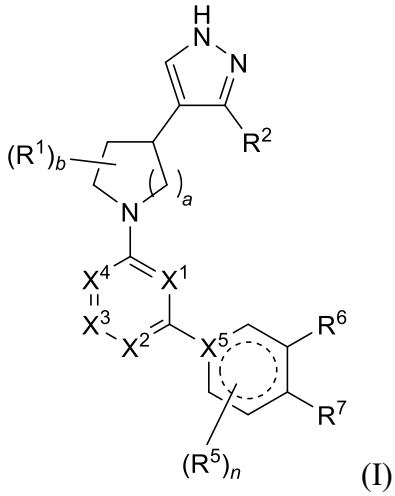
We Claim:

1. A compound having the formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is N or CH;

X^2 is N or CH;

X^3 is N or CR^3;

X^4 is N or CR^4;

X^5 is selected from the group consisting of C, CH and N;

a is selected from 1 or 2;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, oxo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, and -$NR^{11}R^{12}$;

or alternatively, two R^1 attached to the same carbon or to adjacent carbons are taken together to form a 3- to 6-membered ring, which may optionally contain 0 to 2 ring heteroatoms selected from O, S and N, and which may be unsubstituted or optionally substituted by 1 to 3 substituents selected from halo, C_1-C_3 alkyl, NH_2, OH, and O-C_1-C_3 alkyl;

b is selected from 0, 1, and 2;

R^2 is selected from H, halo, C_1-C_3 alkyl, NH_2, OH, and O-C_1-C_3 alkyl;

R^3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-

C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^3 and R^4 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)N$R^{11}R^{12}$, and -NR^{11}-(C_1-C_6 alkyl)-OR^{11};

each R^5 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, oxo, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

n is 0 to 3;

R^6 and R^7 are independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-C(=O)N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^6 and R^7 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6

alkynyl, C_3-C_7 cycloalkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, 3- to 10-membered heterocyclyl, -C_1-C_6 alkyl-(C_3-C_7 cycloalkyl), -C_1-C_6 alkyl-(C_5-C_{10} aryl), -C_1-C_6 alkyl-(C_5-C_{10} heteroaryl), -C_1-C_6 alkyl-(3- to 10-membered heterocyclyl), halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, and -C(=O)-N(R^8)(R^9), and wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

R^8 and R^9 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, wherein each alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl and aralkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

alternatively R^8 and R^9 are taken together with the nitrogen to which they are attached provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, C_1-C_6 fluoroalkyl, C_1-C_3 perfluoro alkyl, -OR^{11}, oxo, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

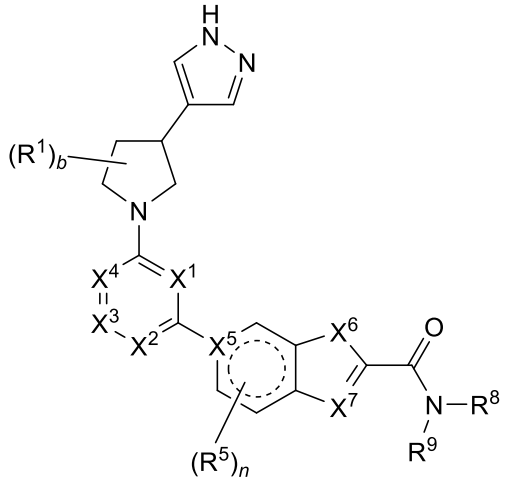
each *x* is independently selected from 0 and 1; and

each R^{11} and R^{12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -

NH_2, C_1-C_3 perfluoroalkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.or a pharmaceutically acceptable salt thereof, wherein:

2. The compound according to claim 1, having the formula II:



II

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is N or CH;

X^2 is N or CH;

X^3 is N or CR^3;

X^4 is N or CR^4;

X^5 is selected from the group consisting of C, CH and N;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, oxo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, and -$NR^{11}R^{12}$;

or alternatively, two R^1 attached to the same carbon or to adjacent carbons are taken together to form a 3- to 6-membered ring, which may optionally contain 0 to 2 ring heteroatoms selected from O, S and N, and which may be unsubstituted or optionally substituted by 1 to 3 substituents selected from halo, C_1-C_3 alkyl, NH_2, OH, and O-C_1-C_3 alkyl;

b is selected from 0, 1, and 2;

