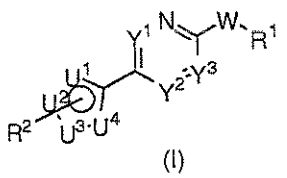
that PGD_2 produced by H-PGDS plays a role in fever induction (*Journal of Physiology and Pharmacology,* 60(2), **2009**, 145-150).

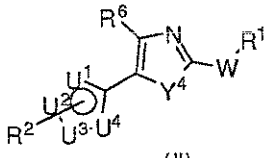
Compounds have now been found that are inhibitors of H-PGDS, and at expected efficacious doses, do not significantly inhibit L-PGDS.

Summary ~~of the Invention~~

The exemplary embodiments may be directed to multiheterocyclic (multiheteroaryl) compounds of structural formulas (I) or (II), respectively, that may be used to treat or prevent allergic, inflammatory, and/or immune disorders, including the prevention and treatment of prostaglandin D_2 mediated diseases and conditions that may be modulated by the inhibition of hematopoietic prostaglandin D synthase (H-PGDS), wherein R^1, R^2, U^1, U^2, U^3, U^4, Y^1, Y^2, Y^3, Y^4, and W, are defined herein:

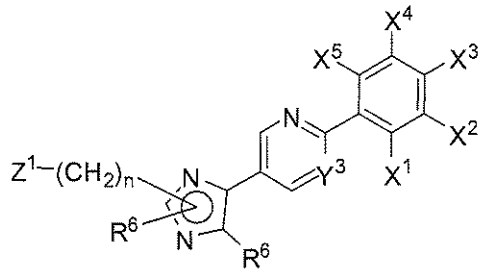


(I)



(II)

In one aspect, there is provided a compound according to Formula (III):



(III)

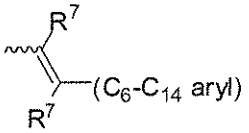
wherein:

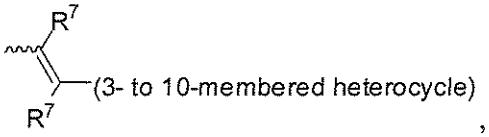
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

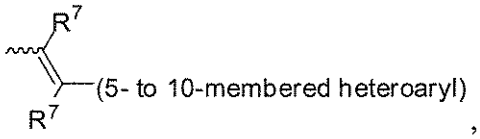
Y^3 is CH or N;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle, wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

p is 1, 2, or 3;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$-(three- to ten-membered heterocycle) wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyclyl), $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, phenyl, naphthyl, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

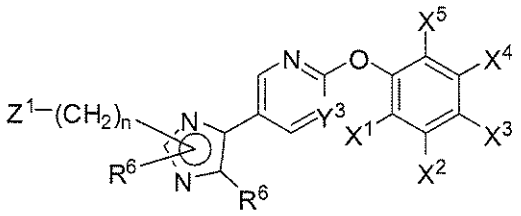
Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, $\text{-S-}(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl; and

R^7 is hydrogen or methyl.

In another aspect, there is provided a compound according to Formula (VI):



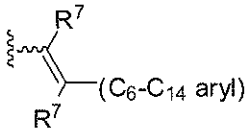
(VI)

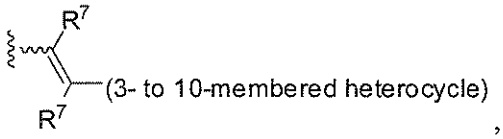
wherein:

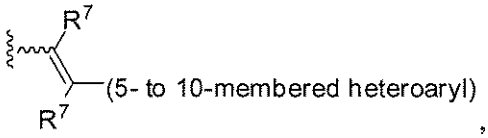
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N or C-R^6;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with -$(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with -$(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

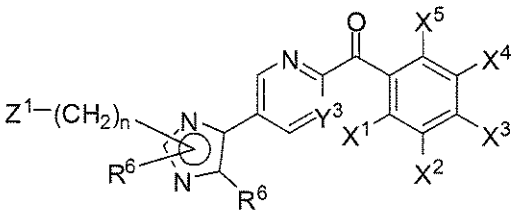
the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

In another aspect, there is provided a compound according to Formula (IX):



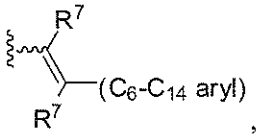
(IX)

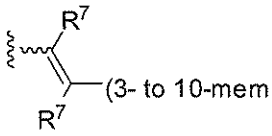
wherein:

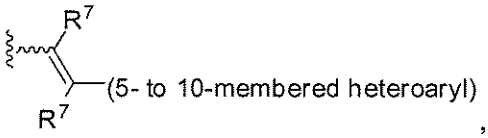
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N or C-R^6;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

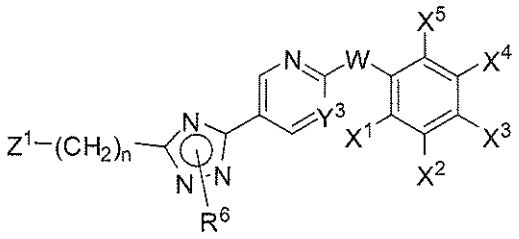
the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

In another aspect, there is provided a compound according to Formula (XVII):



(XVII)

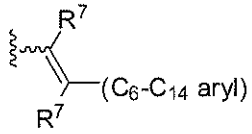
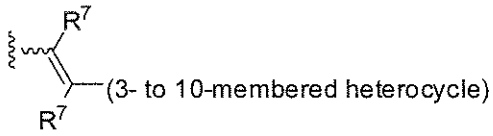
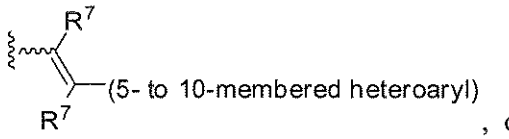
wherein:

each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N or C-R^6;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 
, 
, 
, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with -$(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with -$(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

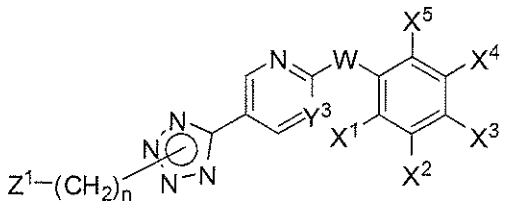
the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

In another aspect, there is provided a compound according to Formula (XVIII):



(XVIII)

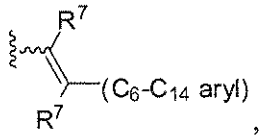
wherein:

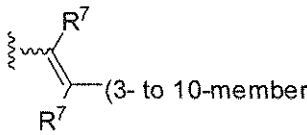
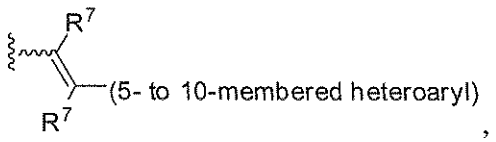
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 
,


, 
, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$ or $SO_2NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above.

