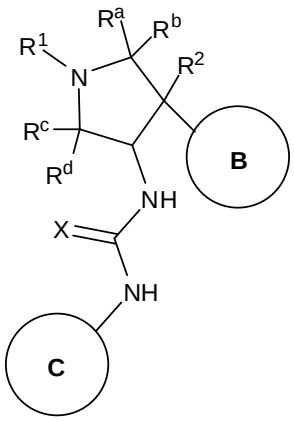
CLAIMS

1. A compound of Formula **I**:



I

or stereoisomers, tautomers, or pharmaceutically acceptable salts, solvates or prodrugs thereof, wherein:

Ring B and the NH-C(=X)-NH moiety are in the *trans* configuration;

R^a, R^b, R^c and R^d are independently selected from H and (1-3C)alkyl,

or R^c and R^d are independently selected from H and (1-3C)alkyl, and R^a and R^b together with the atom to which they are attached form a cyclopropyl ring;

X is O;

R^1 is (1-3C alkoxy)(1-6C)alkyl, (trifluoromethoxy)(1-6C)alkyl, (1-3C alkylsulfanyl)(1-6C)alkyl, monofluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, tetrafluoro(2-6C)alkyl, pentafluro(2-6C)alkyl, cyano(1-6C)alkyl, aminocarbonyl(1-6C)alkyl, hydroxy(1-6C)alkyl, dihydroxy(2-6C)alkyl, (1-6C)alkyl, (1-3Calkylamino)(1-3C)alkyl, (1-4C alkoxycarbonyl)(1-6C)alkyl, amino(1-6C)alkyl, hydroxy(1-3C alkoxy)(1-6C)alkyl, di(1-3C alkoxy)(1-6C)alkyl, (1-3C alkoxy)trifluoro(1-6C)alkyl, hydroxytrifluoro(1-6C)alkyl, (1-4C alkoxycarbonyl)(1-3C alkoxy)(1-6C)alkyl or hydroxycarbonyl(1-3C alkoxy)(1-6C)alkyl;

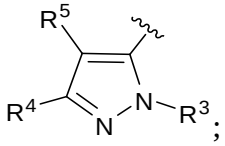
R^2 is H, F, or OH;

Ring B is Ar^1 or $hetAr^1$;

Ar^1 is phenyl optionally substituted with one or more substituents independently selected from halogen, CF_3, CF_3O-, (1-4C)alkoxy, hydroxy(1-4C)alkyl, (1-6C)alkyl and CN;

$hetAr^1$ is a 5-6 membered heteroaryl having 1-3 ring heteroatoms independently selected from N, S and O, and optionally substituted with one or more substituents independently selected from (1-6C)alkyl, halogen, OH, CF_3, NH_2 and hydroxy(1-2C)alkyl;

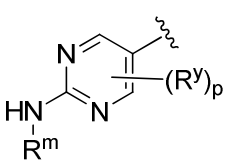
Ring C is

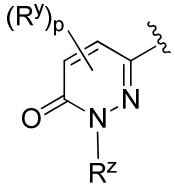


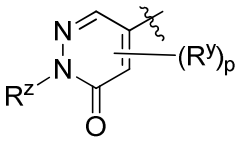
R^3 is Ar^2;

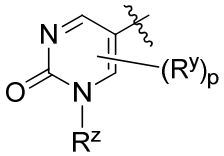
Ar^2 is phenyl optionally substituted with one or more substituents independently selected from halogen and (1-6C)alkyl;

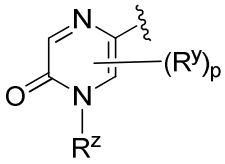
R^4 is selected from (1-6C alkyl)SO_2-, (1-6C alkyl)C(=O)- and from the structures:

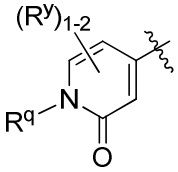


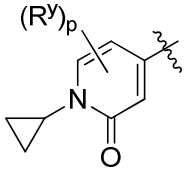


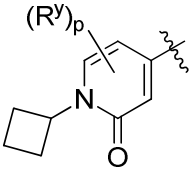


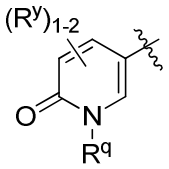


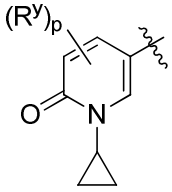


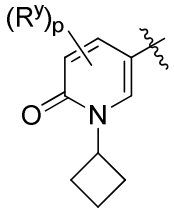


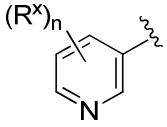


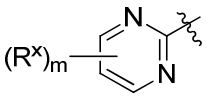


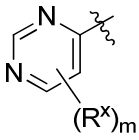


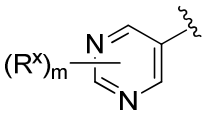


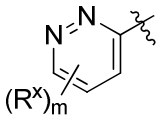


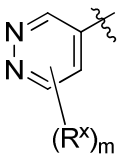


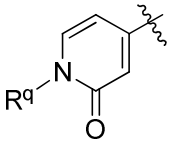


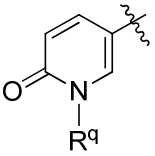


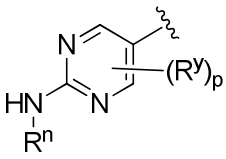












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R^m is (1-3C)alkyl substituted with 1-3 fluoros, or (3-4C)cycloalkyl;

