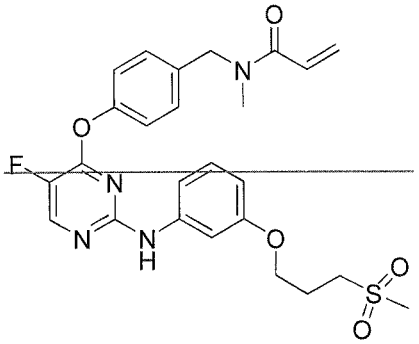
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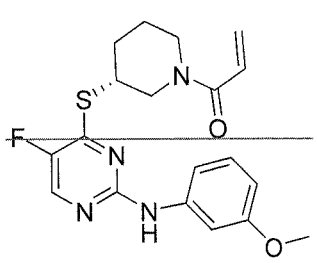
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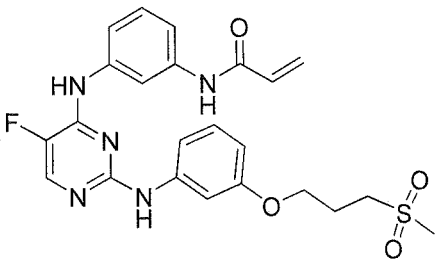
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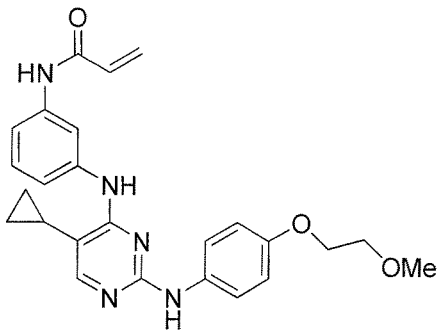
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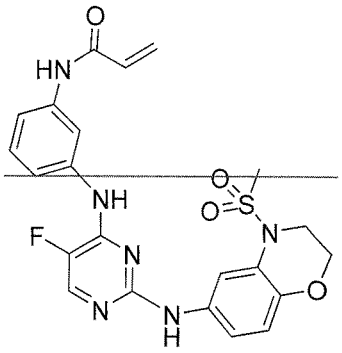
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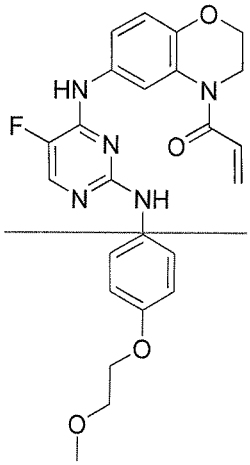
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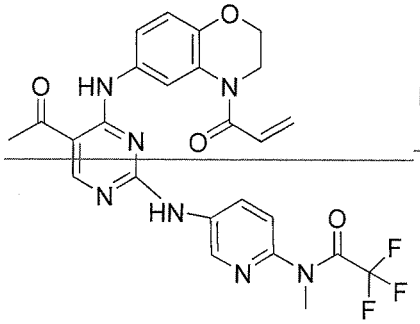
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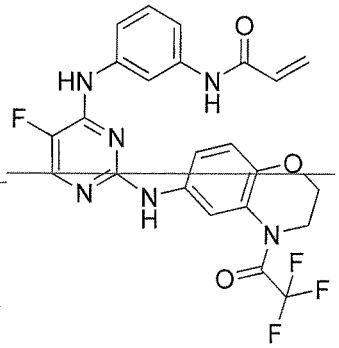
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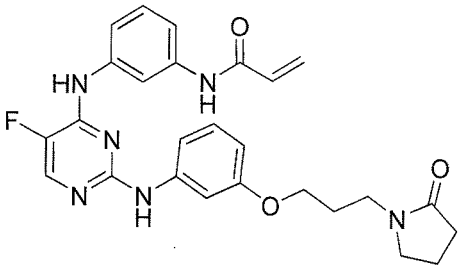
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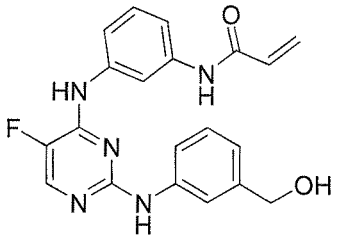
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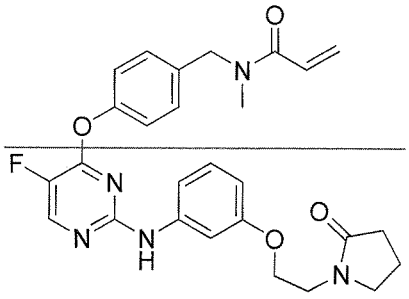
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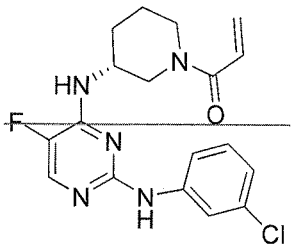
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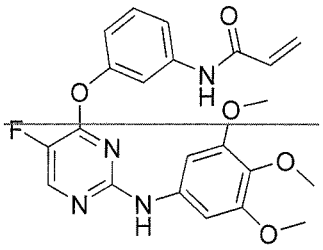
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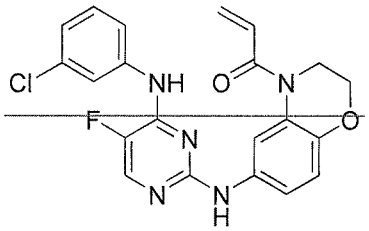
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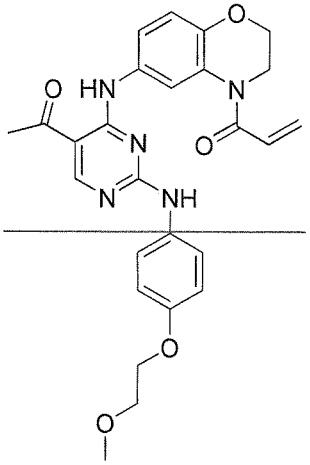
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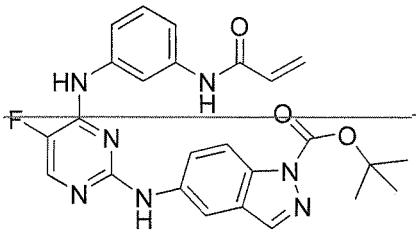
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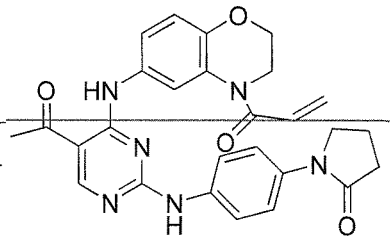
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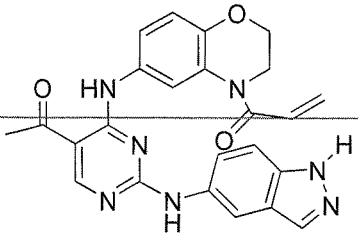
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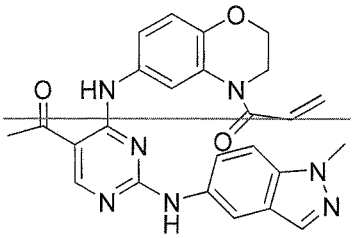
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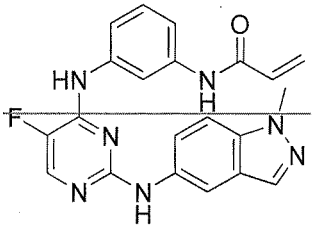
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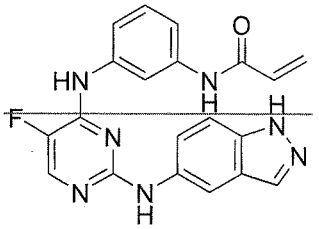
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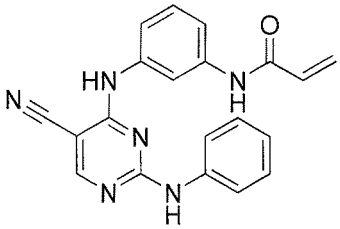
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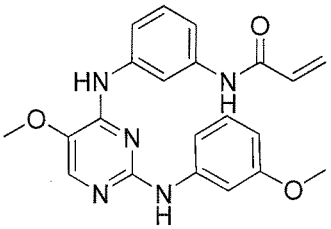
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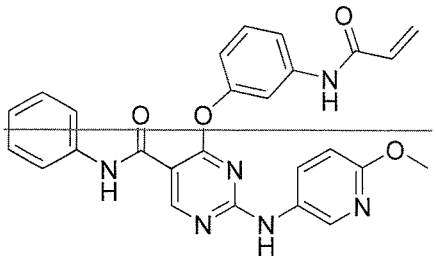
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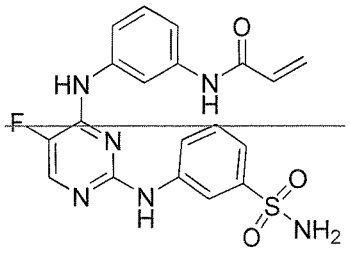
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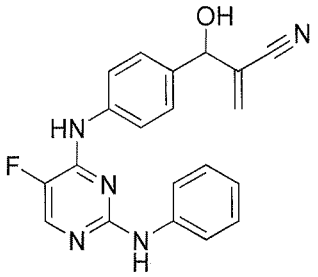
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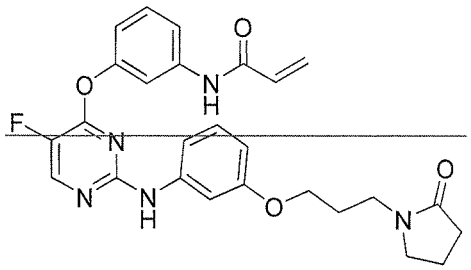
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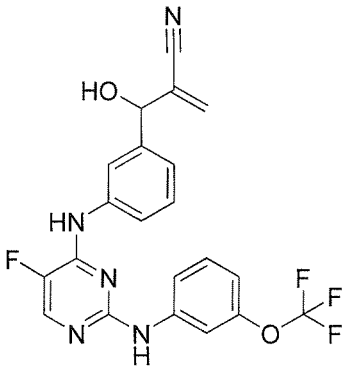
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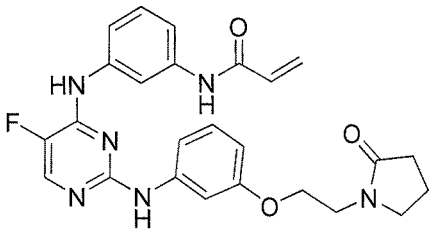
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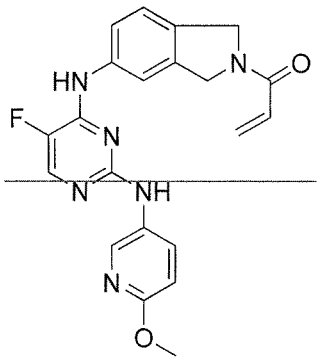
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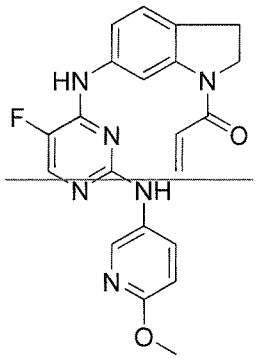
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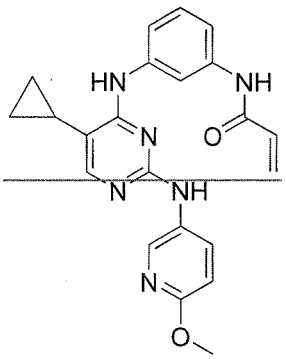
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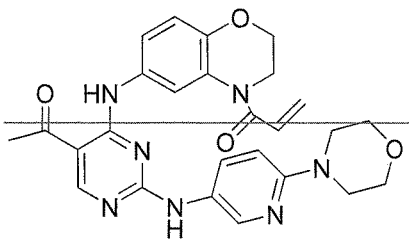
