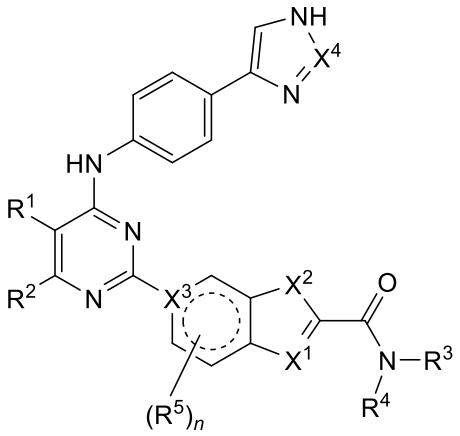
We Claim:

1. A compound having the formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 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^2 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^1 and R^2 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^4 is N or CH;

R^3 and R^4 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)$NR^{11}R^{12}$;

alternatively R^3 and R^4 are taken together with the nitrogen to which they are attached to 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 hetero 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, halo, -CN, 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};

the dotted lines represent optional double bonds;

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}, -$NR^{11}R^{12}$, -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};

n is 0 to 3;

X^1 is selected from the group consisting of CR^6 and N;

X^2 is selected from the group consisting of CHR^6, NR^7, O and S;

X^3 is selected from the group consisting of C, CH and N;

each R^6 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, -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};

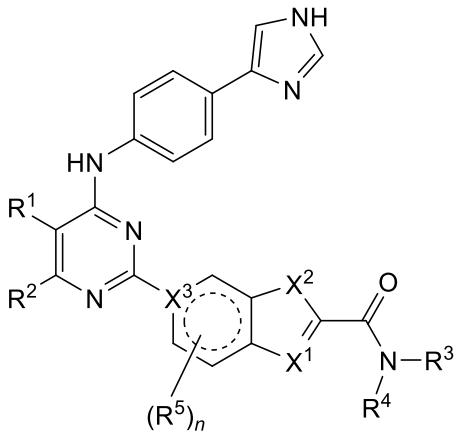
each R^7 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-$C(=O)R^{11}$, -(C_1-C_6 alkyl)$_x$-$C(=O)OR^{11}$, and -(C_1-C_6 alkyl)$_x$-$C(=O)NR^{11}R^{12}$;

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 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

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



(II)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 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^2 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^1 and R^2 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^3 and R^4 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)$_x$-$C(=O)NR^{11}R^{12}$;

alternatively R^3 and R^4 are taken together with the nitrogen to which they are attached to 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 hetero 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, halo, -CN, 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)$_x$-$C(=O)OR^{11}$;

the dotted lines represent optional double bonds;

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

n is 0 to 3;

X^1 is selected from the group consisting of CR^6 and N;

X^2 is selected from the group consisting of CHR^6, NR^7, O and S;

X^3 is selected from the group consisting of C, CH and N;

each R^6 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, $-OR^{11}$, -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};

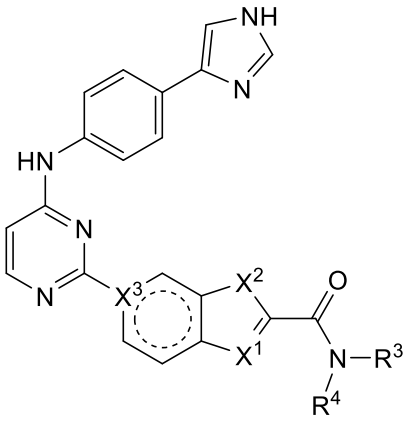
each R^7 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$;

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 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

3. A compound according to claim 1, having the formula IIa:



(IIa)

or a pharmaceutically acceptable salt thereof, wherein:

R^3 and R^4 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)$_x$-$C(=O)NR^{11}R^{12}$;

alternatively R^3 and R^4 are taken together with the nitrogen to which they are attached to 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 hetero 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, halo, -CN, 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)$_x$-$C(=O)OR^{11}$;

the dotted lines represent optional double bonds;

X^1 is selected from the group consisting of CR^6 and N;

X^2 is selected from the group consisting of CHR^6, NR^7, O and S;

X^3 is selected from the group consisting of C, CH and N;

each R^6 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, -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)$_x$-$C(=O)OR^{11}$;

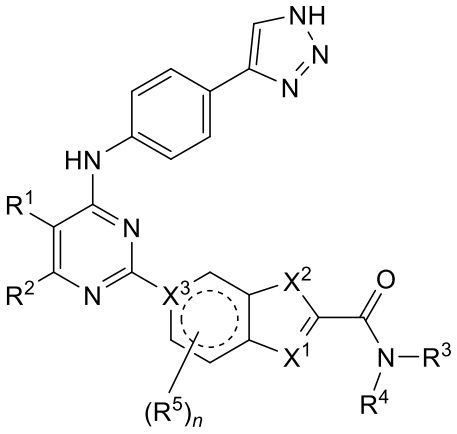
each R^7 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-$C(=O)R^{11}$, -(C_1-C_6 alkyl)$_x$-$C(=O)OR^{11}$, and -(C_1-C_6 alkyl)$_x$-$C(=O)NR^{11}R^{12}$;

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 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

4. A compound according to claim 1, having the formula III:



(III)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 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^2 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^1 and R^2 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^3 and R^4 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)$NR^{11}R^{12}$;

alternatively R^3 and R^4 are taken together with the nitrogen to which they are attached to 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 hetero 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, halo, -CN, 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};

the dotted lines represent optional double bonds;

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}, -$NR^{11}R^{12}$, -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};

n is 0 to 3;