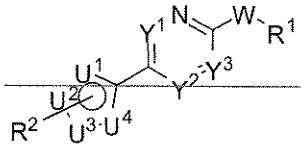
In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above, and a second pharmacologically active compound.

Another ~~aspect of the~~ exemplary embodiments may be a pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to either of formulas (I) or (II), or an equivalent thereof, or an *N*-oxide thereof, or a pharmaceutically acceptable salt or solvate thereof, in admixture with a pharmaceutically acceptable carrier.

Another ~~aspect of the~~ exemplary embodiments may be directed to a method of treating immunological disorders, particularly allergic and/or inflammatory disorders, and more particularly disorders such as allergic rhinitis, asthma, chronic obstructive pulmonary disease (COPD), arthritis, dermal inflammation, ocular inflammation, wound healing, and dermal scarring in a patient in need thereof by administering to the patient a

~~What is claimed is:~~

~~1. A compound of Formula (I):~~



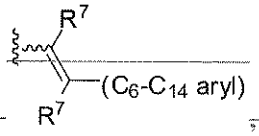
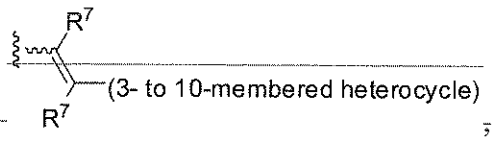
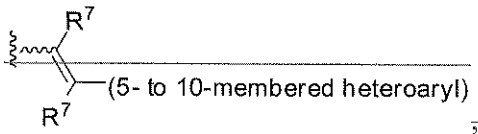
(I)

~~wherein:~~

~~R^1 is $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl; wherein each phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl of R^1 may be optionally substituted with no more than two of each or a combination of fluoro, hydroxy, CH_2OH, carboxy, carboxymethyl, or carboxyethyl;~~

~~R^2 is $(CH_2)_nZ^1$ or $(CH_2)_nZ^2$;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_6$-$C_{14})$ aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl,~~  ~~,~~  ~~,~~  ~~, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;~~

~~Z^2 is cyano, trifluoromethyl, $(CF_2)_pCF_3$, SR^3, NR^4R^5, $N(H)C(O)R^3$, $N(H)CO_2R^3$, $N(H)C(O)NR^4R^5$, $N(H)SO_2R^3$, vinyl, or ethynyl when n is 1, 2, 3 or 4;~~

~~Z^2 may also be cyano, trifluoromethyl, $(CF_2)_pCF_3$, SR^3, NR^4R^5, $N(H)C(O)R^3$, $N(H)CO_2R^3$, $N(H)C(O)NR^4R^5$, $N(H)SO_2R^3$, vinyl, or ethynyl when n is 0, except when R^2 is covalently bonded to a U^1, U^2, U^3, or U^4 that is a nitrogen atom;~~

~~R^3 is hydrogen, $(C_1$-$C_6)$ alkyl, trifluoromethyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;~~

~~m is 0, 1, 2, 3, or 4;~~

~~q is 0, 1, 2, 3, or 4;~~

~~Q is hydrogen, $(C_1$-$C_6)$ alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_3$-$C_6)$ cycloalkyl, $(C_6$-$C_{14})$ aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;~~

~~Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;~~

~~Q may also be hydroxy, $(C_1$-$C_6)$ alkoxy, sulfhydryl, S-$(C_1$-$C_6)$ alkyl, or NR^4R^5 when q is 2, 3, or 4;~~

~~p is 1, 2, or 3;~~

~~R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;~~

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$ alkyl, $(C_3\text{-}C_6)$ alkenyl, $(C_3\text{-}C_6)$ alkynyl, $(CH_2)_m(C_3\text{-}C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$ alkyl, CH_2CF_3, $(C_3\text{-}C_6)$ cycloalkyl, $CH_2(C_3\text{-}C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 and Z^2 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$ alkoxy, $(C_1\text{-}C_3)$ alkyl, $(C_1\text{-}C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$ alkyl, carbamoyl, or sulfamoyl;

W is a covalent bond, O, S, SO, SO_2, CH_2, CHOH, CO, or NH;

U^1, U^2, U^3, U^4, and a carbon atom form a five-membered heteroaryl ring; wherein one of U^1, U^2, U^3, and U^4 of the five-membered heteroaryl ring is covalently bonded to the R^2 group; wherein the U^1, U^2, U^3, or U^4 that is covalently bonded to the R^2 group is a carbon atom or a nitrogen atom; wherein when the U^1, U^2, U^3, or U^4 that is covalently bonded to the R^2 group is a nitrogen atom, one, two, or all of the other three of the group consisting of U^1, U^2, U^3, and U^4 is N and each remaining of the group consisting of U^1, U^2, U^3, and U^4 that is not N is C-R^6; wherein when the U^1, U^2, U^3, or U^4 that is

~~covalently bonded to the R^2 group is a carbon atom, one of the other three of the group consisting of U^1, U^2, U^3, and U^4 is N-R^6, O, or S, and each of remaining of the group consisting of U^1, U^2, U^3, and U^4 is C-R^6 or N;~~

~~Y^1, Y^2, Y^3, a nitrogen atom, and two carbon atoms form a six-membered heteroaryl ring; wherein no more than one of the group consisting of Y^1, Y^2, and Y^3 is N; and wherein all Y^1, Y^2, and Y^3 that are not N are C-R^6;~~

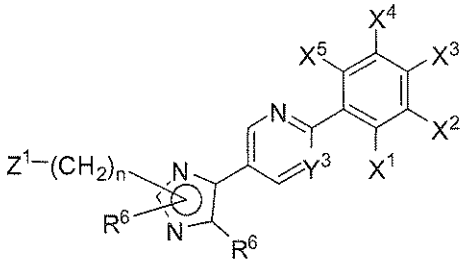
~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and~~

~~each R^7 is independently hydrogen or methyl;~~

~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof.~~

What is claimed is:

~~21~~. A compound ~~of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (I) comprises a compound~~ according to Formula (III):



(III)

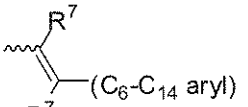
wherein:

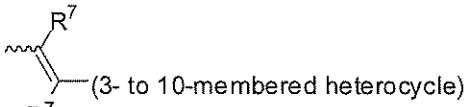
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