R^n is (1-3C)alkyl;

R^q is (1-3C)alkyl optionally substituted with 1-3 fluoros;

R^x is (1-6C)alkyl, halogen, CN, hydroxy(1-6C)alkyl, trifluoro(1-6C)alkyl, (3-6C)cycloalkyl, (3-6C cycloalkyl)CH_2-, (3-6C cycloalkyl)C(=O)-, (1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkylsulfonyl, NH_2, (1-6C alkyl)amino, di(1-6C alkyl)amino, trifluoro(1-3C)alkoxy or trifluoro(1-6C)alkyl;

n is 0, 1, 2, 3 or 4;

m is 0, 1, 2 or 3;

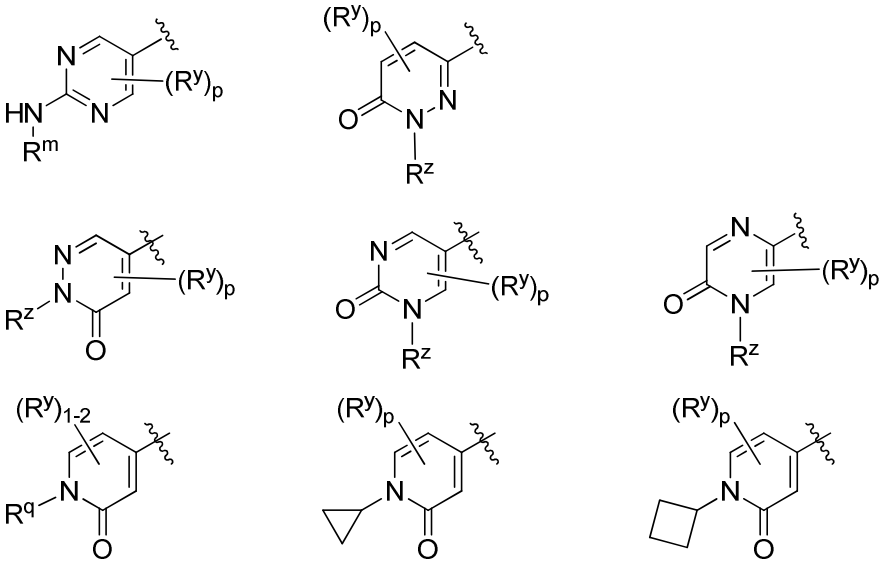
R^y is F or (1-3C)alkyl optionally substituted with 1-3 fluoros;

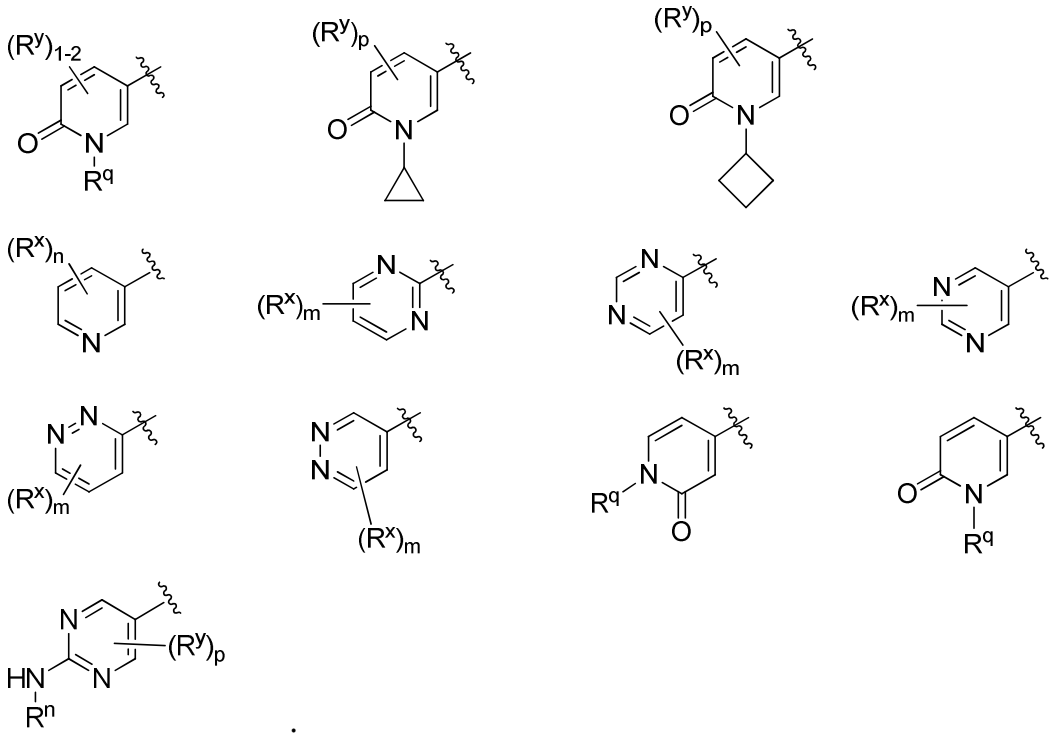
p is 0, 1 or 2;

R^z is (3-4C)cycloalkyl, or (1-3C)alkyl optionally substituted with 1-3 fluoros; and

R^5 is (1-6C)alkyl, monofluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, tetrafluoro(2-6C)alkyl, or pentafluoro(2-6C)alky.