R^3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-

C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^3 and R^4 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)N$R^{11}R^{12}$, and -NR^{11}-(C_1-C_6 alkyl)-OR^{11};

each R^5 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, oxo, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

n is 0 to 3;

X^6 is selected from the group consisting of NR^{10}, O and S;

X^7 is selected from the group consisting of CH and N;

R^8 and R^9 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, $C_{6\text{-}12}$ aralkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, wherein each alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl and aralkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

alternatively R^8 and R^9 are taken together with the nitrogen to which they are attached provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring

heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, C_1-C_6 fluoroalkyl, C_1-C_3 perfluoro alkyl, -OR^{11}, oxo, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

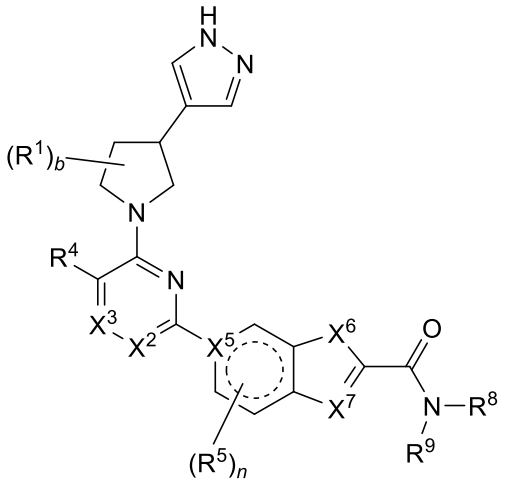
R^{10} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, 3- to 10-membered heterocyclyl, -C_1-C_6 alkyl-(C_3-C_7 cycloalkyl), -C_1-C_6 alkyl-(C_5-C_{10} aryl), -C_1-C_6 alkyl-(C_5-C_{10} heteroaryl), -C_1-C_6 alkyl-(3- to 10-membered heterocyclyl), -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-OR^{11}, and -C(=O)-N(R^{11})(R^{12}), and wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

each *x* is independently selected from 0 and 1; and

each R^{11} and R^{12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -NH_2, C_1-C_3 perfluoroalkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

3. The compound according to claim 1, having the formula III:



III

or a pharmaceutically acceptable salt thereof, wherein:

X^2 is N or CH;

X^3 is N or CR^3;

X^5 is selected from the group consisting of C, CH and N;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, oxo, -CN, C_1-C_3 perfluoro alkyl, $-OR^{11}$, and $-NR^{11}R^{12}$;

or alternatively, two R^1 attached to the same carbon or to adjacent carbons are taken together to form a 3- to 6-membered ring, which may optionally contain 0 to 2 ring heteroatoms selected from O, S and N, and which may be unsubstituted or optionally substituted by 1 to 3 substituents selected from halo, C_1-C_3 alkyl, NH_2, OH, and O-C_1-C_3 alkyl;

b is selected from 0, 1, and 2;

R^3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, $-OR^{11}$, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, $-NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, $-OR^{11}$, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, $-NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-

C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^3 and R^4 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)N$R^{11}R^{12}$, and -NR^{11}-(C_1-C_6 alkyl)-OR^{11};

each R^5 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, oxo, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

n is 0 to 3;

X^6 is selected from the group consisting of NR^{10}, O and S;

X^7 is selected from the group consisting of CH and N;

R^8 and R^9 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, $C_{6\text{-}12}$ aralkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-N$R^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)N$R^{11}R^{12}$, wherein each alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl and aralkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

alternatively R^8 and R^9 are taken together with the nitrogen to which they are attached provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, C_1-C_6 fluoroalkyl, C_1-C_3 perfluoro alkyl, -OR^{11}, oxo, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -N$R^{11}R^{12}$, -O-(C_1-C_6 alkyl)-