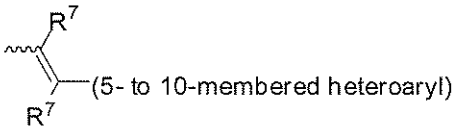
Y^3 is CH or N;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, ~~$SO2NR^4R^5$~~ $SO_2NR^4R^5$, ~~$SO2R^3$~~ SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle, wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

p is 1, 2, or 3;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$-(three- to ten-membered heterocycle) wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered ~~heterocyclyl~~heterocyclyl), $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$ or, $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$-alkyl, CH_2CF_3, $(C_3$-$C_6)$-cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, phenyl, naphthyl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

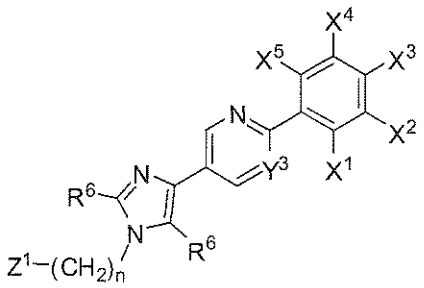
Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, -S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$-alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl; and

R^7 is hydrogen or methyl.

~~32~~. A compound of claim ~~21~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (III) comprises a compound according to Formula (IV):



(IV)

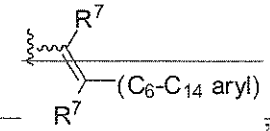
~~wherein:~~

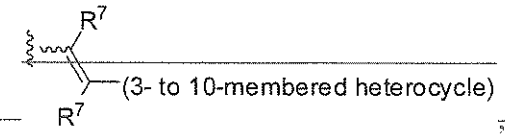
~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

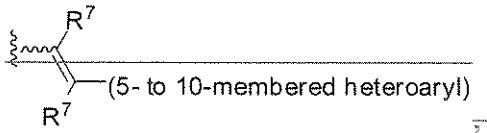
~~Y^3 is CH or N;~~

~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_6$-$C_{14})$ aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

; 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

~~R^3 is hydrogen, $(C_1$-$C_6)$ alkyl, trifluoromethyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$-(three- to ten-membered heterocycle);~~

wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^4 and R^5 are independently hydrogen, (C_1-C_6) alkyl, (C_3-C_6) alkenyl, (C_3-C_6) alkynyl, $(CH_2)_m(C_3-C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$(three- to ten-membered heterocycyl), $(CH_2)_m$(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, (C_1-C_6) alkyl, CH_2CF_3, (C_3-C_6) cycloalkyl, $CH_2(C_3-C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

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

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

Q is hydrogen, (C_1-C_6) alkyl, $(CH_2)_pCF_3$, (C_3-C_6) alkenyl, (C_3-C_6) alkynyl, (C_3-C_6) cycloalkyl, (C_6-C_{14}) aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

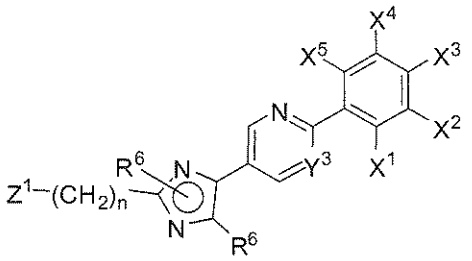
Q may also be hydroxy, (C_1-C_6) alkoxy, sulfhydryl, S-(C_1-C_6) alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

~~phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$-alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl; and~~

~~R^7 is hydrogen or methyl.~~

~~43~~. A compound of claim ~~21~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (III) comprises a compound according to Formula (V):



(V)

~~wherein:~~

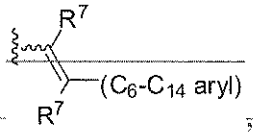
~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

~~Y^3 is CH or N;~~

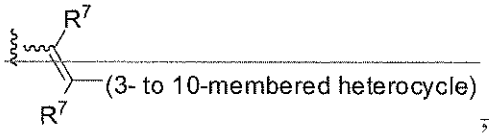
~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino;~~

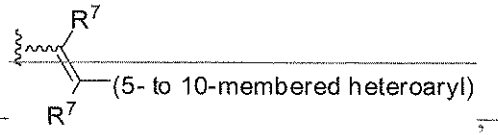
~~n is 0, 1, 2, 3, or 4;~~

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl,~~

~~$(CH_2)_pCF_3$, a five to ten membered heteroaryl,~~ 

~~;~~



~~,~~ 

~~, or a three to ten membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;~~

~~R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five to ten membered heteroaryl), or $(CH_2)_m$-(three to ten membered heterocycle); wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;~~

~~R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three to ten membered heterocycyl), $(CH_2)_m$-(five to ten membered heteroaryl);~~

~~the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S* dioxide;~~

~~the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$-alkyl, CH_2CF_3, $(C_3$-$C_6)$-cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;~~

~~m is 0, 1, 2, 3, or 4;~~

~~q is 0, 1, 2, 3, or 4;~~

~~Q is hydrogen, $(C_1$-$C_6)$ alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_3$-$C_6)$ cycloalkyl, $(C_6$-$C_{14})$ aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;~~

~~Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;~~

~~Q may also be hydroxy, $(C_1$-$C_6)$ alkoxy, sulfhydryl, S-$(C_1$-$C_6)$ alkyl, or NR^4R^5 when q is 2, 3, or 4;~~

~~p is 1, 2, or 3;~~

~~phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl; and~~

~~R^7 is hydrogen or methyl.~~

~~54~~54. A compound of claim ~~43~~43, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

Y^3 is N;

each X^1, X^3, X^4, and X^5 is hydrogen;

X^2 is hydrogen or fluoro;

each R^6 is independently hydrogen, methyl, or trifluoromethyl;

n is 0, 1, or 2;

Z^1 is phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, piperidin-4-yl, piperidin-3-yl, piperidin-3(*R*)-yl, piperidin-3(*S*)-yl, piperidin-2-yl, piperidin-2(*R*)-yl, piperidin-2(*S*)-yl, pyrrolidin-3-yl, pyrrolidin-3(*R*)-yl, pyrrolidin-3(*S*)-yl, pyrrolidin-2-yl, pyrrolidin-2(*R*)-yl, pyrrolidin-2(*S*)-yl, or azetidin-3-yl;

the nitrogen atom of a piperidinyl, a pyrrolidinyl, or a azetidinyl ring is substituted with -$(CH_2)_qQ$;

q is 0, 1, or 2;

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $-CH_2CF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, phenyl, naphthyl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, or $(CH_2)_m$-(five- to ten-membered heteroaryl); and

m is 0, 1, or 2.

~~65~~. A compound of claim ~~54~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

Z^1 is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl; and

wherein said phenyl or pyridyl rings of Z^1 are optionally substituted with one or two of any one or combination of the following: halo, hydroxy, methoxy, methyl, or trifluoromethyl.