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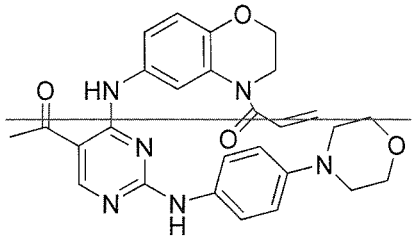
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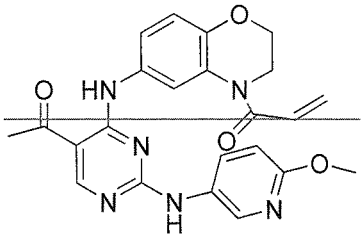
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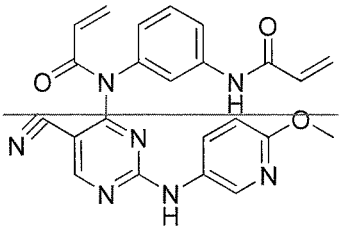
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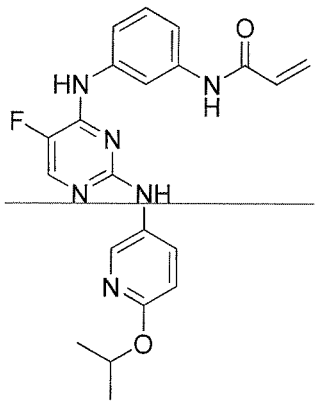
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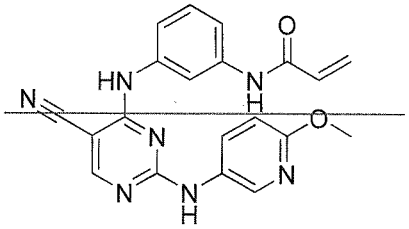
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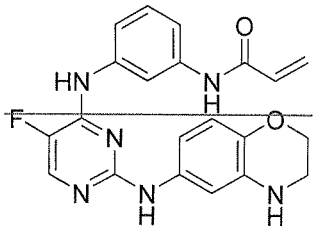
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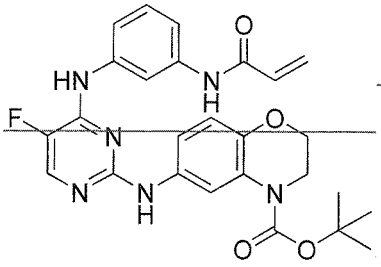
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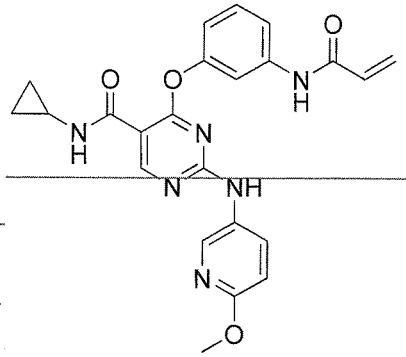
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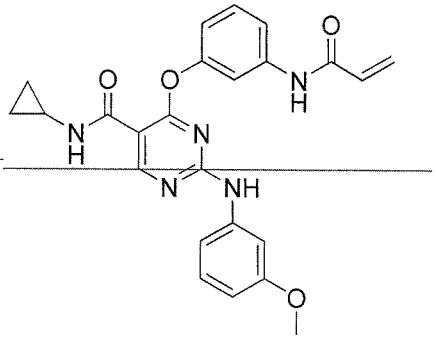
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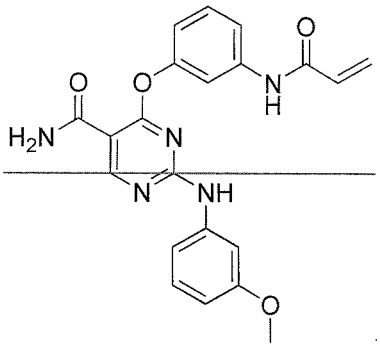
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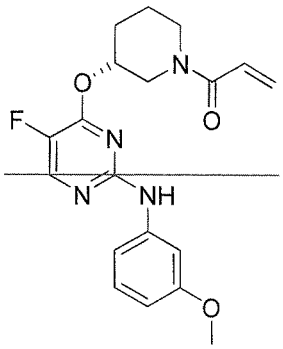
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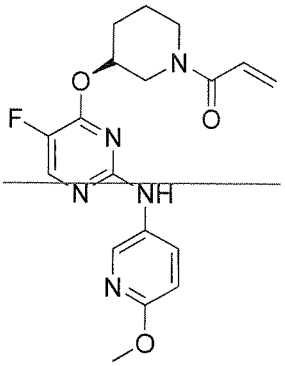
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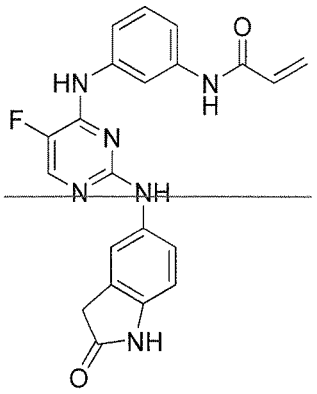
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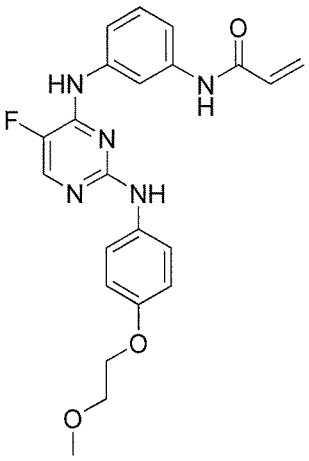
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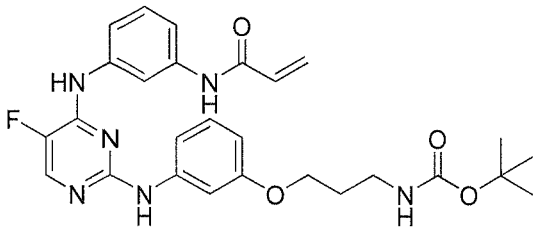
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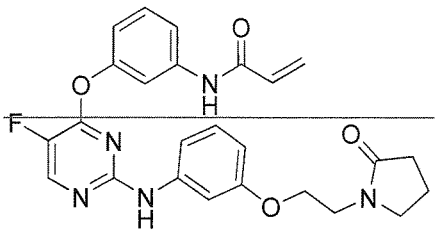
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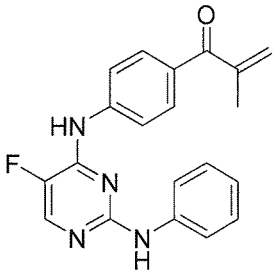
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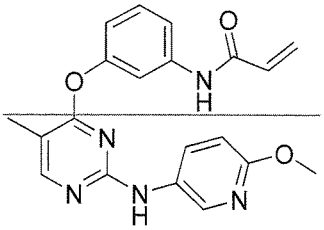
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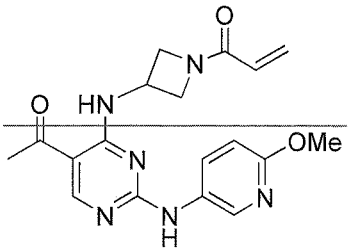
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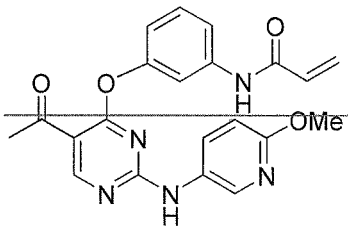
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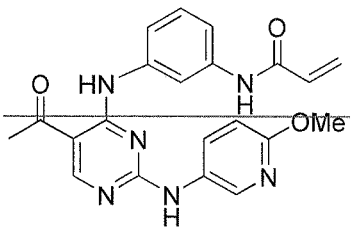
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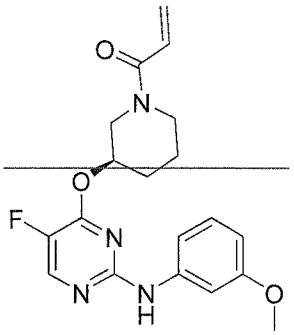
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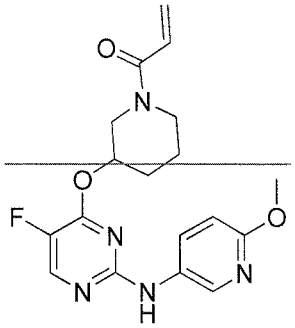
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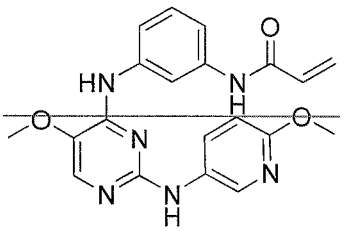
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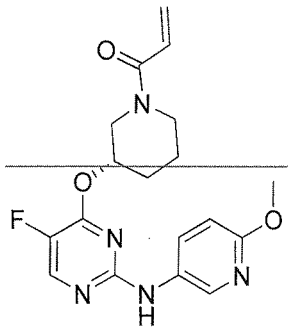
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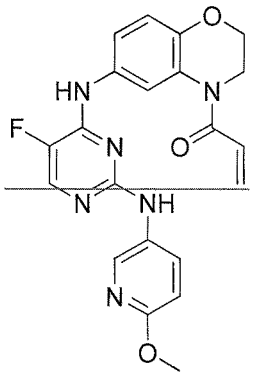
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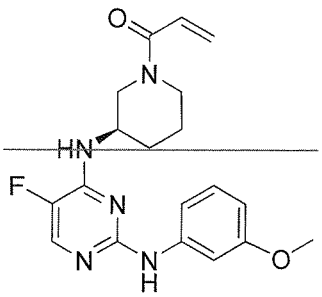
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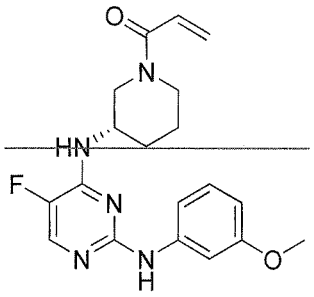
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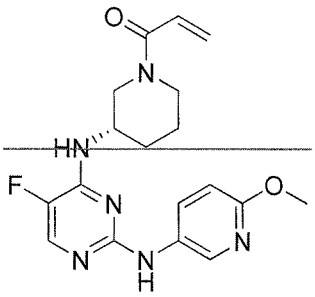
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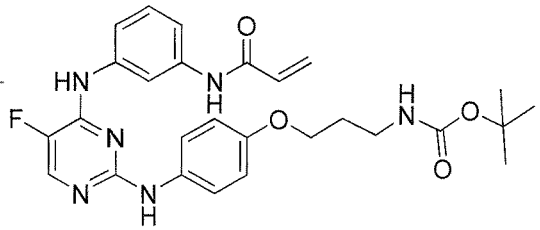
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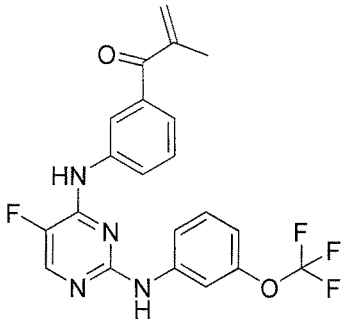
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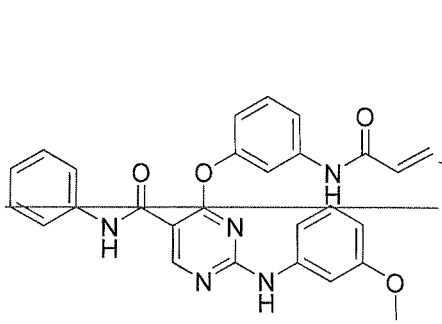
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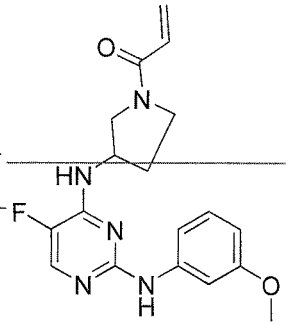