2. A compound according to claim 1, wherein R^4 is selected from the structures:





3. A compound according to any one of claims 1-2, wherein R^1 is selected from (1-3C alkoxy)(1-6C)alkyl, difluoro(1-6C)alkyl and trifluoro(1-6C)alkyl.

4. A compound according to claim 3, wherein R^1 is (1-3C alkoxy)(1-6C)alkyl.

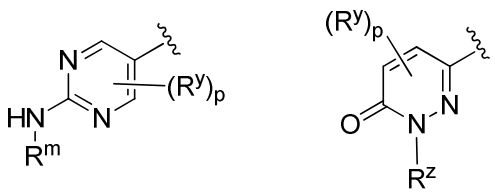
5. A compound according to any one of claims 1-4, wherein Ring B is Ar^1.

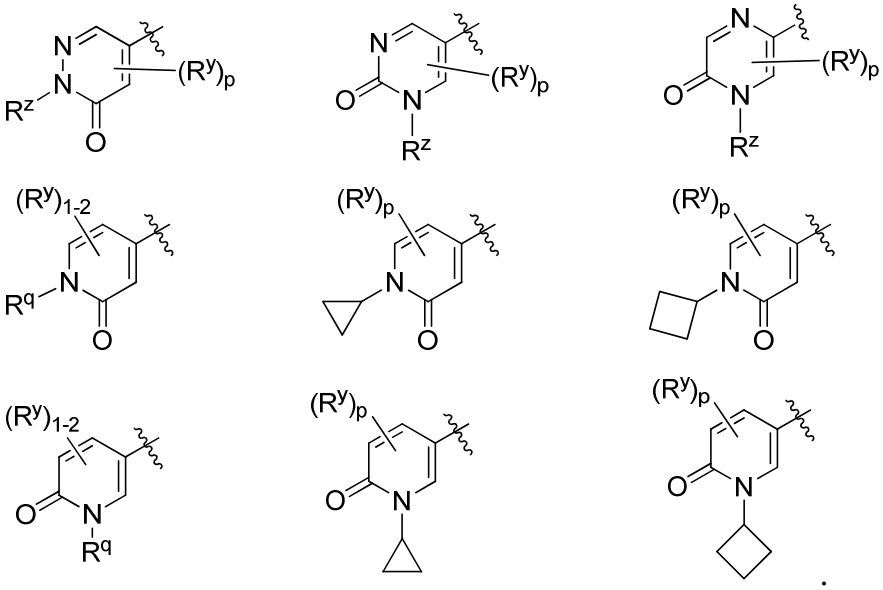
6. The compound of claim 5, wherein Ar^1 is phenyl optionally substituted with one or more halogens.

7. A compound according to any one of claims 1-4, wherein Ring B is $hetAr^1$.

8. A compound according to claim 7, wherein Ring B is pyridyl optionally substituted with 1-2 groups independently selected from (1-6C)alkyl or halogen.

9. A compound according to any one of claims 1-8, wherein R^4 is selected from the structures:





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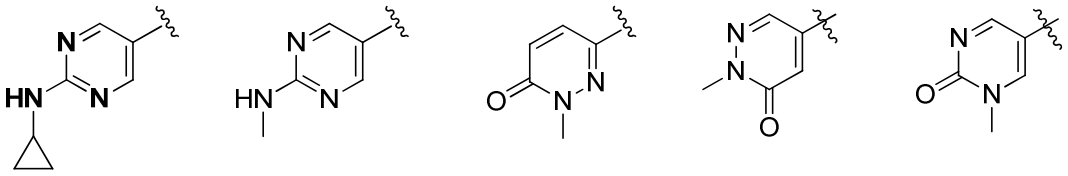
10. A compound according to claim 9, wherein R^4 is selected from the structures:



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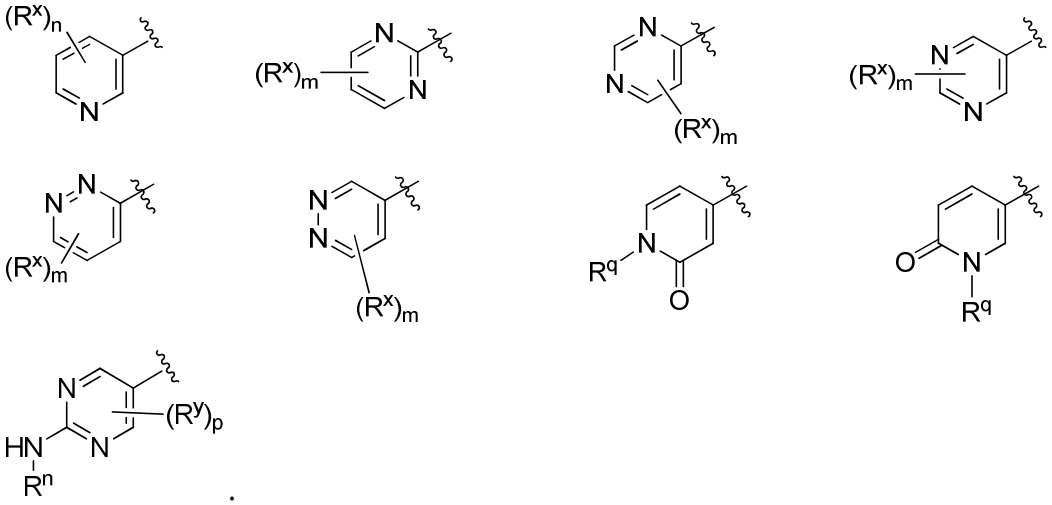
11. A compound according to any one of claims 1-8, wherein R^4 is selected from the structures:



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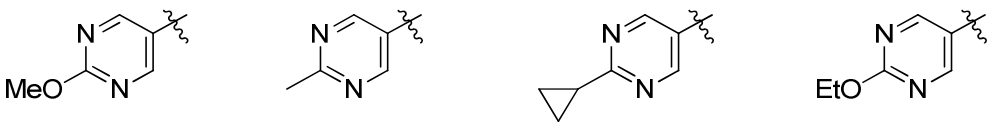
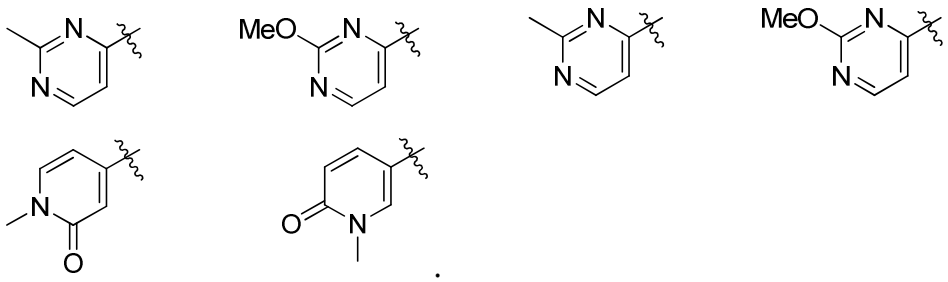
12. A compound according to claim 11, wherein n is 0 or 1 and m is 0 or 1.

13. A compound according to claim 12, wherein R^4 is selected from the structures:





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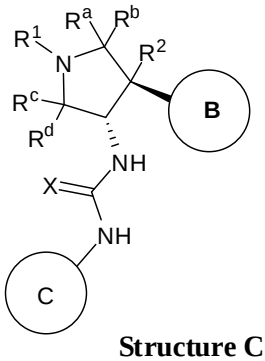
14. A compound according to any one of claims 1-13, wherein R^5 is (1-6C)alkyl.

15. A compound according to any one of claims 1-14, wherein R^2 is H.

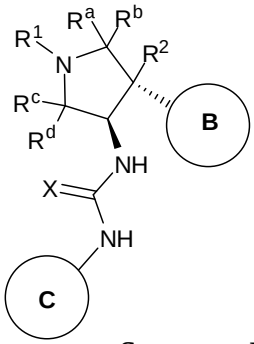
16. A compound according to any one of claims 1-15, wherein R^a, R^b, R^c and R^d are H.

17. A compound according to any one of claims 1-16, wherein Ring B and the -NH-C(=X)-NH- moiety of Formula **I** are trans in the absolute configuration shown in structure C:



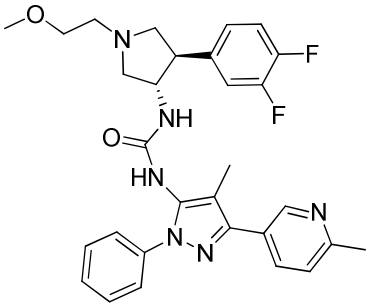
Structure C.

18. A compound according to any one of claims 1-16, wherein Ring B and the -NH-C(=X)-NH- moiety of Formula **I** are *trans* in the absolute configuration shown in structure D:



Structure D.