~~76~~76. A compound of claim ~~65~~65, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

Z^1 is piperidin-4-yl, piperidin-3-yl, piperidin-3(*R*)-yl, piperidin-3(*S*)-yl, piperidin-2-yl, piperidin-2(*R*)-yl, piperidin-2(*S*)-yl, pyrrolidin-3-yl, pyrrolidin-3(*R*)-yl, pyrrolidin-3(*S*)-yl, pyrrolidin-2-yl, pyrrolidin-2(*R*)-yl, pyrrolidin-2(*S*)-yl, or azetidin-3-yl;

q is 0 or 1;

Q is (C_1-C_4)-alkyl, -CH_2CF_3, (C_3-C_6)-cycloalkyl, phenyl, ~~C(O)R^3, CO_2R^3,~~ C(O)NHR^5, a five- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

R^3 is hydrogen, (C_1-C_4)-alkyl, trifluoromethyl, $(CH_2)_m$(C_3-C_6)-cycloalkyl, $(CH_2)_m$phenyl, or $(CH_2)_m$-(five- to six-membered heteroaryl); and

m is 0, 1, or 2.

~~87~~. A compound of claim 43, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ or a pharmaceutically acceptable salt thereof, wherein:

Y^3 is CH;

each X^1, X^3, X^4, and X^5 is hydrogen;

X^2 is hydrogen or fluoro;

R^6 is hydrogen, methyl, or trifluoromethyl;

n is 0, 1, or 2;

Z^1 is phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, piperidin-4-yl, piperidin-3-yl, piperidin-3(*R*)-yl, piperidin-3(*S*)-yl, piperidin-2-yl, piperidin-2(*R*)-yl, piperidin-2(*S*)-yl, pyrrolidin-3-yl, pyrrolidin-3(*R*)-yl, pyrrolidin-3(*S*)-yl, pyrrolidin-2-yl, pyrrolidin-2(*R*)-yl, pyrrolidin-2(*S*)-yl, or azetidin-3-yl;

the nitrogen atom of a piperidinyl, a pyrrolidinyl, or a azetidinyl ring of Z^1 is substituted with $-(CH_2)_qQ$;

q is 0, 1, or 2;

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $-CH_2CF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, phenyl, naphthyl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, or $(CH_2)_m$-(five- to ten-membered heteroaryl); and

m is 0, 1, or 2.

~~98~~. A compound of claim ~~87~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

Z^1 is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl; and

said phenyl or pyridyl rings may be optionally substituted with one or two of any one or combination of the following: halo, hydroxy, methoxy, methyl, or trifluoromethyl.

~~109~~. A compound of claim ~~87~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

Z^1 is piperidin-4-yl, piperidin-3-yl, piperidin-3(R)-yl, piperidin-3(S)-yl, piperidin-2-yl, piperidin-2(R)-yl, piperidin-2(S)-yl, pyrrolidin-3-yl, pyrrolidin-3(R)-yl, pyrrolidin-3(*S*)-yl, pyrrolidin-2-yl, pyrrolidin-2(*R*)-yl, pyrrolidin-2(*S*)-yl, or azetidin-3-yl;

q is 0 or 1;

Q is (C_1-C_4)-alkyl, -CH_2CF_3, (C_3-C_6)-cycloalkyl, phenyl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NHR^5$, a five- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

R^3 is hydrogen, (C_1-C_4)-alkyl, trifluoromethyl, $(CH_2)_m$(C_3-C_6)-cycloalkyl, $(CH_2)_m$phenyl, or $(CH_2)_m$-(five- to six-membered heteroaryl); and

m is 0, 1, or 2.

~~11~~10. A compound of claim ~~10~~9, ~~or an equivalent thereof, or a hydrate, solvate, or N-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein:

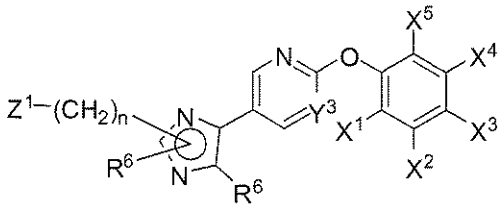
q is 0;

Q is hydrogen, (C_1-C_6)-alkyl, $(CH_2)_pCF_3$, (C_3-C_6)- alkenyl, (C_3-C_6)-alkynyl, (C_3-C_6)-cycloalkyl, (C_6-C_{14})-aryl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NHR^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl;

phenyl or heteroaryl rings are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, (C_1-C_3)-

alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl.

~~1211~~. A compound ~~of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (I) comprises a compound~~ according to Formula (VI):



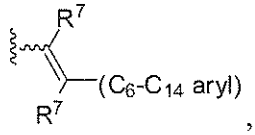
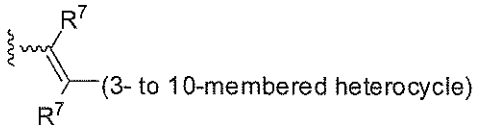
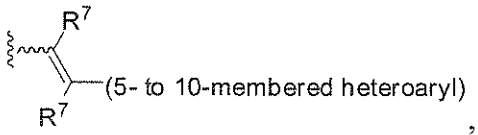
(VI)

wherein:

each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N or C-R^6;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, , , , or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, $-S\text{-}(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

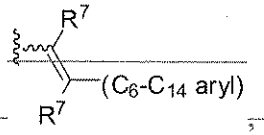
R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

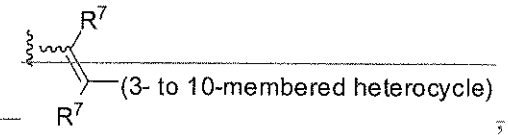
~~R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;~~

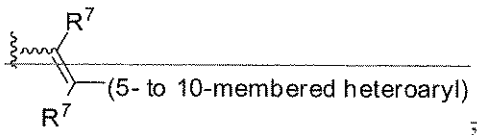
R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered ~~heterocycyl~~heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyeyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$-alkyl, CH_2CF_3, $(C_3$-$C_6)$-cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$-alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$ or, $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

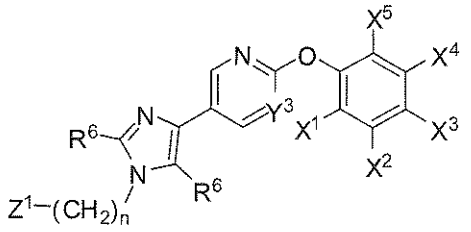
phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

~~wherein Y^3 is N or C-R^6;~~

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~13~~12. A compound of claim ~~12~~11, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (VI) comprises a compound according to Formula (VII):