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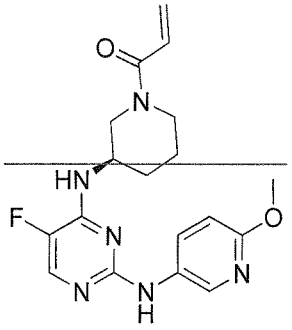
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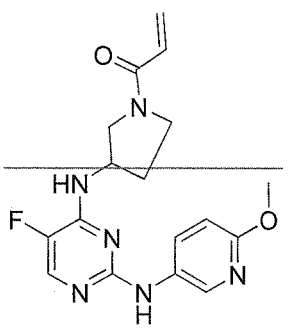
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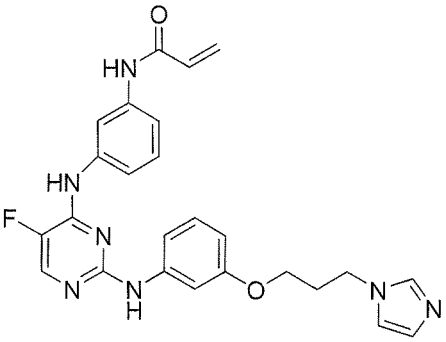
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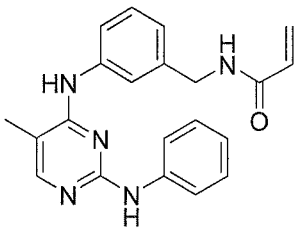
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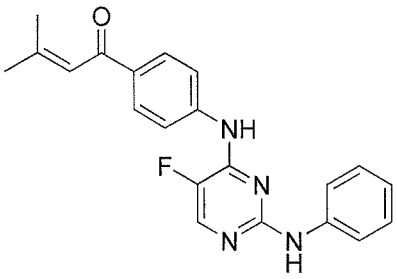
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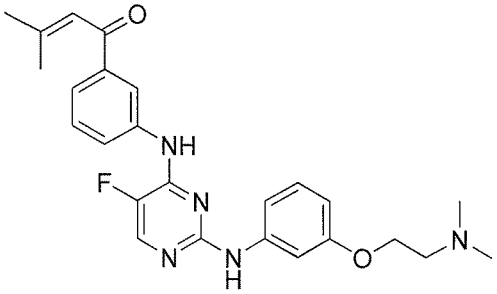
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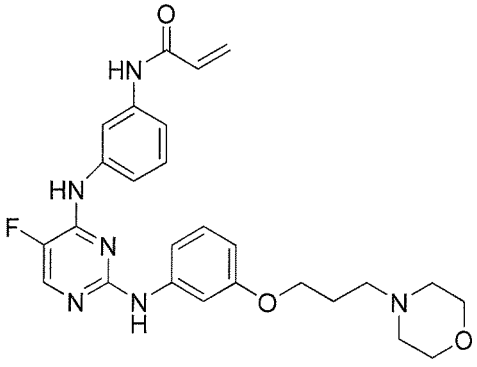
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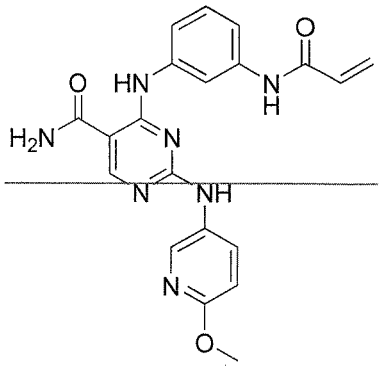
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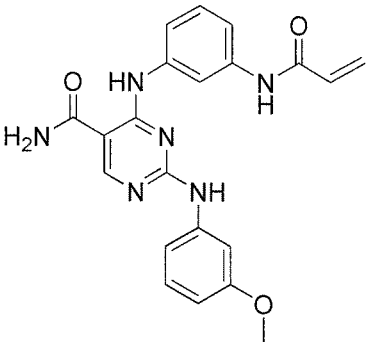
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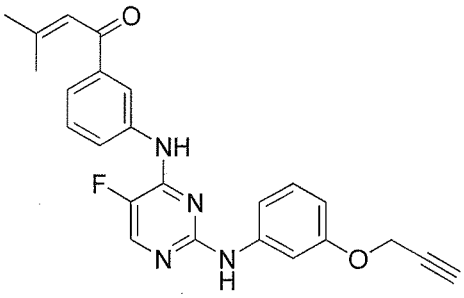
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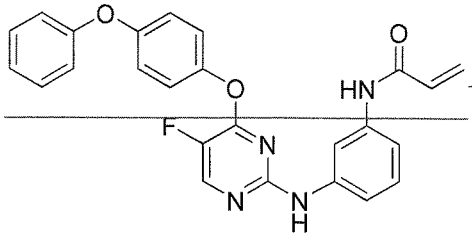
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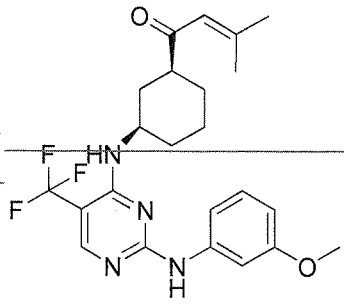
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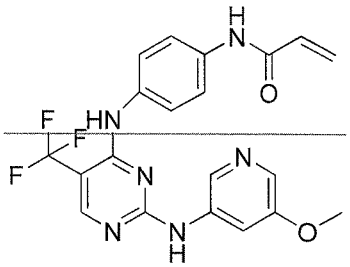
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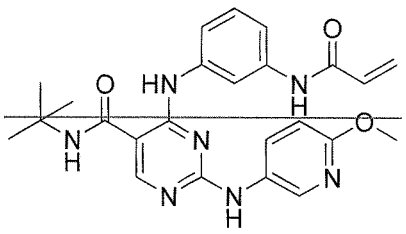
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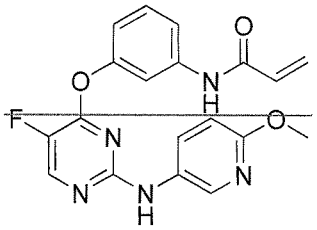
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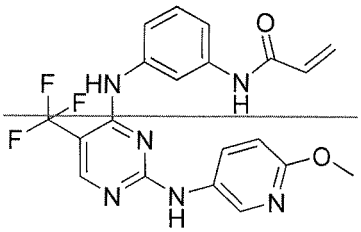
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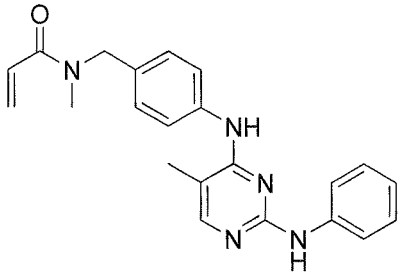
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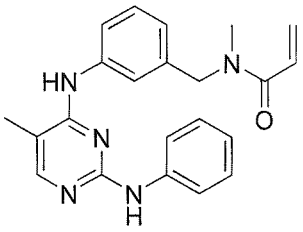
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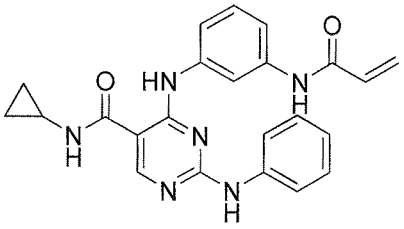
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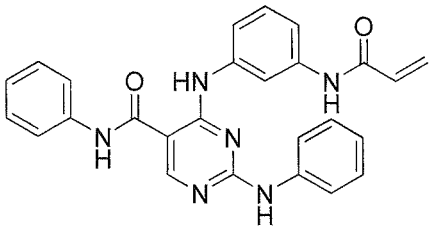
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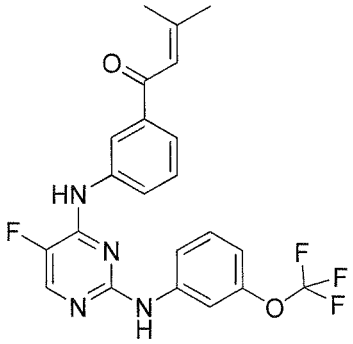
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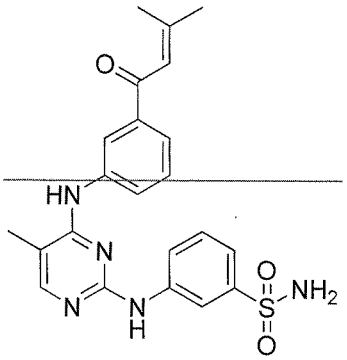
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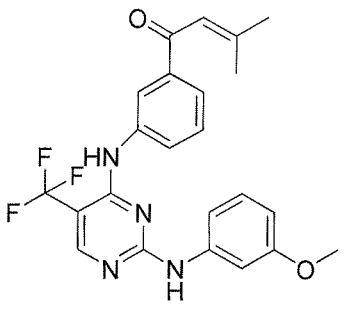
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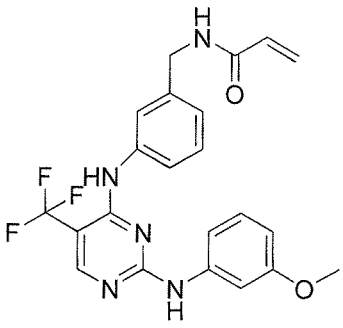
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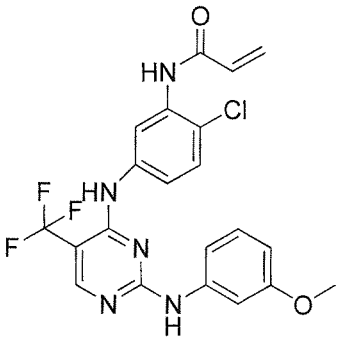
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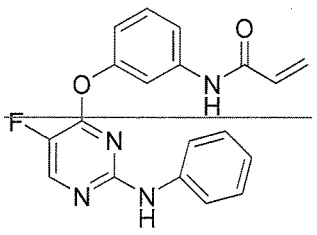
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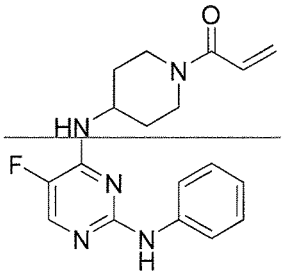
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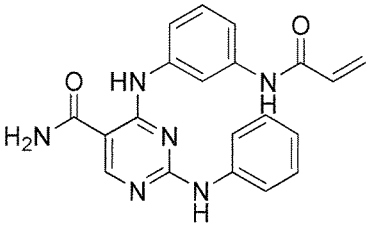
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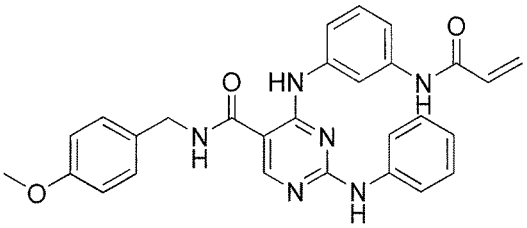
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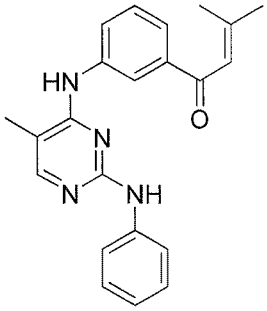
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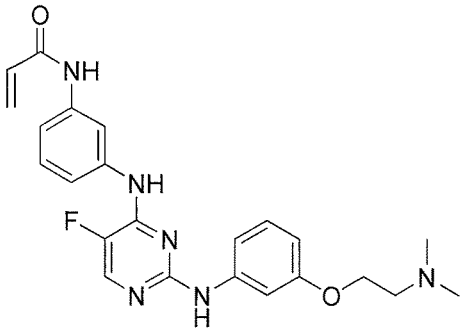
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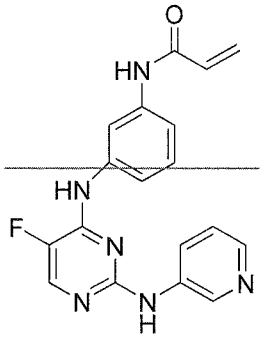