19. A compound of claim 1, which is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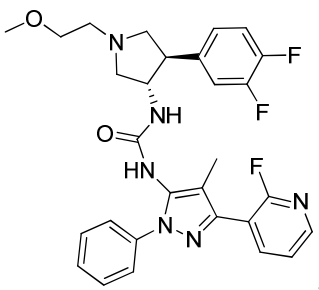
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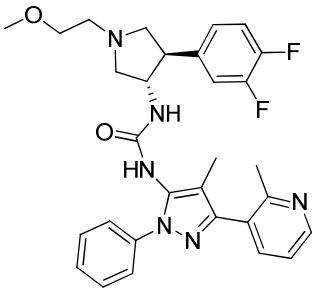

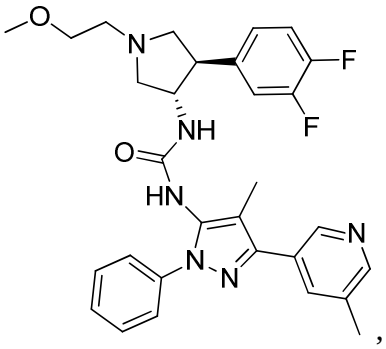
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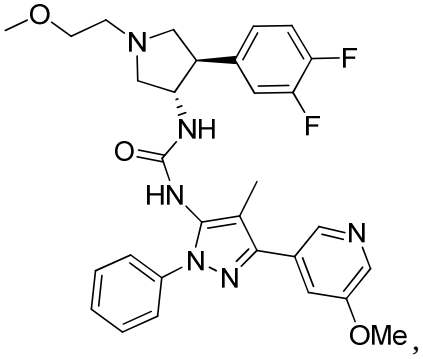
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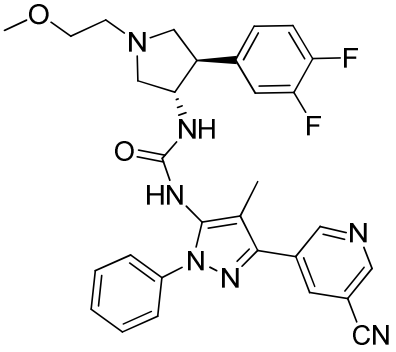