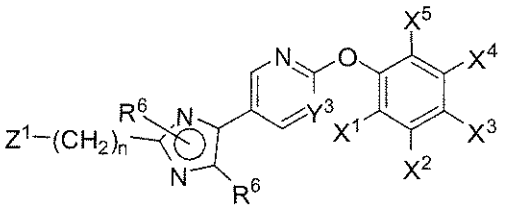
(VII)

~~wherein:~~

~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and~~

~~each R^7 is independently hydrogen or methyl.~~

~~1413~~. A compound of claim ~~1211~~, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (VI) comprises a compound according to Formula (VIII):

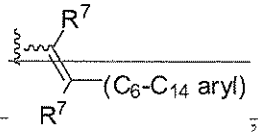
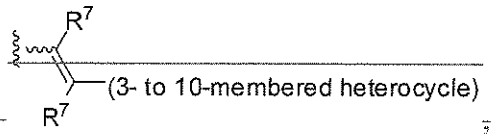
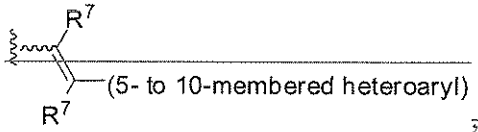


(VIII)

~~wherein:~~

~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl,~~  ~~,~~  ~~,~~  ~~, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qO$;~~

R^3 is hydrogen, (C_1-C_6)-alkyl, trifluoromethyl, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, $(CH_2)_m(C_3-C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, (C_1-C_6)-alkyl, $(CH_2)_pCF_3$, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, (C_3-C_6)-cycloalkyl, (C_6-C_{14})-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, (C_1-C_6)-alkoxy, sulfhydryl, S-(C_1-C_6)-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, (C_1-C_6)-alkyl, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, $(CH_2)_m(C_3-C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

~~the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;~~

~~the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;~~

~~phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;~~

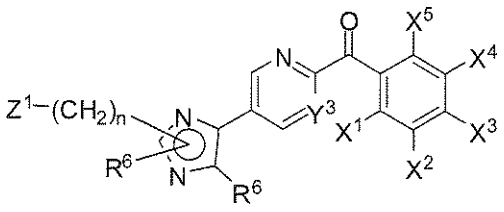
~~wherein Y^3 is N or C-R^6;~~

~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and~~

~~each R^7 is independently hydrogen or methyl.~~

~~15~~14. A compound ~~of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~

~~wherein the compound according to Formula (I) comprises a compound~~ according to Formula (IX):



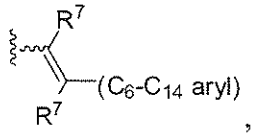
(IX)

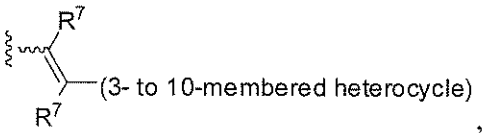
wherein:

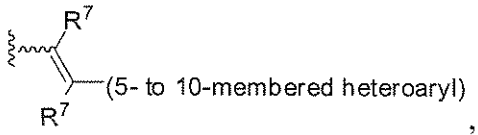
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

Y^3 is N or C-R^6;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

~~R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a 2 (minus 2) oxidation state;~~

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered ~~heterocycyl~~heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

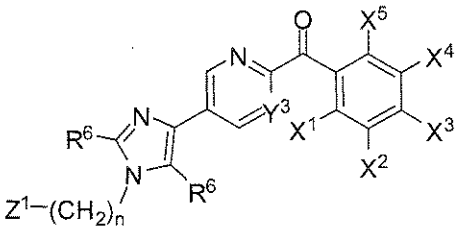
phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

~~wherein Y^3 is N or C-R^6;~~

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~16~~15. A compound of claim ~~15~~14, ~~or an equivalent thereof, or a hydrate, solvate, or N-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (IX) comprises a compound according to Formula (X):

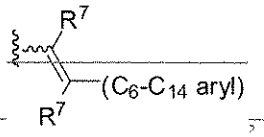


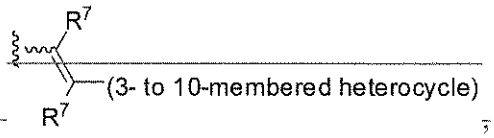
(X)

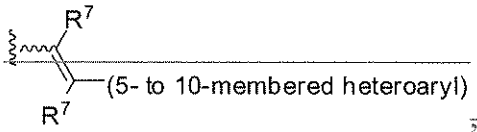
~~wherein:~~

~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$-alkyl, CH_2CF_3, $(C_3$-$C_6)$-cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

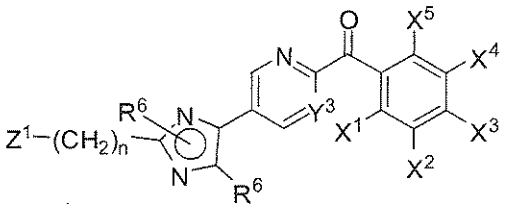
phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$-alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~17~~16. A compound of claim ~~15~~14, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~ wherein the compound according to Formula (IX) comprises a compound according to Formula (XI):

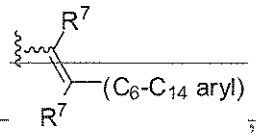


(XI)

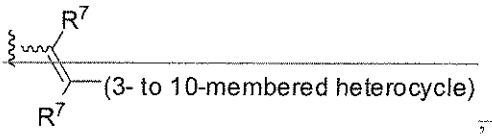
~~wherein:~~

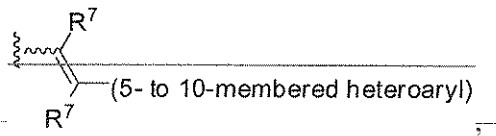
~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_6$-$C_{14})$ aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl,~~ 

;



,


, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, (C_1-C_6)-alkyl, trifluoromethyl, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, $(CH_2)_m(C_3-C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, (C_1-C_6)-alkyl, $(CH_2)_pCF_3$, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, (C_3-C_6)-cycloalkyl, (C_6-C_{14})-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, (C_1-C_6)-alkoxy, sulfhydryl, $S-(C_1-C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$-alkyl, CH_2CF_3, $(C_3$-$C_6)$-cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

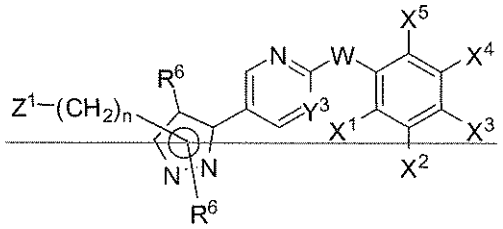
phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$-alkoxy, $(C_1$-$C_3)$-alkyl, $(C_1$-$C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~18. A compound of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (I) comprises a compound according to Formula (XII):~~