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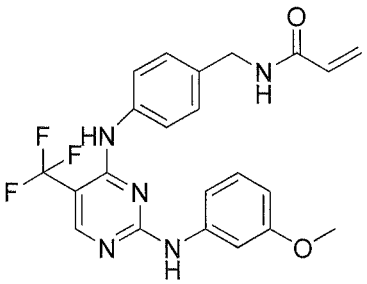
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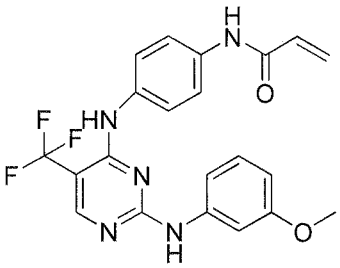
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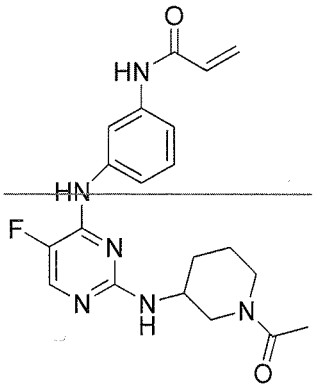
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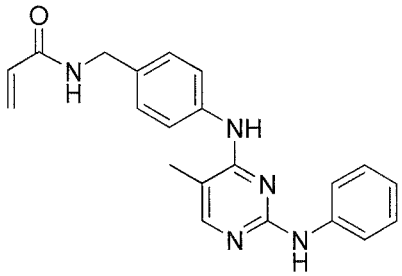
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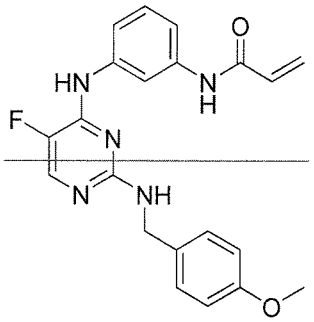
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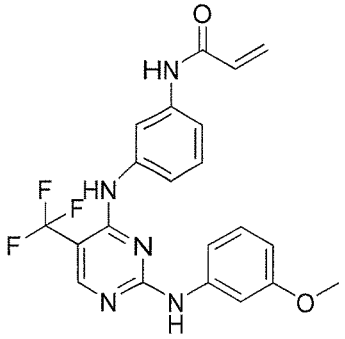
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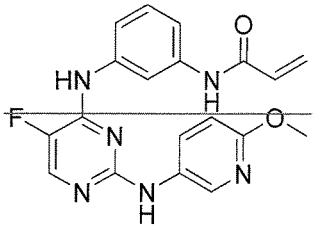
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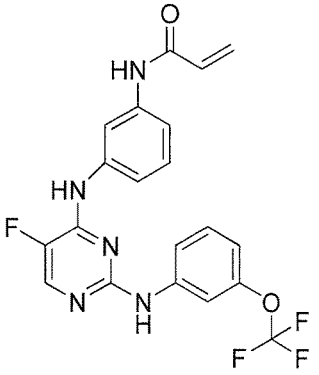
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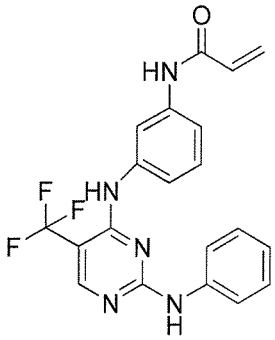
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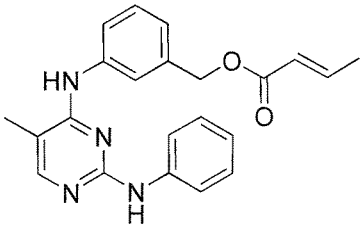
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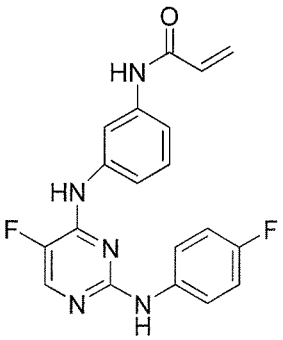
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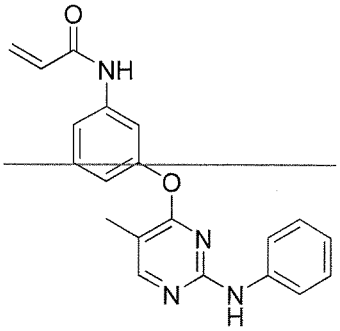
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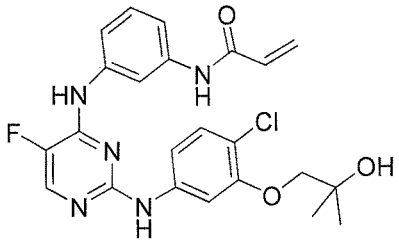
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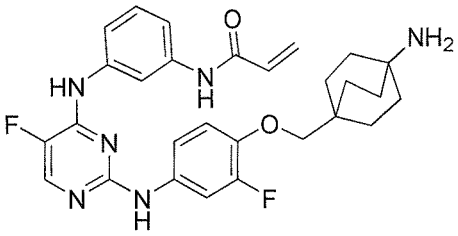
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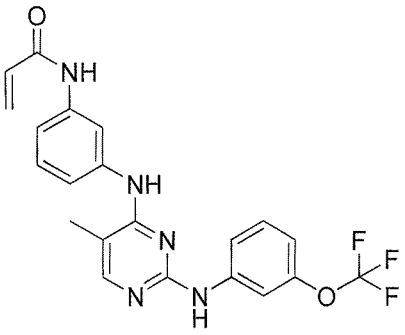
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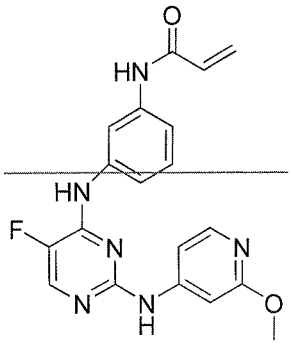
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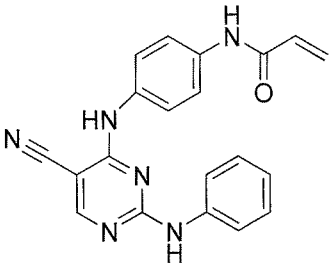
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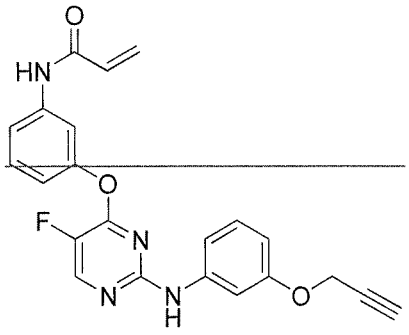
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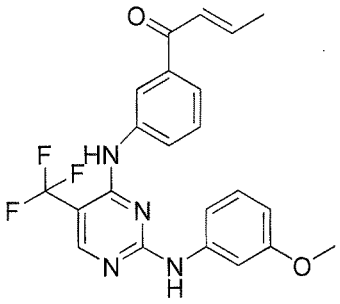
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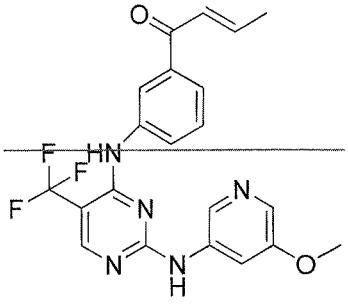
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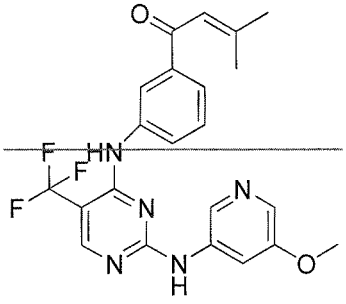
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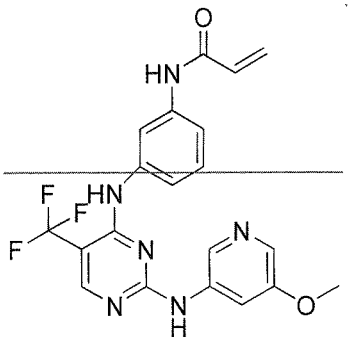
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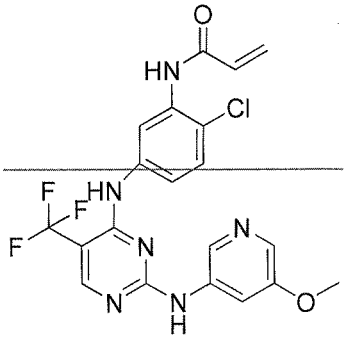
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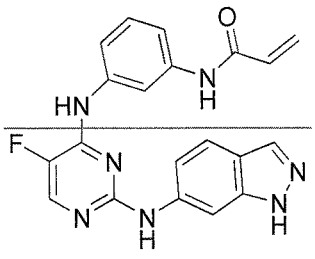
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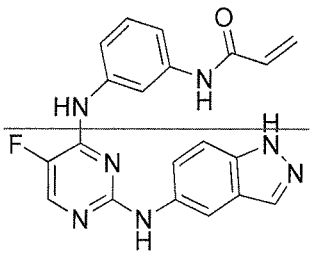
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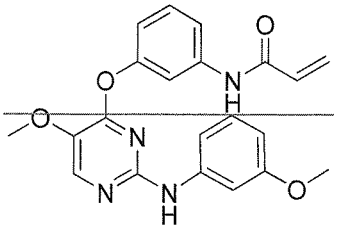
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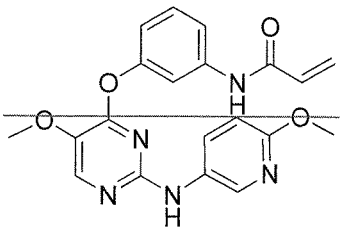
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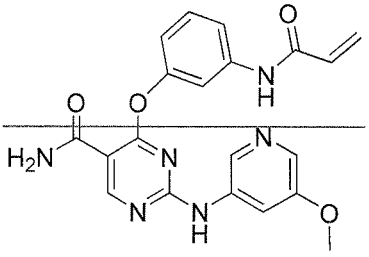
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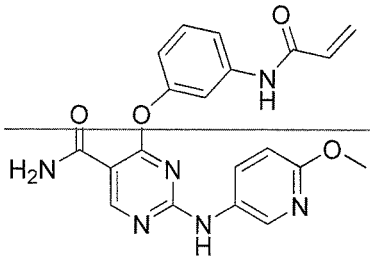
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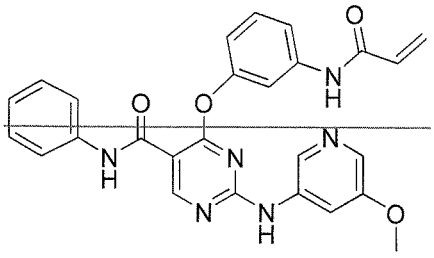
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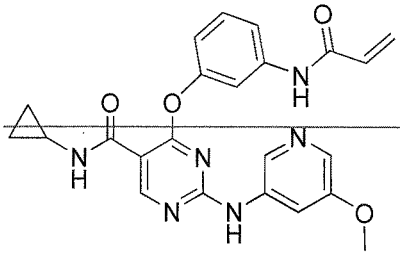
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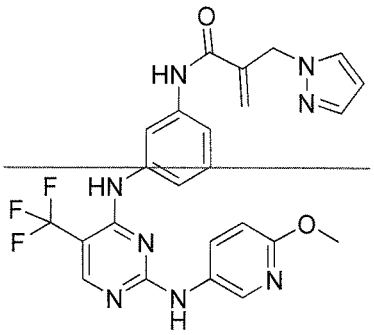
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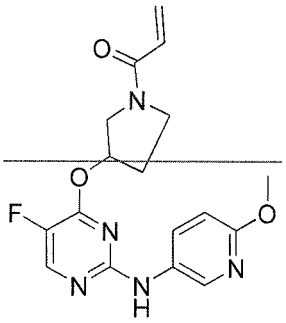