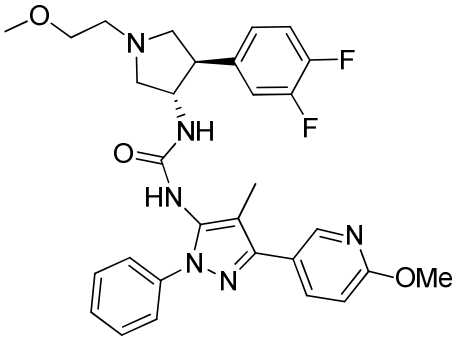
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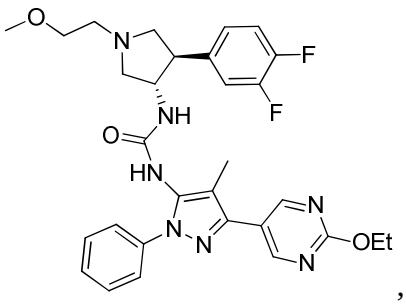
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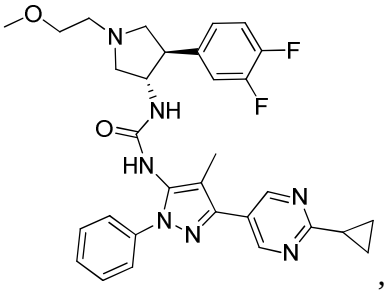
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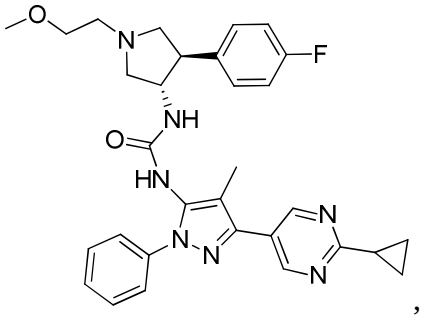
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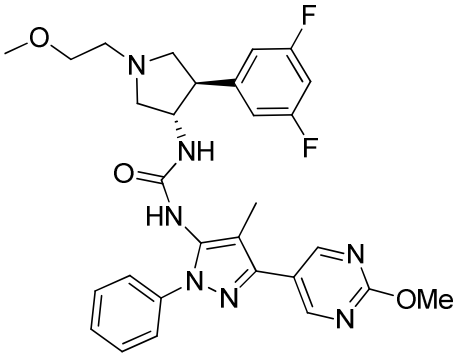
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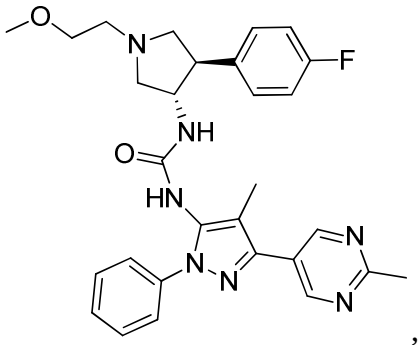
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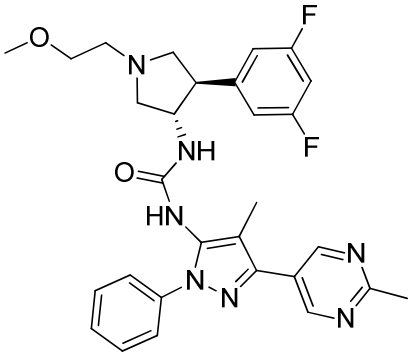
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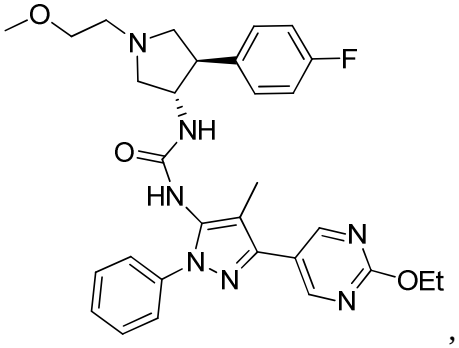
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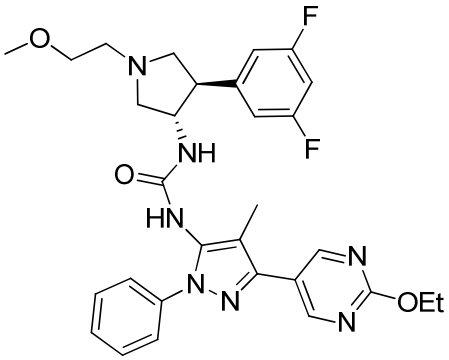
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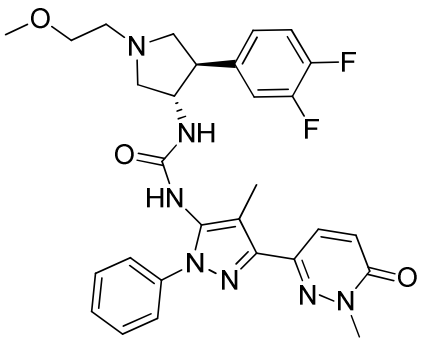
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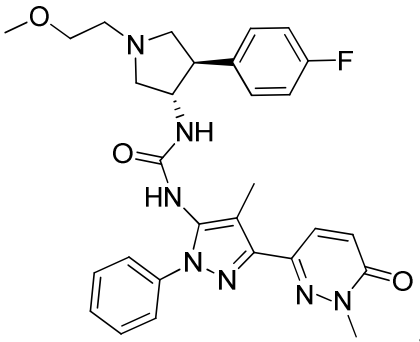
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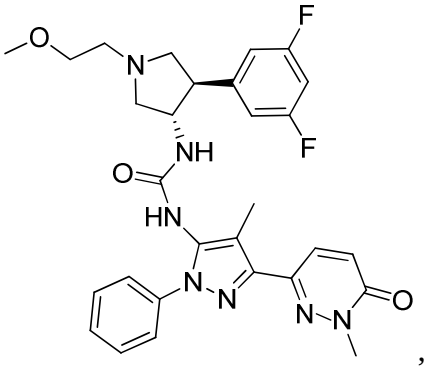