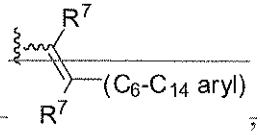
(XII)

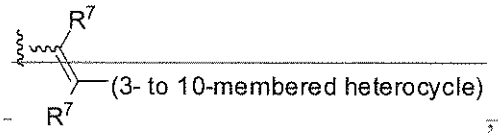
~~wherein:~~

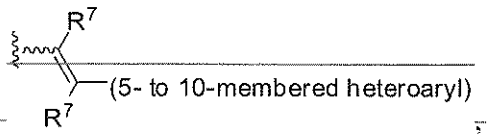
~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

~~W is a covalent bond, O, or CO;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl,~~  ~~;~~





~~, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;~~

~~R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;~~

~~m is 0, 1, 2, 3, or 4;~~

~~q is 0, 1, 2, 3, or 4;~~

~~Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;~~

~~Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;~~

~~Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;~~

~~p is 1, 2, or 3;~~

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;

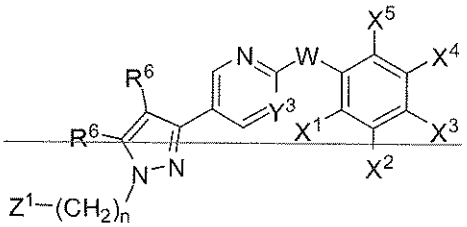
wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

19. A compound of claim **18**, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,

wherein the compound according to Formula (XII) comprises a compound according to Formula (XIII):



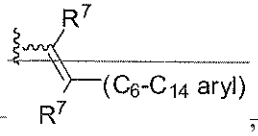
(XIII)

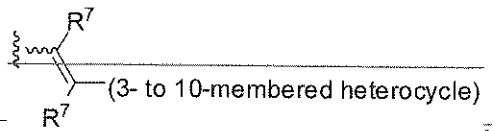
wherein:

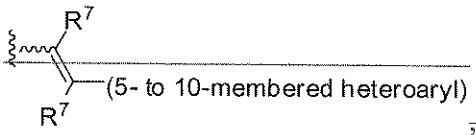
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more

nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyeyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine S-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

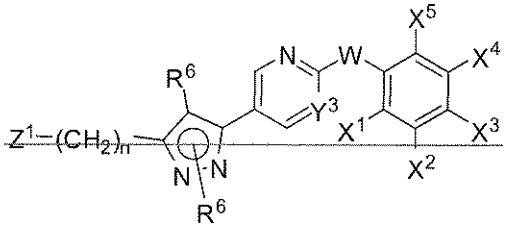
phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

20. A compound of claim 18, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (XII) comprises a compound according to Formula (XIV):



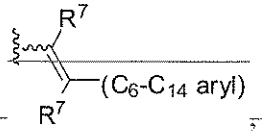
(XIV)

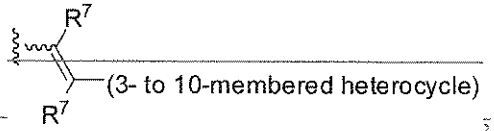
wherein:

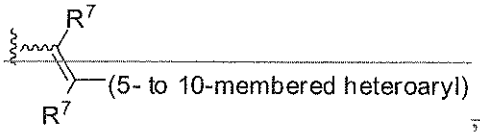
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

; 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen

atom of the piperazine ring is substituted with hydrogen, (C_1-C_6)-alkyl, CH_2CF_3, (C_3-C_6)-cycloalkyl, CH_2(C_3-C_6)-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

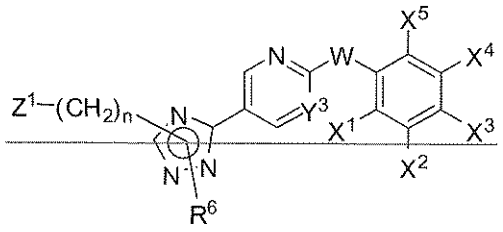
phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, (C_1-C_3)-alkoxy, (C_1-C_3)-alkyl, (C_1-C_3)-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy(C_1-C_3)-alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

21. A compound of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (I) comprises a compound according to Formula (XV):



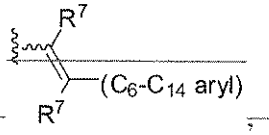
(XV)

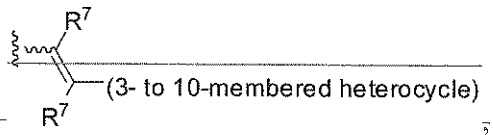
wherein:

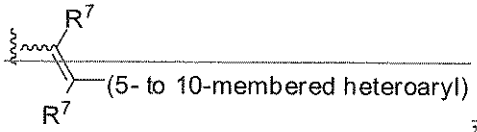
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen

atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

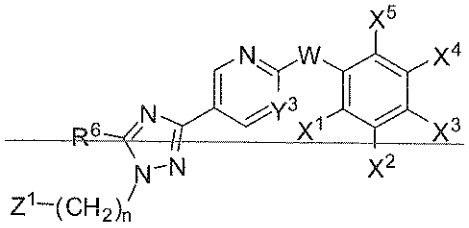
phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$-alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

22. A compound of claim 21, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (XV) comprises a compound according to Formula (XVI):



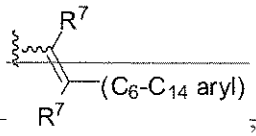
(XVI)

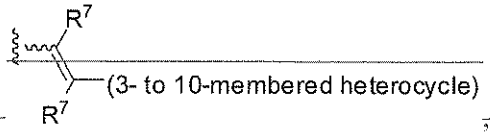
wherein:

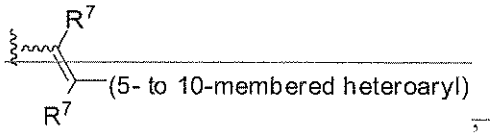
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_6$-$C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered heterocyeyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

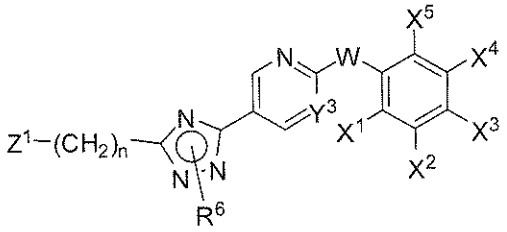
phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;

wherein Y^3 is N or C-R^6;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~23~~17. A compound ~~of claim 21, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (XV) comprises a compound~~ according to Formula (XVII):



(XVII)