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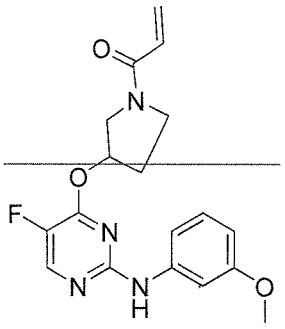
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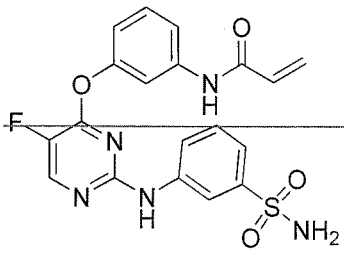
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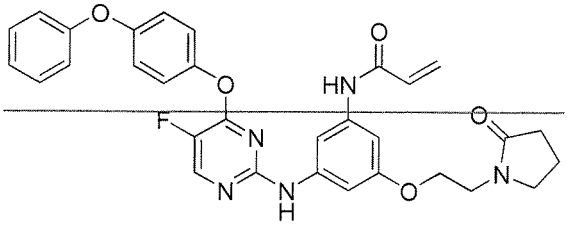
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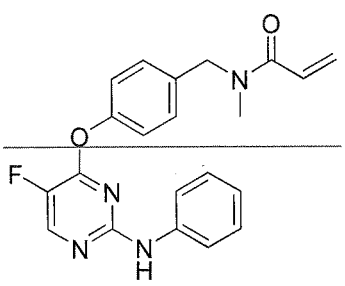
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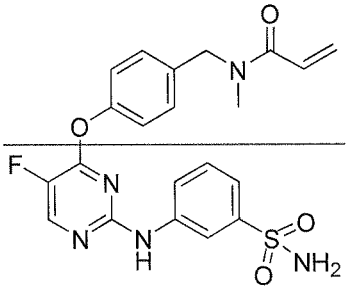
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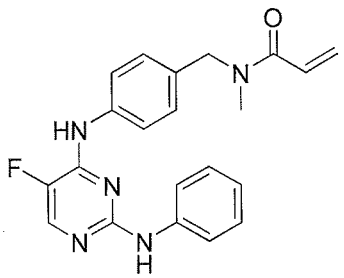
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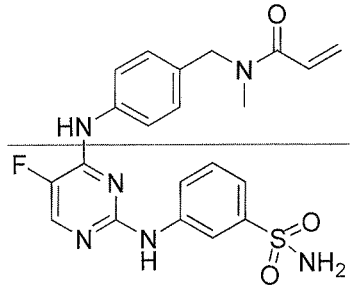
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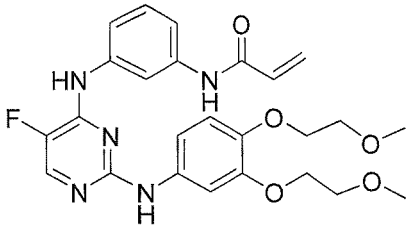
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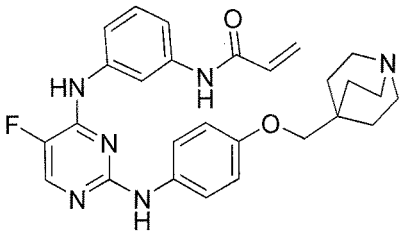
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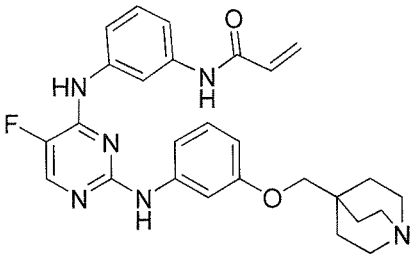
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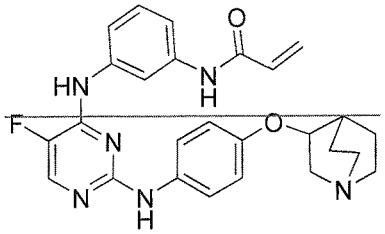
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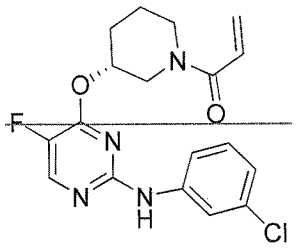
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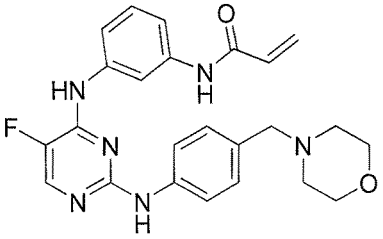
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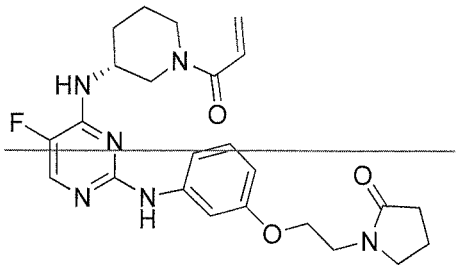
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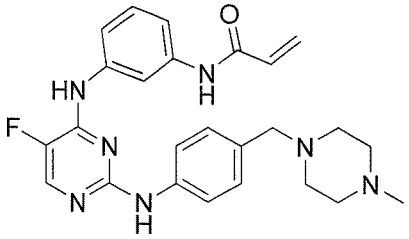
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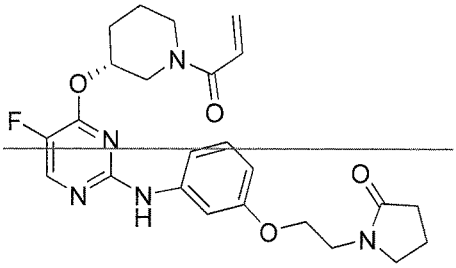
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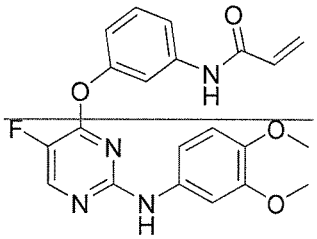
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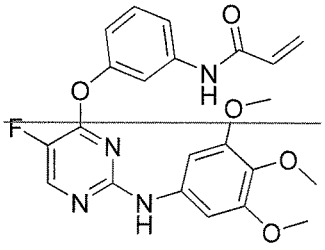
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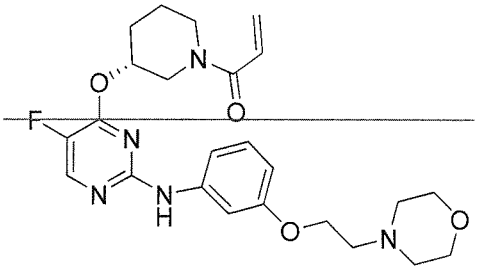
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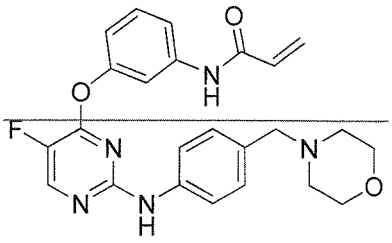
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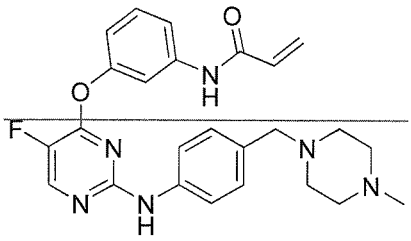
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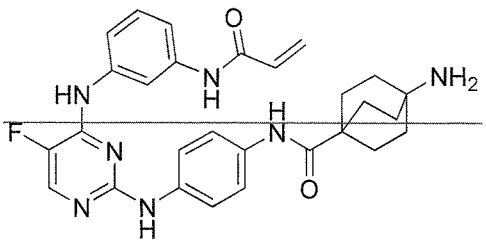
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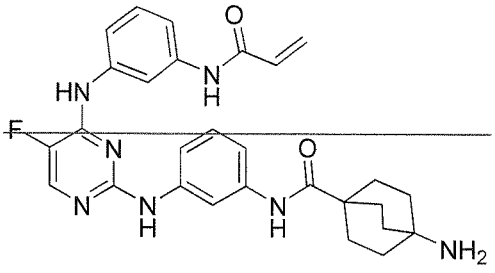
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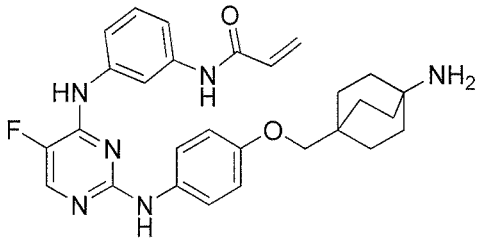
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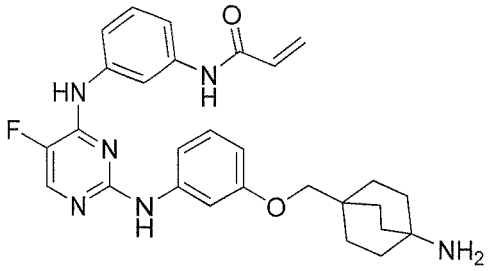
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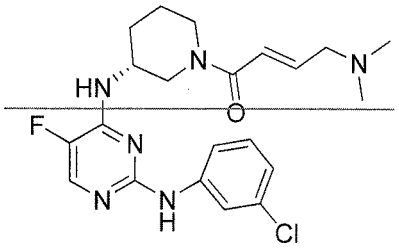
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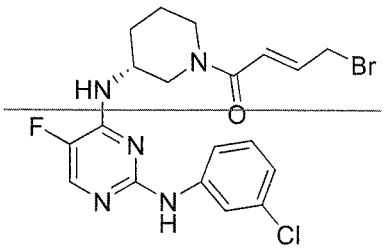
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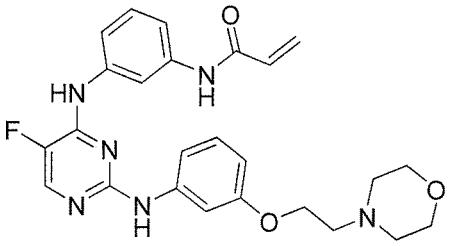
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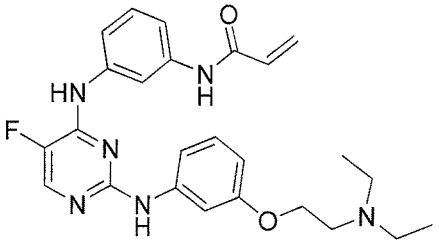
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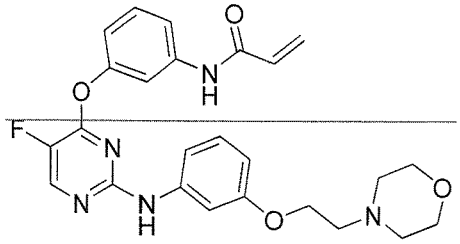
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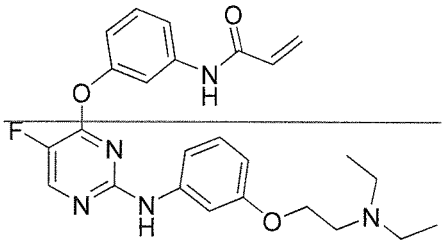
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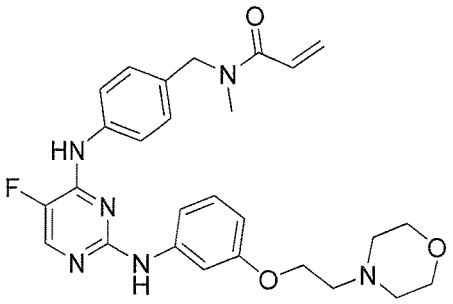