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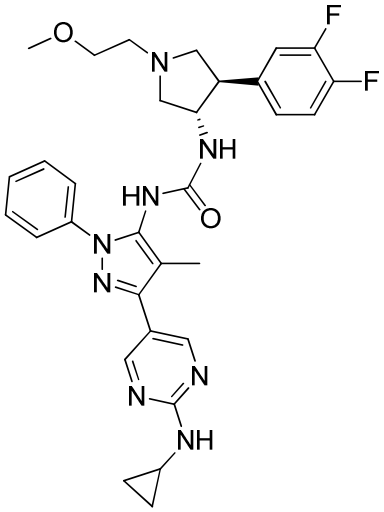
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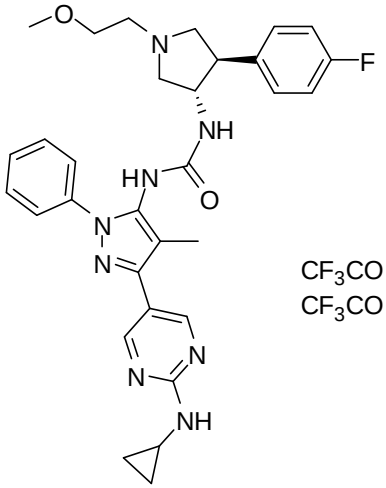
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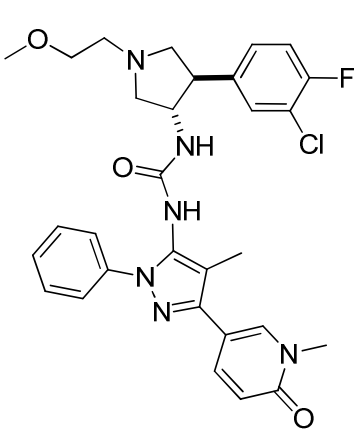
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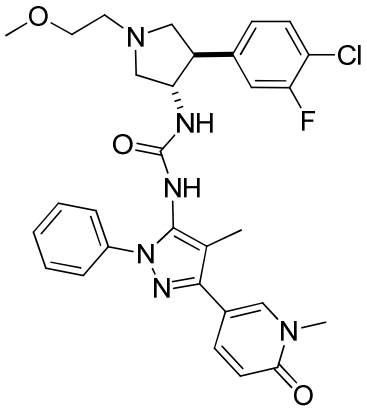
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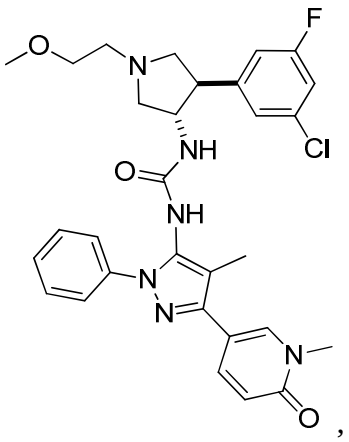
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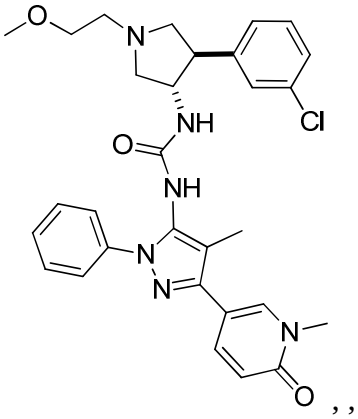
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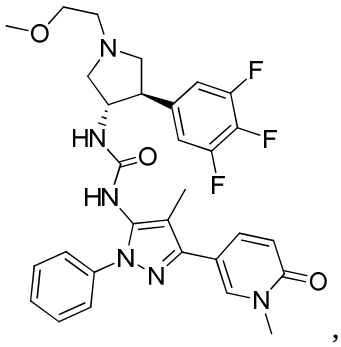
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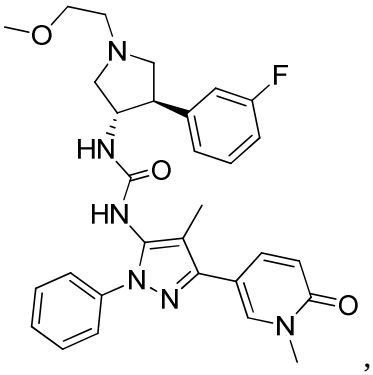
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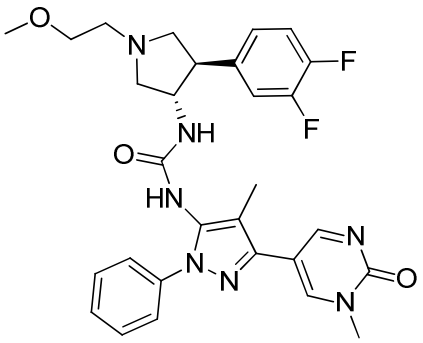
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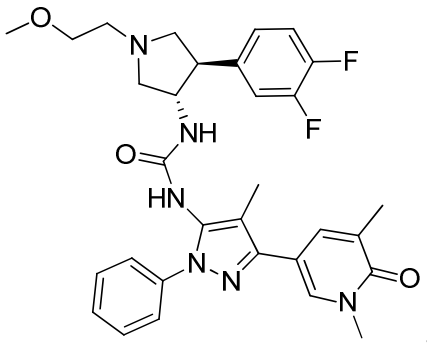
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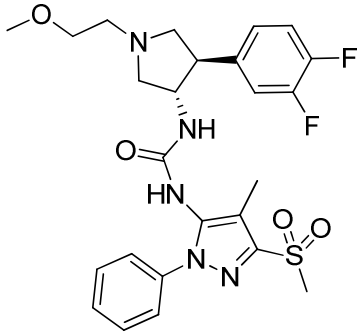
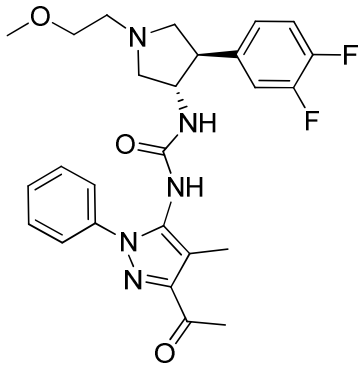
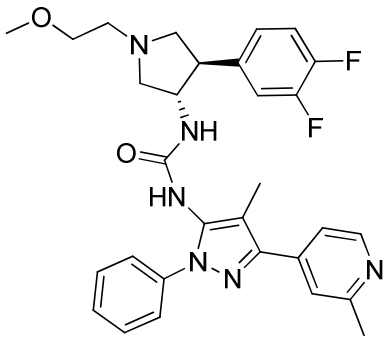