$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

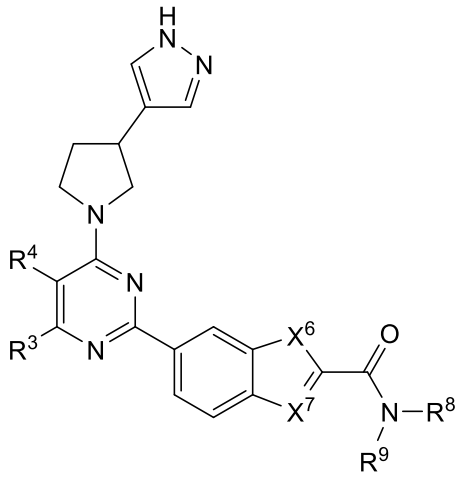
R^{10} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, 3- to 10-membered heterocyclyl, -C_1-C_6 alkyl-(C_3-C_7 cycloalkyl), -C_1-C_6 alkyl-(C_5-C_{10} aryl), -C_1-C_6 alkyl-(C_5-C_{10} heteroaryl), -C_1-C_6 alkyl-(3- to 10-membered heterocyclyl), -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-OR^{11}, and -C(=O)-N(R^{11})(R^{12}), and wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

each *x* is independently selected from 0 and 1; and

each R^{11} and R^{12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -NH_2, C_1-C_3 perfluoroalkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

4. The compound according to claim 1, having the formula IV:



IV

or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^3 and R^4 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)$NR^{11}R^{12}$, and -NR^{11}-(C_1-C_6 alkyl)-OR^{11};

X^6 is selected from the group consisting of NR^{10}, O and S;

X^7 is selected from the group consisting of CH and N;

R^8 and R^9 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, $C_{6\text{-}12}$ aralkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, wherein each alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl and aralkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

alternatively R^8 and R^9 are taken together with the nitrogen to which they are attached provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6

alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, C_1-C_6 fluoroalkyl, C_1-C_3 perfluoro alkyl, -OR^{11}, oxo, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

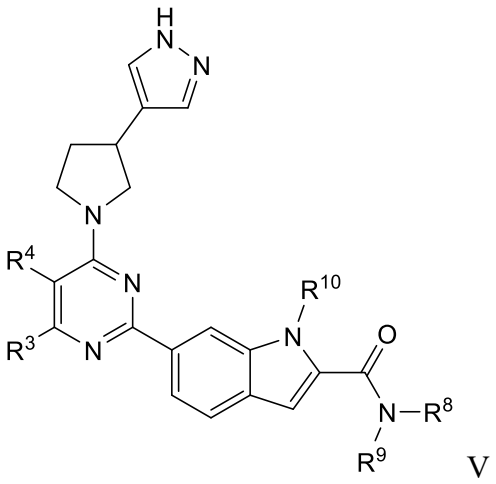
R^{10} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, 3- to 10-membered heterocyclyl, -C_1-C_6 alkyl-(C_3-C_7 cycloalkyl), -C_1-C_6 alkyl-(C_5-C_{10} aryl), -C_1-C_6 alkyl-(C_5-C_{10} heteroaryl), -C_1-C_6 alkyl-(3- to 10-membered heterocyclyl), -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-OR^{11}, and -C(=O)-N(R^{11})(R^{12}), and wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

each *x* is independently selected from 0 and 1; and

each R^{11} and R^{12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -NH_2, C_1-C_3 perfluoroalkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

5. The compound according to claim 1, having the formula V:



V

or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

alternatively, R^3 and R^4 are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, C_1-C_3 perfluoro alkyl, -NR^{11}-(C_1-C_6 alkyl)$NR^{11}R^{12}$, and -NR^{11}-(C_1-C_6 alkyl)-OR^{11};

R^8 and R^9 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, $C_{6\text{-}12}$ aralkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, wherein each alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl and aralkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

alternatively R^8 and R^9 are taken together with the nitrogen to which they are attached provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, C_1-C_6 fluoroalkyl, C_1-C_3 perfluoro alkyl, -

OR^{11}, oxo, -O-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-OR^{11}, -$NR^{11}R^{12}$, -O-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -O-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, -C(=O)-R^{11}, -C(=O)OR^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$, -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, and -NR^{11}-(C_1-C_6 alkyl)$_x$-C(=O)OR^{11};