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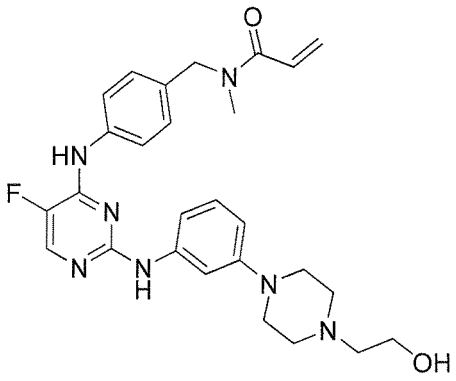
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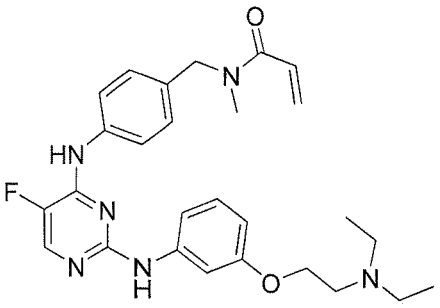
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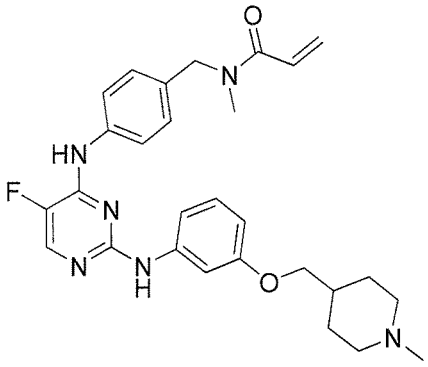
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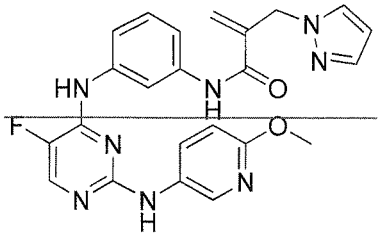
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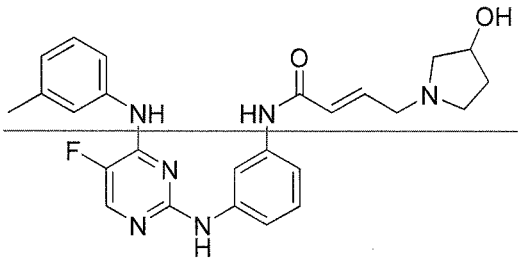
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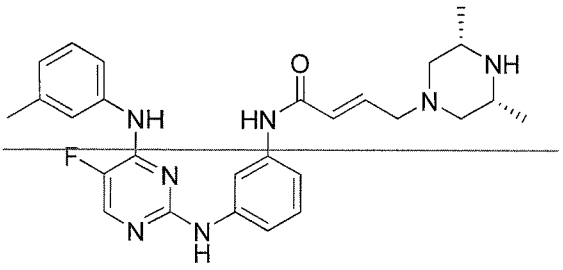
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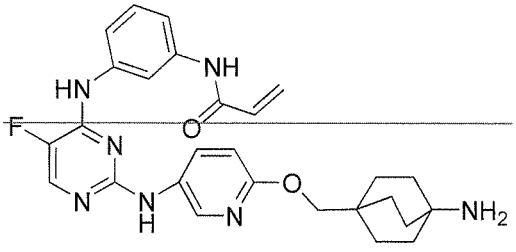
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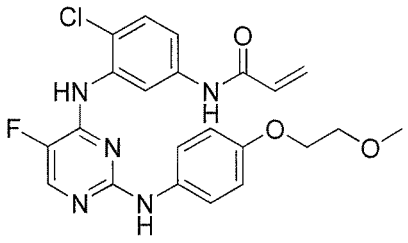
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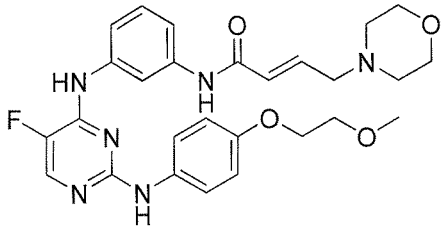
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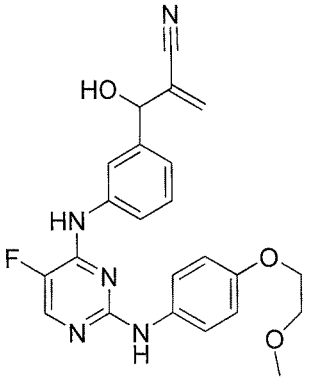
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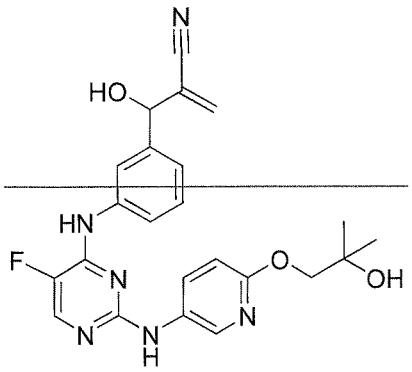
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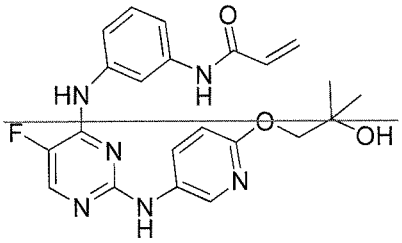
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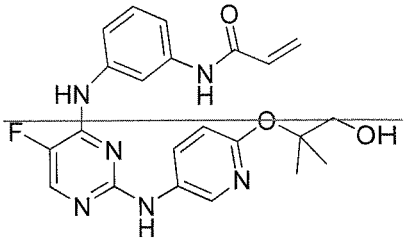
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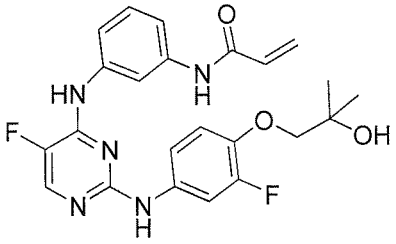
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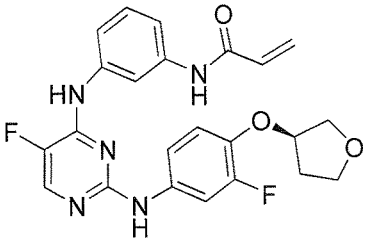
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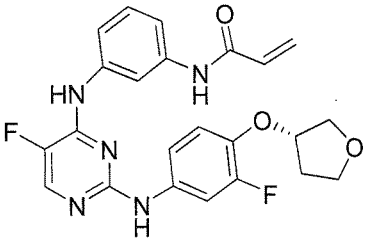
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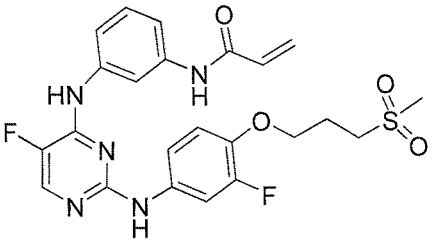
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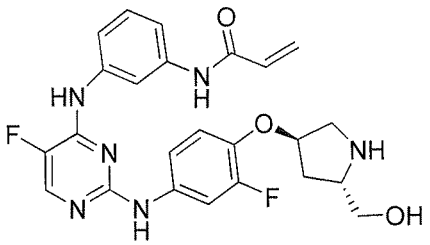
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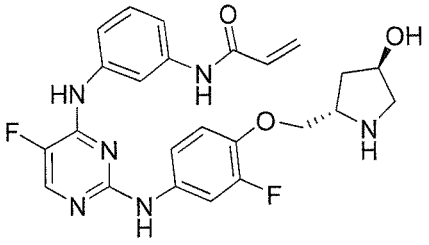
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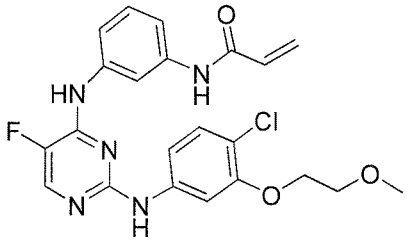
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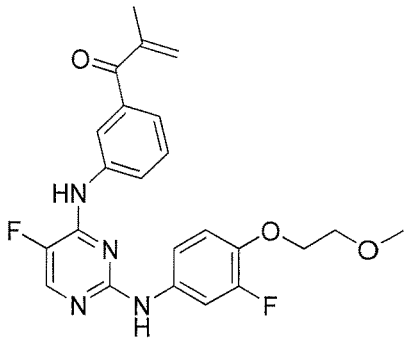
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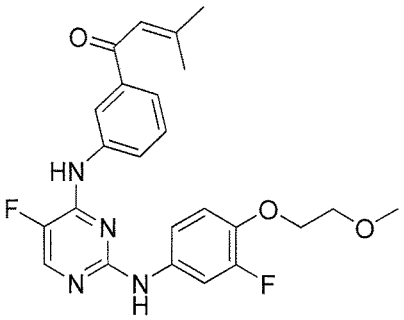
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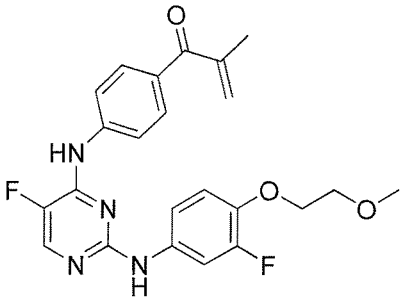
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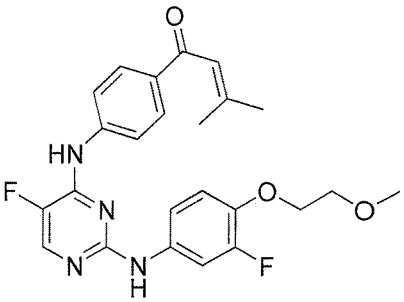
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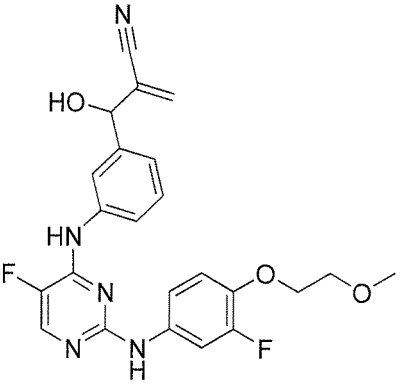
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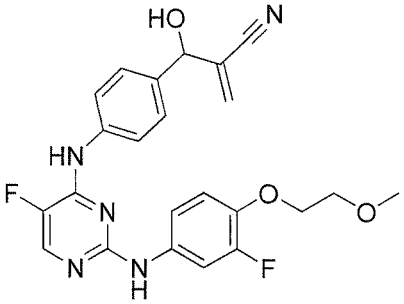
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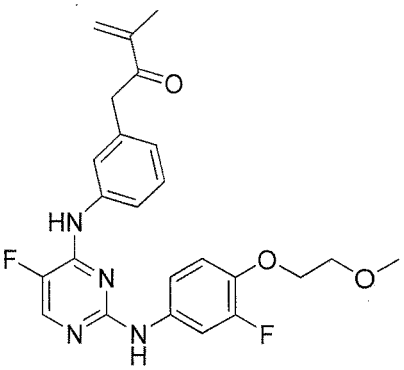
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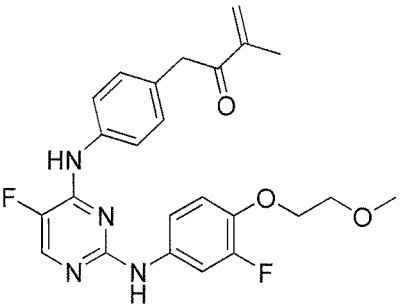
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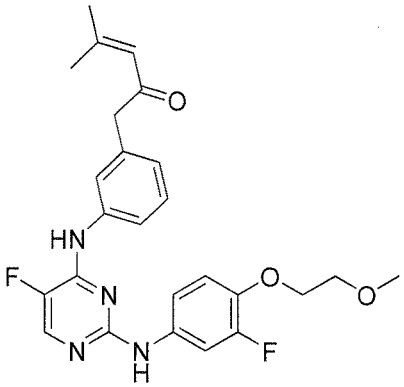
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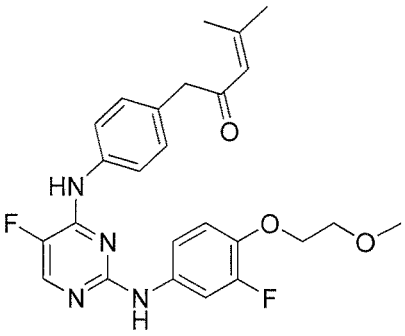
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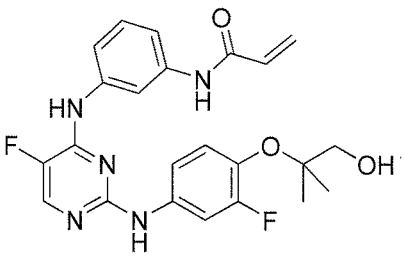
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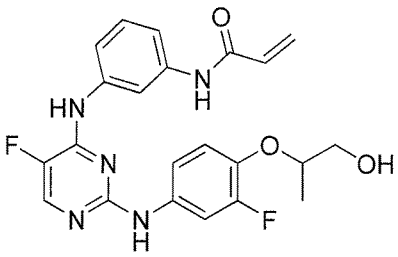
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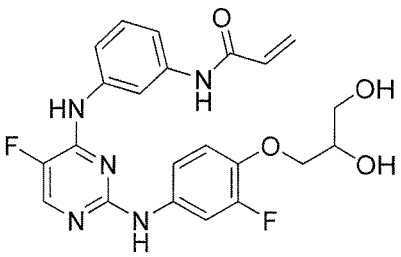