X^1 is selected from the group consisting of CR^6 and N;

X^2 is selected from the group consisting of CHR^6, NR^7, O and S;

X^3 is selected from the group consisting of C, CH and N;

each R^6 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, -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};

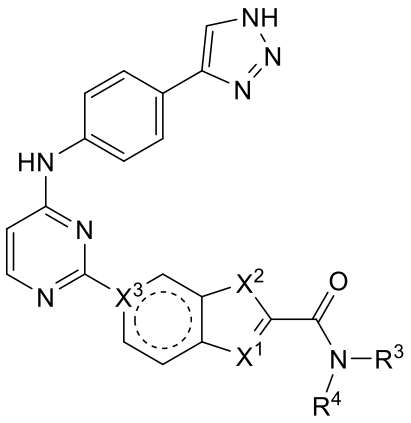
each R^7 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$;

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 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

5. A compound according to claim 1, having the formula IIIa:



(IIIa)

or a pharmaceutically acceptable salt thereof, wherein:

R^3 and R^4 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)$NR^{11}R^{12}$;

alternatively R^3 and R^4 are taken together with the nitrogen to which they are attached to 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 hetero 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, halo, -CN, 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};

the dotted lines represent optional double bonds;

X^1 is selected from the group consisting of CR^6 and N;

X^2 is selected from the group consisting of CHR^6, NR^7, O and S;

X^3 is selected from the group consisting of C, CH and N;

each R^6 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, -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};

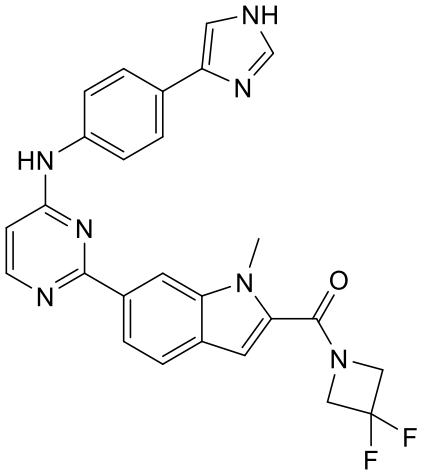
each R^7 is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{11}, -(C_1-C_6 alkyl)-$NR^{11}R^{12}$, -(C_1-C_6 alkyl)$_x$-C(=O)R^{11}, -(C_1-C_6 alkyl)$_x$-C(=O)OR^{11}, and -(C_1-C_6 alkyl)$_x$-C(=O)$NR^{11}R^{12}$;

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;

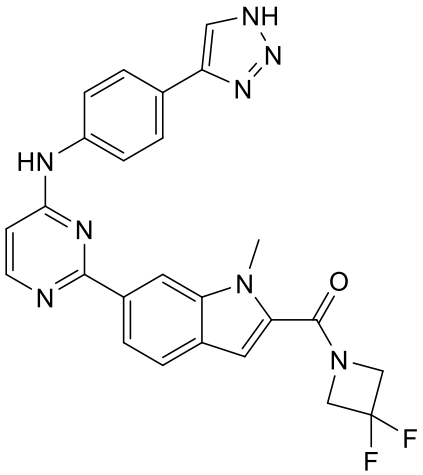
or alternatively, R^{11} and R^{12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted 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 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

6. A compound of claim 1, which is 2-[2-(3,3-difluoroazetidine-1-carbonyl)-1-methyl-1H-indol-6-yl]-N-[4-(1H-imidazol-5-yl)phenyl]pyrimidin-4-amine having the formula:



or a pharmaceutically acceptable salt thereof.

7. A compound of claim 1, which is 2-[2-(3,3-difluoroazetidine-1-carbonyl)-1-methyl-1H-indol-6-yl]-N-[4-(1H-1,2,3-triazol-4-yl)phenyl]pyrimidin-4-amine having the formula:



or a pharmaceutically acceptable salt thereof.

8. Use of an effective amount of a compound according to any of claims 1 to 7 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disease or disorder mediated by ROCK2 in a subject in need thereof.

9. The use of claim 8, 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.

10. The use of claim 9, wherein the disease or disorder is selected from the group consisting of fibrotic diseases, inflammatory diseases, and autoimmune diseases.

11. The use of claim 10, wherein 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.

12. The use of claim 9, wherein the disease or disorder is selected from the group consisting of a cardiovascular disorder, a central nervous system disorder, a neoplastic disease, or a metabolic syndrome.

13. The use of claim 10, wherein the inflammatory disorder is selected from the group consisting of cardiovascular inflammation, pulmonary inflammation, renal inflammation, arteriosclerosis and sepsis.

14. The use of claim 10, wherein 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.

15. The use of claim 12, wherein the neoplastic disease is selected from the group consisting of ovarian cancer, breast cancer and pancreatic cancer.

16. The use of claim 12, wherein 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.

17. The use of claim 9, wherein the pulmonary disease is selected from the group consisting of idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, and asthma.

18. The use of claim 9, wherein 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.

19. The use of claim 9, wherein the renal disease is selected from the group consisting of polycystic kidney disease, renal fibrosis and diabetic renal disease.

20. The use of claim 9, wherein the metabolic disease is selected from the group consisting of insulin resistance, hyperinsulinemia, type 2 diabetes, obesity, metabolic syndrome and glucose intolerance.

21. The use of claim 9, wherein 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).

22. The use of claim 9, wherein the disease is Duchenne muscular dystrophy.

23. The use of claim 9, wherein the viral infection is a coronavirus infections such as SARS-CoV-1, SARS-CoV-2, and MERS-CoV.