R^{10} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, 3- to 10-membered heterocyclyl, -C_1-C_6 alkyl-(C_3-C_7 cycloalkyl), -C_1-C_6 alkyl-(C_5-C_{10} aryl), -C_1-C_6 alkyl-(C_5-C_{10} heteroaryl), -C_1-C_6 alkyl-(3- to 10-membered heterocyclyl), -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$NR^{11}R^{12}$, -(C_1-C_6 alkyl)-OR^{11}, and -C(=O)-N(R^{11})(R^{12}), and wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, oxo, halo, -CN, -OH, and NH_2;

each *x* is independently selected from 0 and 1; and

each R^{11} and R^{12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -NH_2, C_1-C_3 perfluoroalkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

6. The compound according to any one of claims 1 to 5, wherein R^3 is selected to be H.

7. The compound according to any one of claims 1 to 6, wherein R^4 is selected from H, methyl, ethyl, halo, fluoromethyl, difluoromethyl and trifluoromethyl.

8. The compound according to any one of claims 1 to 7, wherein both R^3 and R^4 are H.

9. The compound according to any one of claims 1 to 8, wherein R^8 and R^9 are independently selected from H, C_1-C_6 alkyl, and C_3-C_7 cycloalkyl, wherein each alkyl and cycloalkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl and halo.

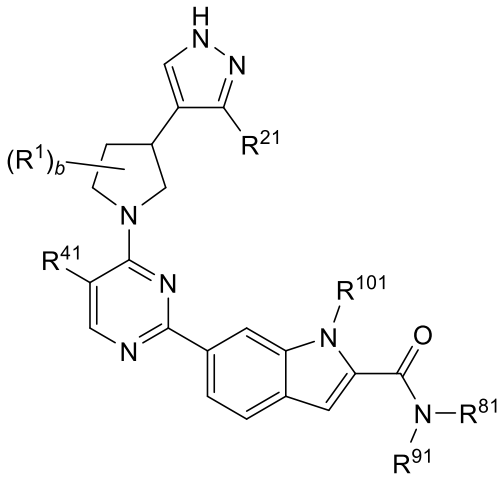
10. The compound according to any one of claims 1 to 9, wherein one of R^8 and R^9 is H and the other is selected from C_1-C_6 alkyl, and C_3-C_7 cycloalkyl, wherein each alkyl and cycloalkyl may optionally be substituted with one to three substituents selected from C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl and halo, particularly fluoro.

11. The compound according to any one of claims 1 to 10, wherein R^8 and R^9 are taken together with the nitrogen to which they are attached to provide a 4- or 5-membered heterocyclic ring, wherein the heterocyclic ring is unsubstituted or is substituted with from 1 to 4 substituents selected from the group consisting of C_1-C_6 alkyl, C_1-C_6-fluoroalkyl and halo, particularly fluoro.

12. The compound according to any one of claims 1 to 11, wherein R^{10} is selected from H and C_1-C_6 alkyl, and particularly R^{10} may be methyl.

13. The compound according to any one of claims 1 to 11, wherein R^{10} is methyl.

14. The compound according to claim 1, having the formula VI:



VI

or a pharmaceutically acceptable salt thereof, wherein:

each R^1 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, oxo, -CN, C_1-C_3 perfluoro alkyl, -OR^{11}, and -$NR^{11}R^{12}$;

or alternatively, two R^1 attached to the same carbon or to adjacent carbons are taken together to form a 3- to 6-membered ring, which may optionally contain 0 to 2 ring heteroatoms selected from O, S and N, and which may be unsubstituted or optionally

substituted by 1 to 3 substituents selected from halo, C_1-C_3 alkyl, NH_2, OH, and O-C_1-C_3 alkyl;

b is selected from 0, 1, and 2;R^{21} is selected from the group consisting of H, methyl, halo, fluoromethyl, difluoromethyl and trifluoromethyl;

R^{41} is selected from the group consisting of H, methyl, ethyl, halo, fluoromethyl, difluoromethyl and trifluoromethyl;