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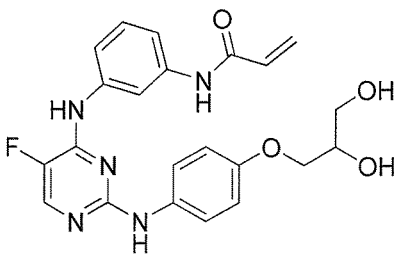
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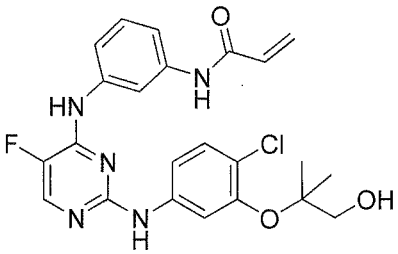
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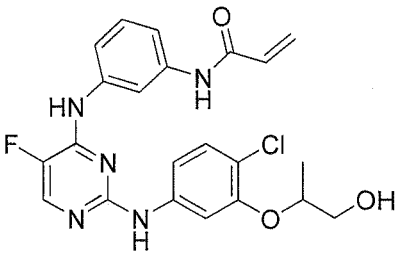
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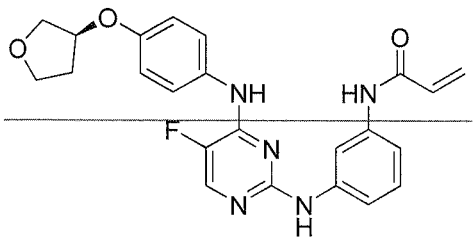
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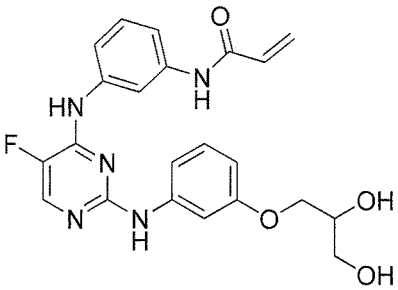
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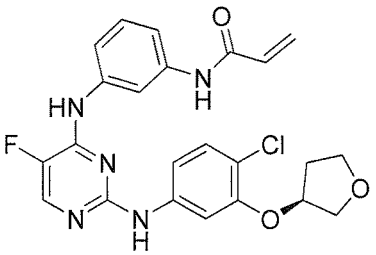
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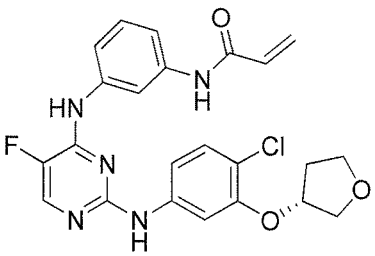
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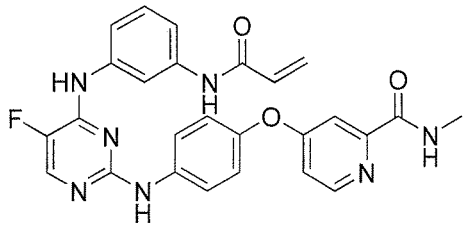
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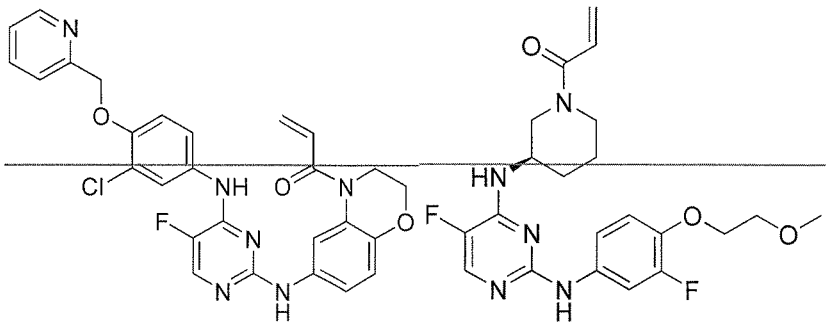
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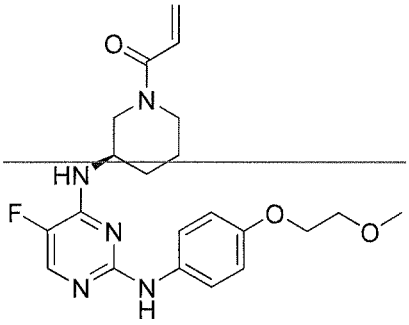
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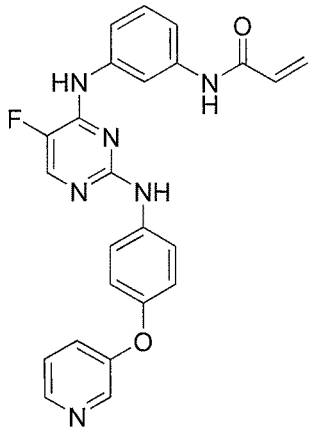
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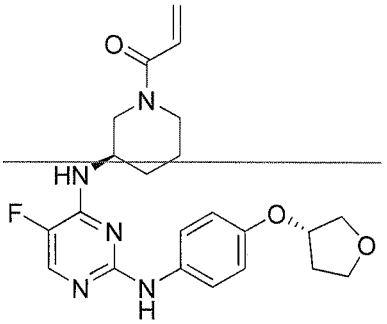
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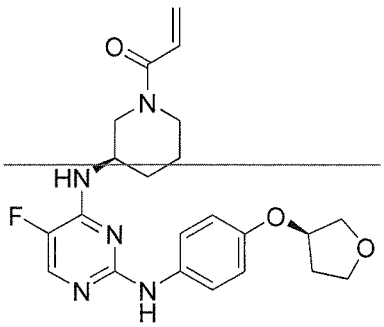
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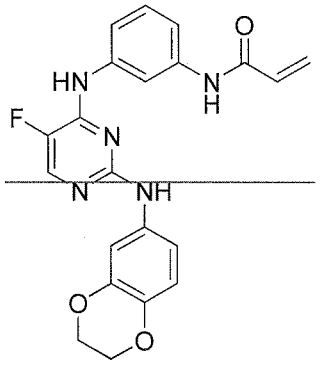
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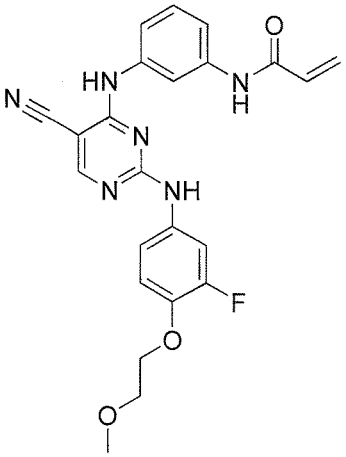
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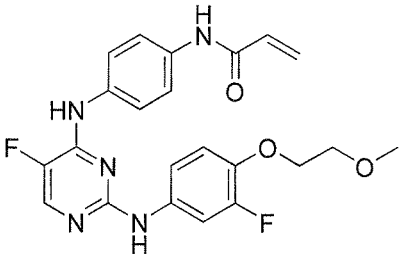
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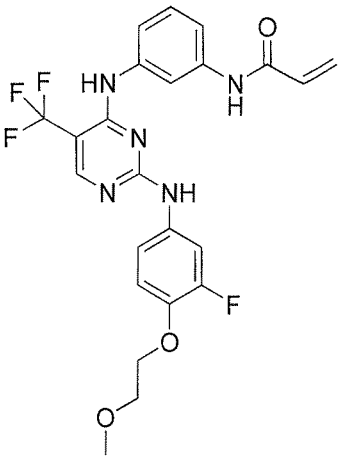
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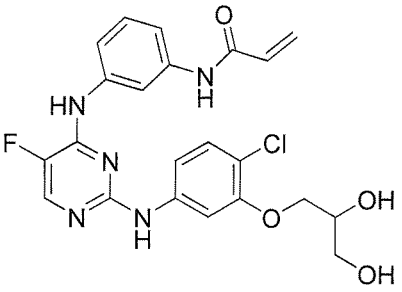
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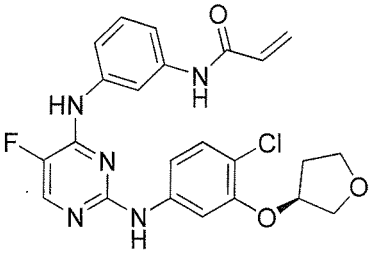
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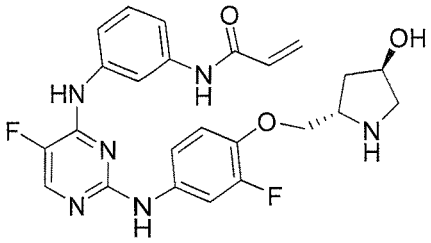
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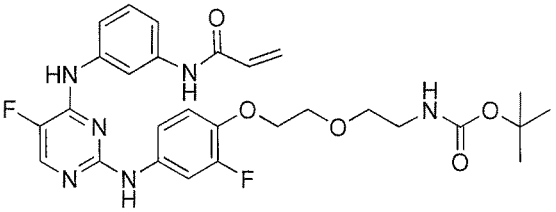
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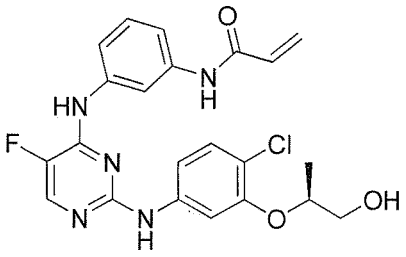
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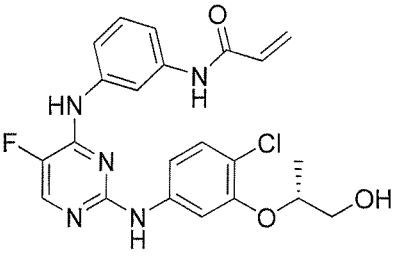
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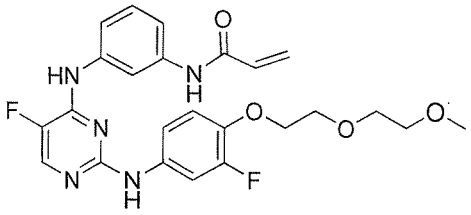
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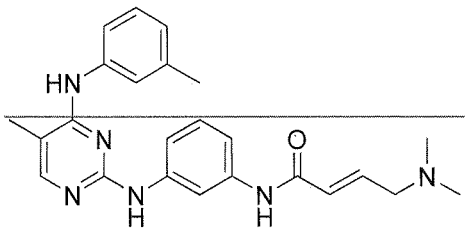
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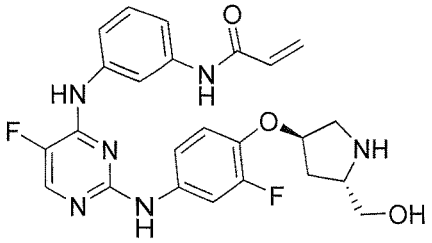
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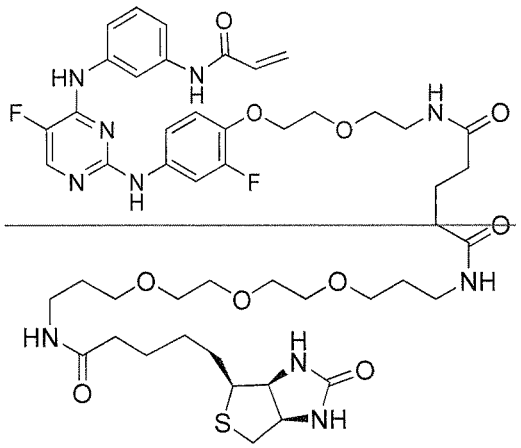
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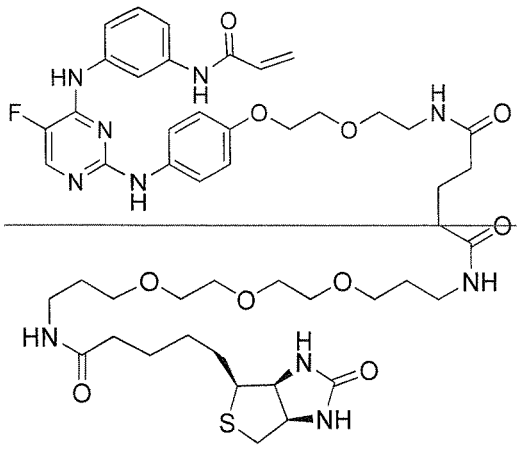
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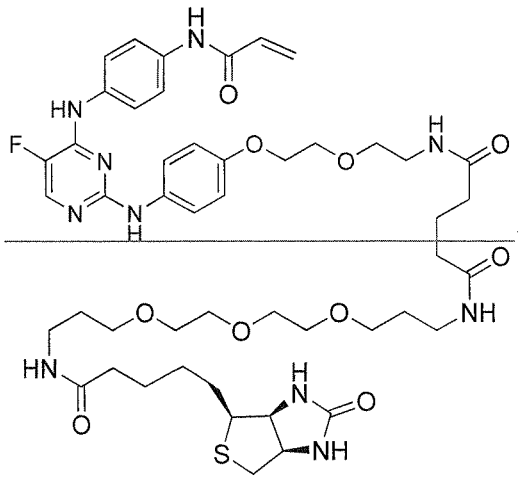
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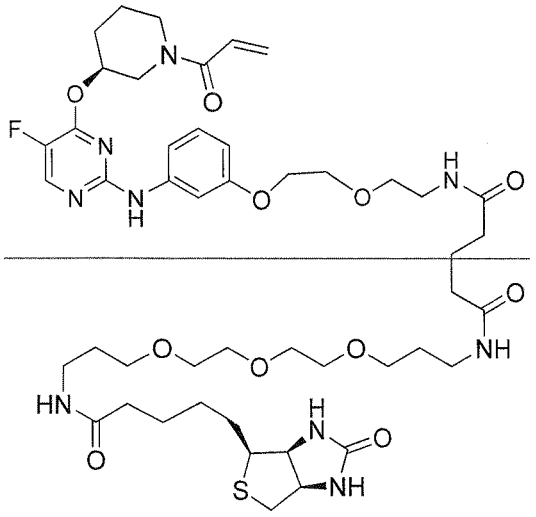
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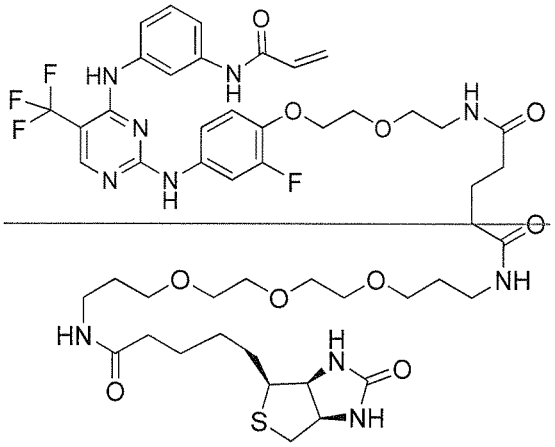
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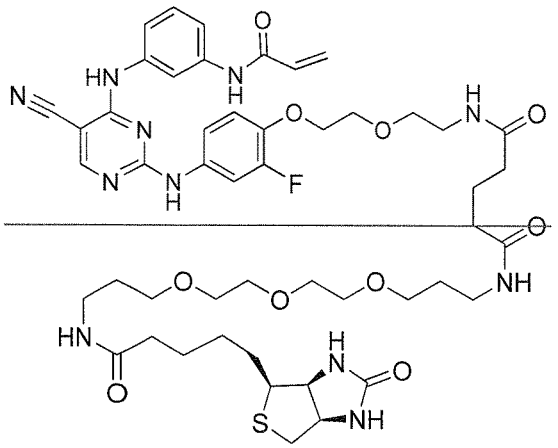