or



or a pharmaceutically acceptable salt thereof.

20. A compound which is:



or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition, which comprises a compound of Formula **I** as defined in any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, or which comprises the compound of claim 20 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

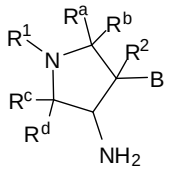
22. A compound of Formula **I** as defined in any one of claims 1 to 19, the compound of claim 20, or a pharmaceutically acceptable salt thereof, for use in the treatment of pain, wherein the pain is mediated by TrkA, cancer, wherein the cancer is associated with overexpression, activation, amplification and/or mutation of Trk kinases, or inflammation/inflammatory diseases associated with the TrkA pathway.

23. Use of a compound of Formula **I** as defined in any one of claims 1 to 19, the compound of claim 20, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating pain, wherein the pain is mediated by TrkA, cancer, wherein the cancer

is associated with overexpression, activation, amplification and/or mutation of Trk kinases, or inflammation/inflammatory diseases associated with the TrkA pathway.

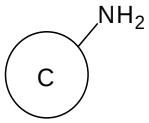
24. A process for the preparation of a compound of claim 1, which comprises:

(a) coupling a corresponding compound having the formula **II**



II

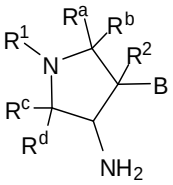
with a corresponding compound having the formula **III**



III

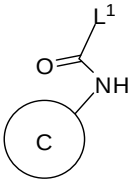
in the presence carbonyldiimidazole and a base; or

(b) coupling a corresponding compound having the formula **II**



II

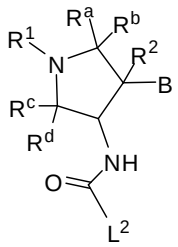
with a corresponding compound having the formula **IV**



IV

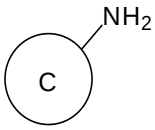
where L^1 is a leaving group, in the presence of a base; or

(c) coupling a corresponding compound having the formula **V**



V

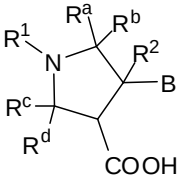
where L^2 is a leaving group, with a corresponding compound having the formula **III**



III

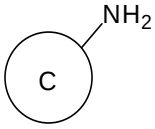
in the presence of a base; or

(d) activating a corresponding compound having the formula **VI**



VI

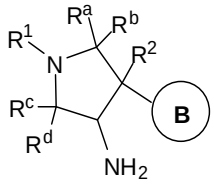
with diphenylphosphoryl azide followed by coupling the activated intermediate with a corresponding compound having the formula **III**



III

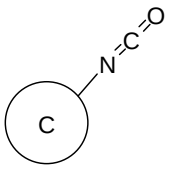
in the presence a base; or

(e) coupling a corresponding compound having the formula **II**



II

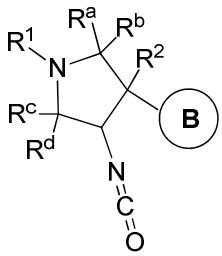
with a corresponding compound having the formula **VII**



VII

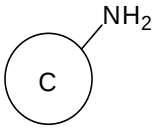
in the presence of a base; or

(f) coupling a corresponding compound having the formula **VIII**



VIII

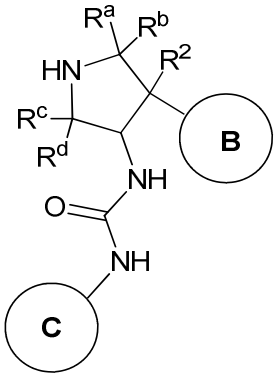
with a corresponding compound having the formula **III**



III

in the presence of a base; or

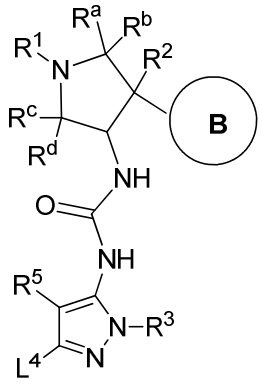
(g) for a compound of Formula **I** where R^1 is (trifluoromethoxy)(1-6C)alkyl, (1-3C alkylsulfanyl)(1-6C)alkyl, monofluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, tetrafluoro(2-6C)alkyl, or pentafluoro(2-6C)alkyl, reacting a corresponding compound having the formula **IX**



IX

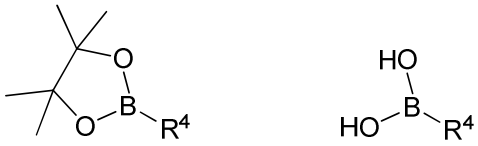
with (trifluoromethoxy)(1-6C)alkyl-L^3,(1-3C alkylsulfanyl)(1-6C)alkyl-L^3, monofluoro(1-6C)alkyl-L^3, difluoro(1-6C)alkyl-L^3, trifluoro(1-6C)alkyl-L^3, tetrafluoro(2-6C)alkyl-L^3, or pentafluoro(2-6C)alkyl-L^3, respectively, where L^3 is a leaving atom or a leaving group, in the presence of a base; or

(h) reacting a compound having the formula **X**:



X

where L^4 is Br or OTf, and R^1, R^a, R^b, C^c, R^d, R^2, R^3 and R^5 are as defined for Formula **I**, provided that R^5 is not halogen, with a corresponding boronic ester or boronic acid having the formula:



respectively, in the presence of a palladium catalyst and a base; and

optionally removing protecting groups and optionally preparing a pharmaceutically acceptable salt thereof.