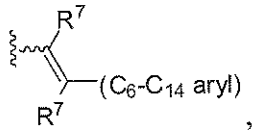
wherein:

each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

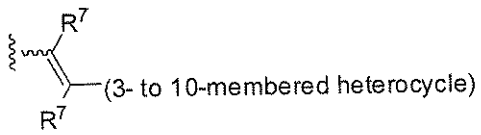
Y^3 is N or C-R^6;

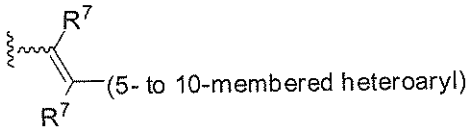
W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, (C_3-C_6)-alkenyl, (C_3-C_6)-alkynyl, (C_6-C_{14})-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

,



, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, ~~$C(O)R^3$, CO_2R^3,~~ $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

~~R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;~~

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered ~~heterocyeyl~~heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

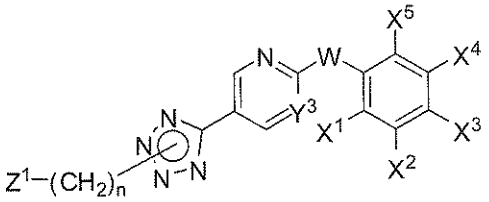
phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

~~wherein Y^3 is N or C-R^6;~~

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~24~~18. A compound ~~of claim 1, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound according to Formula (I) comprises a compound~~ according to Formula (XVIII):



(XVIII)

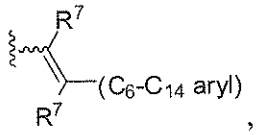
wherein:

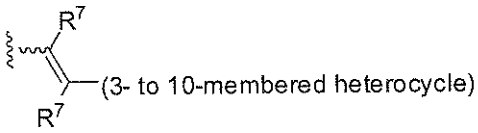
each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;

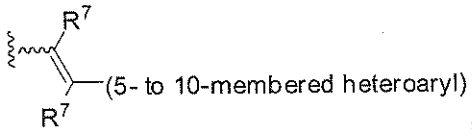
Y^3 is N;

W is a covalent bond, O, or CO;

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

Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_6\text{-}C_{14})$-aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, ,



, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

R^3 is hydrogen, $(C_1\text{-}C_6)$-alkyl, trifluoromethyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1\text{-}C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3\text{-}C_6)$- alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(C_3\text{-}C_6)$-cycloalkyl, $(C_6\text{-}C_{14})$-aryl, ~~$C(O)R^3$~~, ~~CO_2R^3~~, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1\text{-}C_6)$-alkoxy, sulfhydryl, -S-$(C_1\text{-}C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

~~R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a 2 (minus 2) oxidation state;~~

R^4 and R^5 are independently hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-alkenyl, $(C_3\text{-}C_6)$-alkynyl, $(CH_2)_m(C_3\text{-}C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(three- to ten-membered ~~heterocycyl~~heterocyclyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, or $SO_2NR^4R^5$, ~~NR^4R^5, or $N(H)C(O)NR^4R^5$~~ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1\text{-}C_6)$-alkyl, CH_2CF_3, $(C_3\text{-}C_6)$-cycloalkyl, $CH_2(C_3\text{-}C_6)$-cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 are optionally substituted with one-to-three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1\text{-}C_3)$-alkoxy, $(C_1\text{-}C_3)$-alkyl, $(C_1\text{-}C_3)$-alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1\text{-}C_3)$-alkyl, carbamoyl, or sulfamoyl;

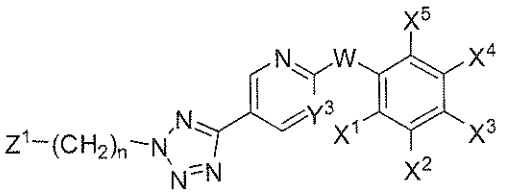
~~wherein Y^3 is N or C-R^6;~~

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl.

~~25~~19. A compound of claim ~~24~~18, ~~or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof,~~

wherein the compound according to Formula (XVIII) comprises a compound according to Formula (XIX):



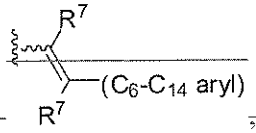
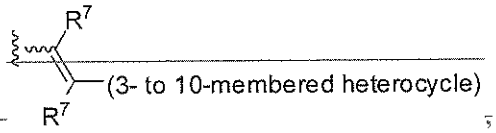
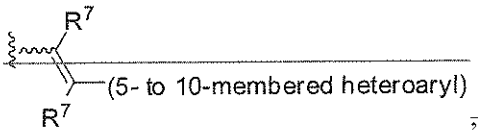
(XIX)

~~wherein:~~

~~each X^1, X^2, X^3, X^4, and X^5 is independently hydrogen or fluoro, with no more than two of X^1, X^2, X^3, X^4, and X^5 being fluoro;~~

~~W is a covalent bond, O, or CO;~~

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

~~Z^1 is hydrogen, OR^3, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, $SO_2NR^4R^5$, SO_2R^3, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_6$-$C_{14})$ aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl,~~  ~~,~~  ~~,~~  ~~, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;~~

~~R^3 is hydrogen, $(C_1$-$C_6)$ alkyl, trifluoromethyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle), wherein any one nitrogen atom of any heterocycle containing one or more~~

nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $-(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $-C(O)R^3$, $-CO_2R^3$, $-C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $-SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, $-S-(C_1$-$C_6)$-alkyl, or $-NR^4R^5$ when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a +2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $-(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $-(CH_2)_m$phenyl, $-(CH_2)_m$-(three- to ten-membered heterocycyl), or $-(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $-C(O)NR^4R^5$, $-SO_2NR^4R^5$, $-NR^4R^5$, or $-N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

~~the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;~~

~~phenyl or heteroaryl rings of Z^1 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;~~

~~wherein Y^3 is N or C-R^6;~~

~~each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and~~

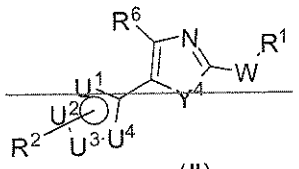
~~each R^7 is independently hydrogen or methyl.~~

~~2620~~**20**. A pharmaceutical composition comprising a compound of claim **1**~~, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient~~.

~~2721~~**21**. A pharmaceutical composition comprising a compound of claim **1**~~, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a~~

pharmaceutically acceptable salt thereof, and a second pharmacologically active compound.