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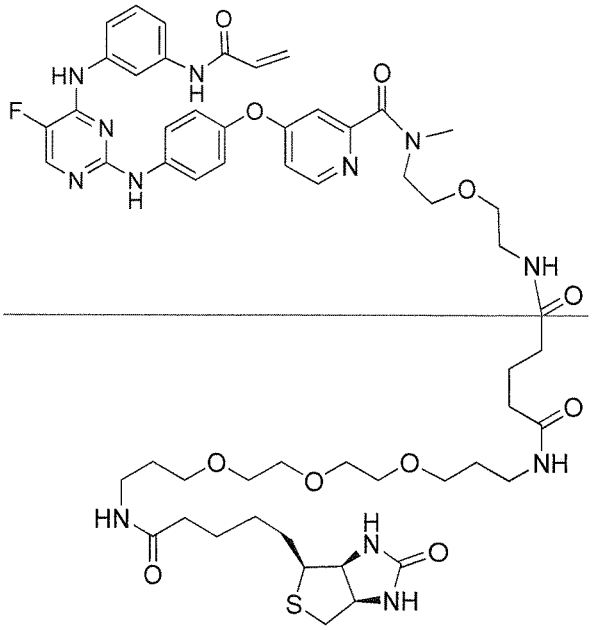
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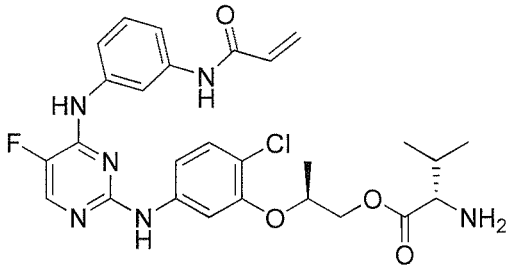
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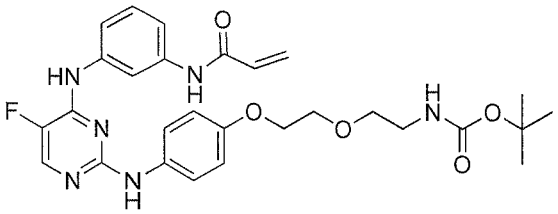
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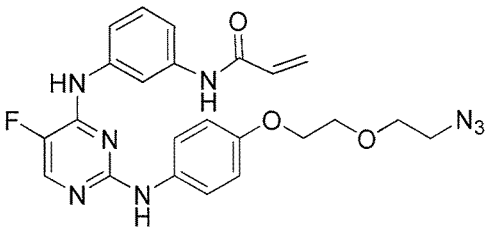
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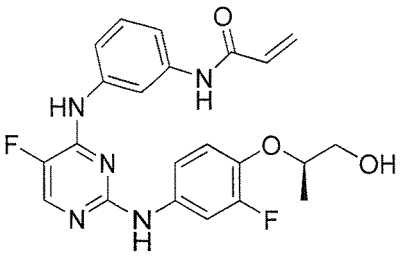
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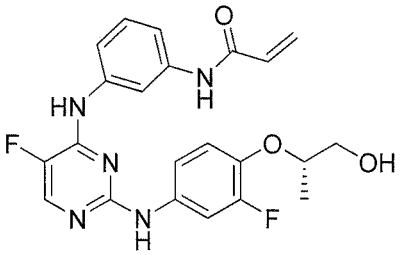
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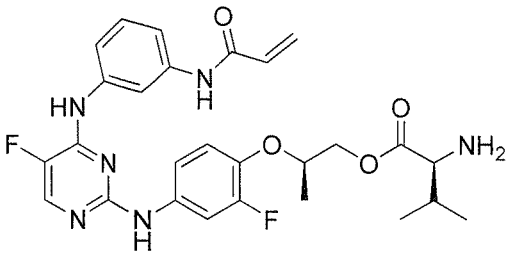
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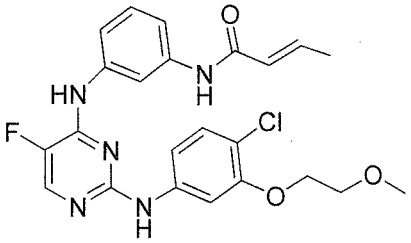
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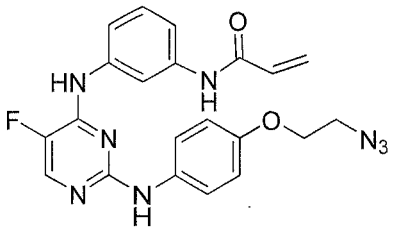
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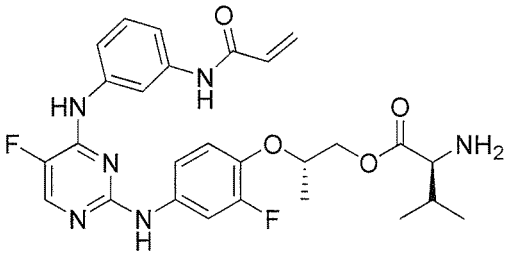
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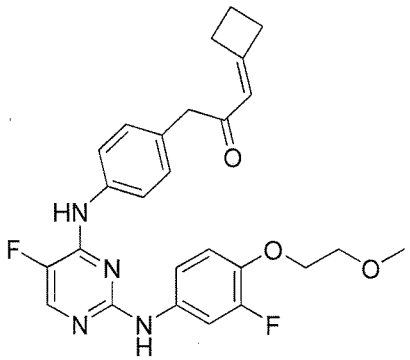
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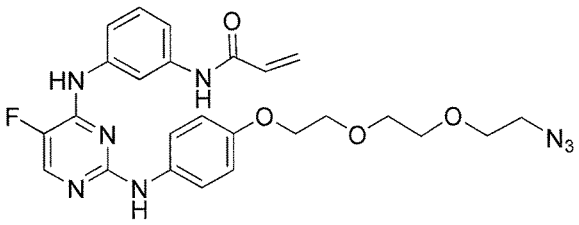
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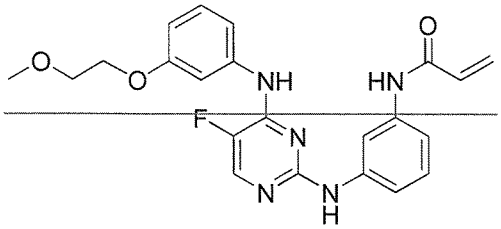
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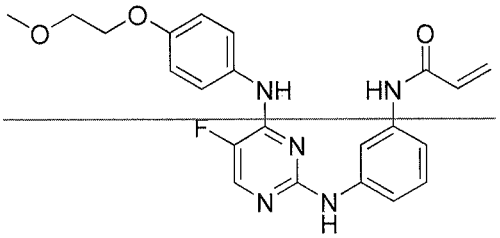
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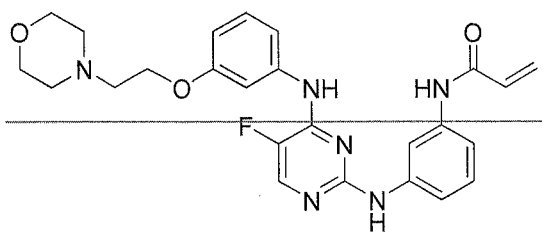
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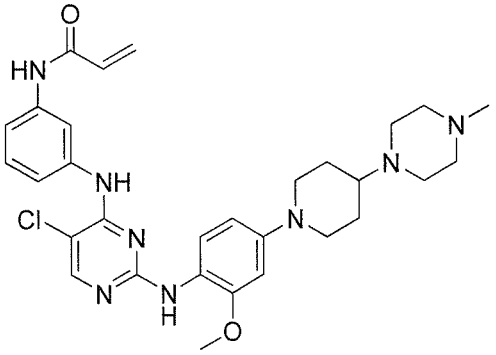
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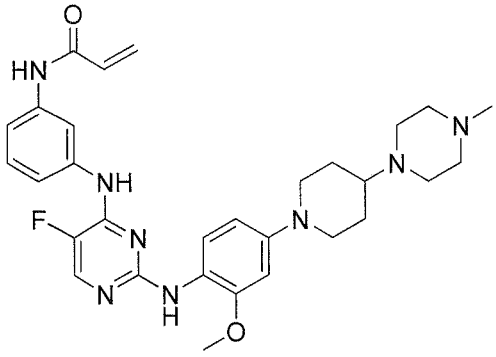
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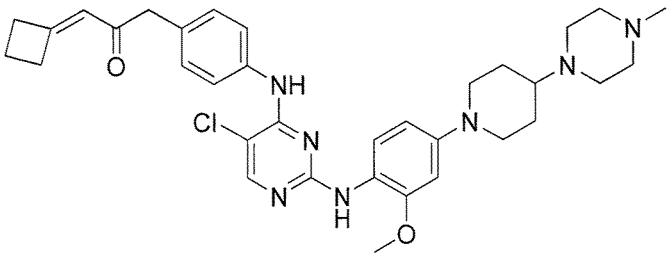
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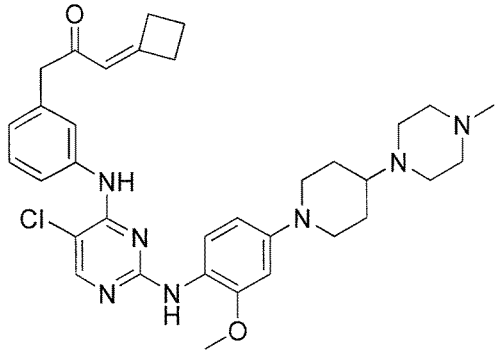
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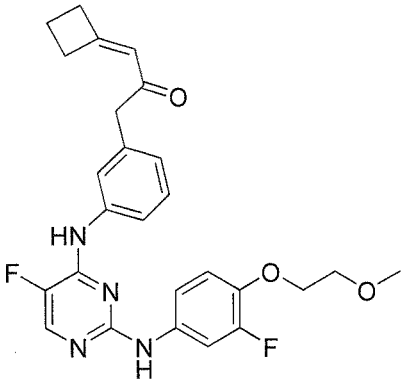
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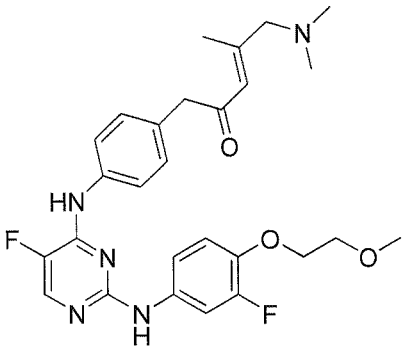
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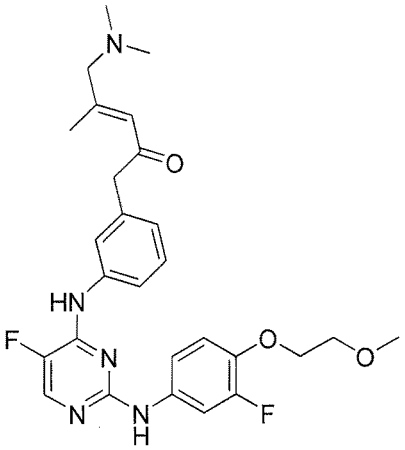
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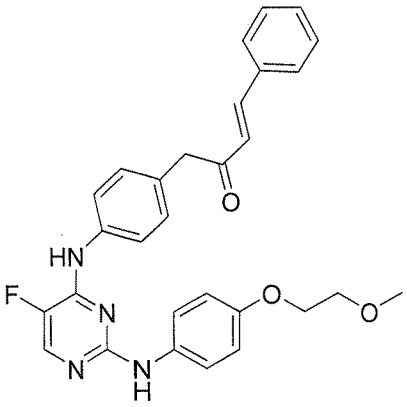
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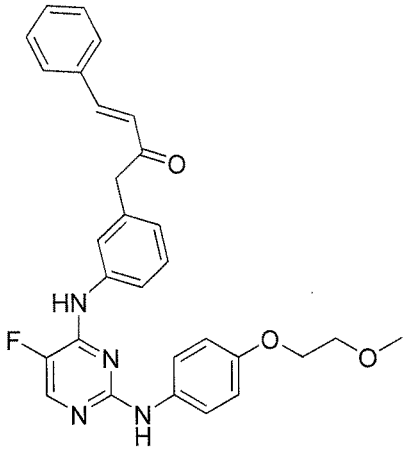
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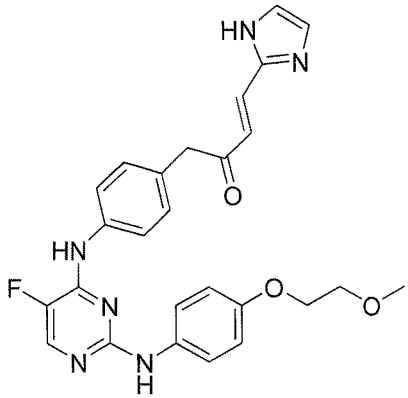
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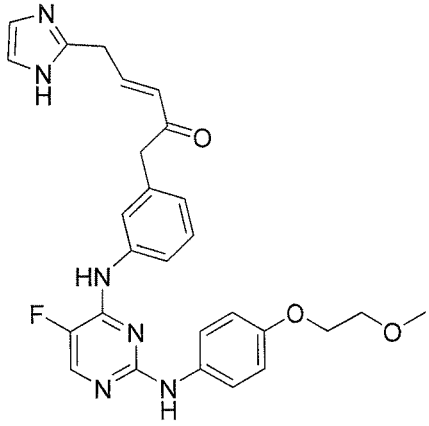
I-390



I-391



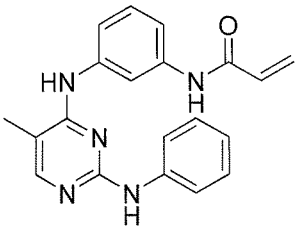
I-392



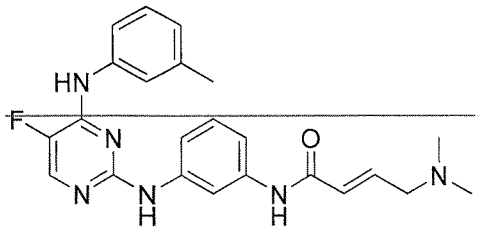
and **I-393**,

or a pharmaceutically acceptable salt thereof.

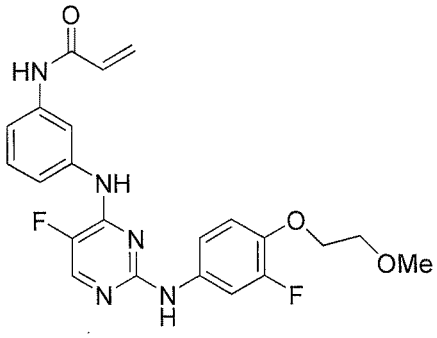
~~58~~53. The use according to claim ~~57~~42 wherein the compound is selected from the group consisting of:



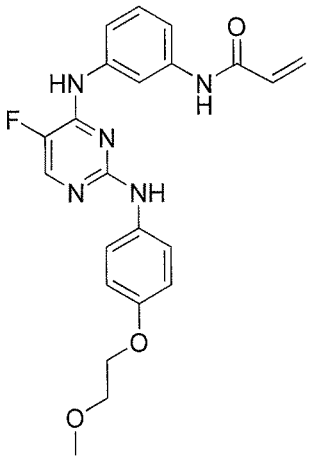
I-7



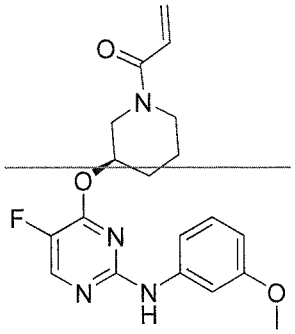
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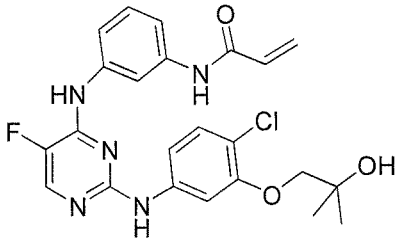
I-96



I-182

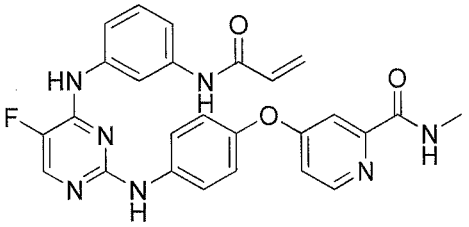


~~I-190~~



I-249

and



I-342,

or a pharmaceutically acceptable salt thereof.