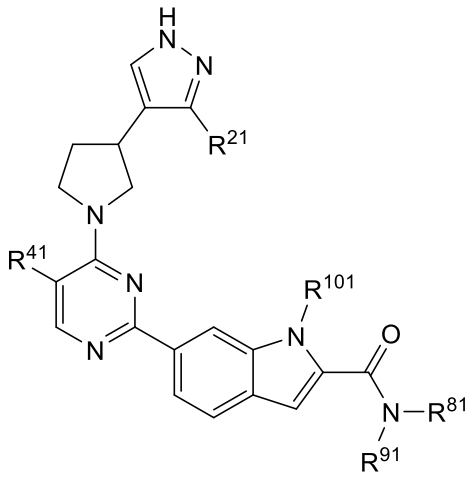
R^{81} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, wherein each alkyl or cycloalkyl may optionally be substituted with one to three substituents selected from halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl;

R^{91} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, wherein each alkyl or cycloalkyl may optionally be substituted with one to three substituents selected from halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl;

alternatively R^{81} and R^{91} are taken together with the nitrogen to which they are attached provide a 4- to 6-membered heterocyclic ring, wherein the heterocyclic ring is unsubstituted or is substituted with from 1 to 4 substituents selected from the group consisting of halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl; and

R^{101} is selected from the group consisting of H and methyl.

15. The compound according to claim 1, having the formula VII:



VII

or a pharmaceutically acceptable salt thereof, wherein:

R^{21} is selected from the group consisting of H, methyl, halo, fluoromethyl, difluoromethyl and trifluoromethyl;

R^{41} is selected from the group consisting of H, methyl, ethyl, halo, fluoromethyl, difluoromethyl and trifluoromethyl;

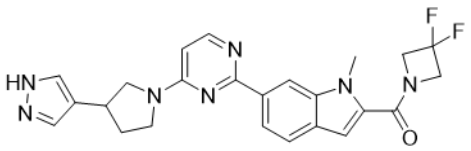
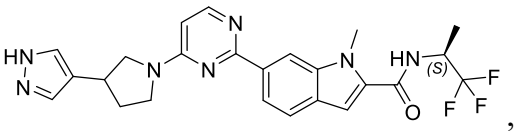
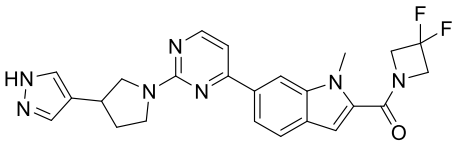
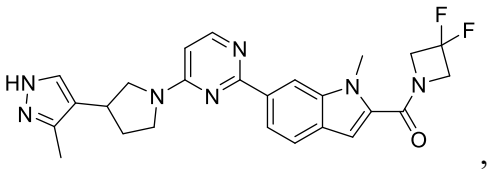
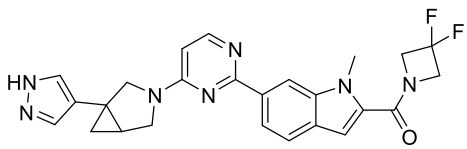
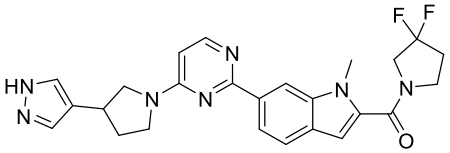
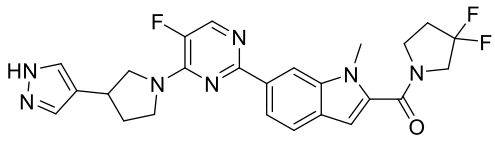
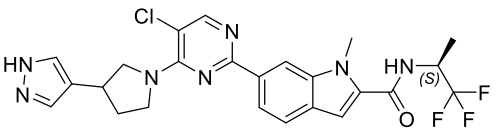
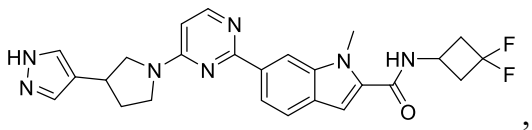
R^{81} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, wherein each alkyl or cycloalkyl may optionally be substituted with one to three substituents selected from halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl;