28. A compound of Formula (II):



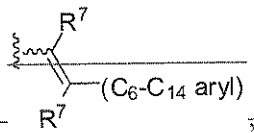
(II)

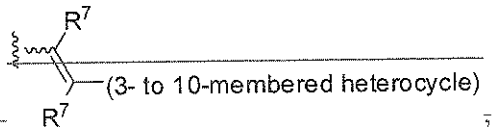
wherein:

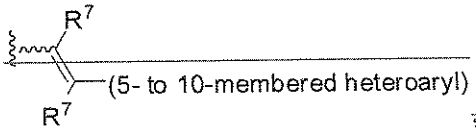
R^1 is $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl; wherein each phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl of R^1 may be optionally substituted with no more than two of each or a combination of fluoro, hydroxy, $-CH_2OH$, carboxy, carboxymethyl, or carboxyethyl;

R^2 is $-(CH_2)_nZ^1$ or $-(CH_2)_nZ^2$;

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

Z^1 is hydrogen, OR^3, $-C(O)R^3$, $-CO_2R^3$, $-C(O)NR^4R^5$, $-SO_2NR^4R^5$, $-SO_2R^3$, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ cycloalkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(C_6$-$C_{14})$ aryl, $(CH_2)_pCF_3$, a five- to ten-membered heteroaryl, 

, 

, 

, or a three- to ten-membered heterocycle; wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $-(CH_2)_qQ$;

Z^2 is cyano, trifluoromethyl, $(CF_2)_pCF_3$, SR^3, NR^4R^5, $N(H)C(O)R^3$, $N(H)CO_2R^3$, $N(H)C(O)NR^4R^5$, $N(H)SO_2R^3$, vinyl, or ethynyl when n is 1, 2, 3 or 4;

Z^2 may also be cyano, trifluoromethyl, $(CF_2)_pCF_3$, SR^3, NR^4R^5, $N(H)C(O)R^3$, $N(H)CO_2R^3$, $N(H)C(O)NR^4R^5$, $N(H)SO_2R^3$, vinyl, or ethynyl when n is 0, except when R^2 is covalently bonded to a U^1, U^2, U^3, or U^4 that is a nitrogen atom;

R^3 is hydrogen, $(C_1$-$C_6)$-alkyl, trifluoromethyl, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(CH_2)_m(C_3$-$C_6)$-cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$-(five- to ten-membered heteroaryl), or $(CH_2)_m$(three- to ten-membered heterocycle); wherein any one nitrogen atom of any heterocycle containing one or more nitrogen atoms that may be substituted with a non-ring atom are substituted with $(CH_2)_qQ$;

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

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

Q is hydrogen, $(C_1$-$C_6)$-alkyl, $(CH_2)_pCF_3$, $(C_3$-$C_6)$-alkenyl, $(C_3$-$C_6)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, $(C_6$-$C_{14})$-aryl, $C(O)R^3$, CO_2R^3, $C(O)NR^4R^5$, a three- to six-membered heterocycle, or a five- to ten-membered heteroaryl when q is 0, 1, 2, 3, or 4;

Q may also be cyano, trifluoromethyl, or $SO_2NR^4R^5$ when q is 1, 2, 3, or 4;

Q may also be hydroxy, $(C_1$-$C_6)$-alkoxy, sulfhydryl, -S-$(C_1$-$C_6)$-alkyl, or NR^4R^5 when q is 2, 3, or 4;

p is 1, 2, or 3;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an N or O atom;

R^3 may also be vinyl or ethynyl when R^3 is not covalently bonded to an S atom possessing a -2 (minus 2) oxidation state;

R^4 and R^5 are independently hydrogen, $(C_1$-$C_6)$ alkyl, $(C_3$-$C_6)$ alkenyl, $(C_3$-$C_6)$ alkynyl, $(CH_2)_m(C_3$-$C_6)$ cycloalkyl, $(CH_2)_m$phenyl, $(CH_2)_m$(three- to ten-membered heterocycyl), or $(CH_2)_m$-(five- to ten-membered heteroaryl);

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a pyrrolidine, a piperidine, a morpholine, a thiomorpholine, or a thiomorpholine *S*-dioxide;

the NR^4R^5 group of any $C(O)NR^4R^5$, $SO_2NR^4R^5$, NR^4R^5, or $N(H)C(O)NR^4R^5$ may also form a piperazine ring, wherein the other nitrogen atom of the piperazine ring is substituted with hydrogen, $(C_1$-$C_6)$ alkyl, CH_2CF_3, $(C_3$-$C_6)$ cycloalkyl, $CH_2(C_3$-$C_6)$ cycloalkyl, phenyl, benzyl, hydroxyethyl, or hydroxypropyl;

phenyl or heteroaryl rings of Z^1 and Z^2 are optionally substituted with one to three of any one or combination of the following: halo, hydroxy, sulfhydryl, $(C_1$-$C_3)$ alkoxy, $(C_1$-$C_3)$ alkyl, $(C_1$-$C_3)$ alkylthio, trifluoromethyl, trifluoromethoxy, cyano, carboxy, carboxy$(C_1$-$C_3)$ alkyl, carbamoyl, or sulfamoyl;

W is a covalent bond, O, S, SO, SO_2, CH_2, CHOH, CO, or NH;

U^1, U^2, U^3, U^4, and a carbon atom form a five-membered heteroaryl ring; wherein one of U^1, U^2, U^3, and U^4 of the five-membered heteroaryl ring is covalently bonded to the R^2 group; wherein the U^1, U^2, U^3, or U^4 that is covalently bonded to the R^2 group is a carbon atom or a nitrogen atom; wherein when the U^1, U^2, U^3, or U^4 that is covalently bonded to the R^2 group is

a nitrogen atom, one, two, or all of the other three of the group consisting of U^1, U^2, U^3, and U^4 is N and each remaining of the group consisting of U^1, U^2, U^3, and U^4 that is not N is C-R^6; wherein when the U^1, U^2, U^3, or U^4 that is covalently bonded to the R^2 group is a carbon atom, one of the other three of the group consisting of U^1, U^2, U^3, and U^4 is N-R^6, O, or S, and each of remaining of the group consisting of U^1, U^2, U^3, and U^4 is C-R^6 or N;

Y^4 is O, S, or N-R^7;

each R^6 is independently hydrogen, methyl, trifluoromethyl, or amino; and

each R^7 is independently hydrogen or methyl;

or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereof.

29. A pharmaceutical composition comprising a compound of claim 28, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a pharmaceutically acceptable salt thereofreof, and a pharmaceutically acceptable excipient.

30. A pharmaceutical composition comprising a compound of claim 28, or an equivalent thereof, or a hydrate, solvate, or *N*-oxide thereof, or a

~~pharmaceutically acceptable salt thereof, and a second pharmacologically active compound.~~

~~31. The compound of claim 1, wherein when W is NH, then the ring incorporating U1, U2, U3, and U4 may not be an imidazole or thiazole ring.~~

~~32. The compound of claim 28, provided that the heterocyclic ring is not a pyrazole.~~