R^{91} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, wherein each alkyl or cycloalkyl may optionally be substituted with one to three substituents selected from halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl;

alternatively R^{81} and R^{91} are taken together with the nitrogen to which they are attached provide a 4- to 6-membered heterocyclic ring, wherein the heterocyclic ring is unsubstituted or is substituted with from 1 to 4 substituents selected from the group consisting of halo, methyl, ethyl, fluoromethyl, difluoromethyl, and trifluoromethyl; and

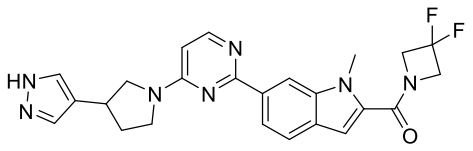
R^{101} is selected from the group consisting of H and methyl.

16. The compound of claim 1, which is selected from a compound having the one of the following structures:


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or a pharmaceutically acceptable salts thereof.

17. The compound of claim 1, which is 2-(3,3-difluoroazetidine-1-carbonyl)-1-methyl-6-{4-[3-(1H-pyrazol-4-yl)pyrrolidin-1-yl]pyrimidin-2-yl}-1H-indole having the formula:



or a pharmaceutically acceptable salt thereof.

18. Use of a compound according to any of claims 1 to 17 in the manufacture of a medicament for the treatment of a disease or disorder mediated by ROCK2 in a subject, wherein an effective amount of the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

19. The use of claim 18, wherein the disease or disorder is selected from the group consisting of fibrotic diseases, inflammatory diseases, autoimmune diseases, cardiovascular disorders, central nervous system disorders, neoplastic diseases, metabolic syndromes, ocular diseases, renal diseases, pulmonary diseases, muscular dystrophy, sickle cell disease, and viral diseases.

20. The use of claim 19, wherein

(i) the autoimmune disease is selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus (SLE; lupus), psoriasis, psoriatic arthritis, multiple sclerosis, Crohn's disease, ulcerative colitis, atopic dermatitis, eczema, or graft-versus-host disease (GVHD; acute and chronic), idiopathic pulmonary fibrosis and scleroderma

(ii) the inflammatory disorder is selected from the group consisting of cardiovascular inflammation, pulmonary inflammation, renal inflammation, arteriosclerosis and sepsis;

(iii) the fibrotic disorder is selected from the group consisting of idiopathic pulmonary fibrosis, renal fibrosis, kidney fibrosis, ocular fibrosis, cardiac fibrosis, NASH, scleroderma, systemic sclerosis, and cirrhosis;

(iv) the neoplastic disease is selected from the group consisting of ovarian cancer, breast cancer and pancreatic cancer;

(v) the cardiovascular disease is selected from the group consisting of hypertension, cardiomyopathy, cardiac remodeling, atherosclerosis, restenosis, cardiac

hypertrophy, cerebral ischemia, cerebral vasospasm, and erectile dysfunction;

(vi) the pulmonary disease is selected from the group consisting of idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, and asthma;

(vii) the central nervous system disorder is selected from the group consisting of neuronal degeneration or spinal cord injury, traumatic brain injury, cerebral cavernous malformation, Huntington's disease, Parkinson's disease, Alzheimer's disease, Amyotrophic lateral sclerosis (ALS), and multiple sclerosis;

(viii) the renal disease is selected from the group consisting of polycystic kidney disease, renal fibrosis and diabetic renal disease;

(ix) the metabolic disease is selected from the group consisting of insulin resistance, hyperinsulinemia, type 2 diabetes, obesity, metabolic syndrome and glucose intolerance;

(x) the ocular disease is selected from the group consisting of ocular hypertension, age related macular degeneration (AMD; wet and dry), choroidal neovascularization (CNV), choroidal tumor, diabetic macular edema (DME), iris neovascularization, uveitis, glaucoma, primary open-angle glaucoma, acute angle-closure glaucoma, pigmentary glaucoma, congenital glaucoma, normal tension glaucoma, secondary glaucoma, neo vascular glaucoma, geographic atrophy, and retinitis of prematurity (ROP);

(xi) the disease is Duchenne muscular dystrophy; or

(xii) the viral infection is a coronavirus infection such as SARS-CoV-1, SARS-CoV-2, and MERS-CoV.