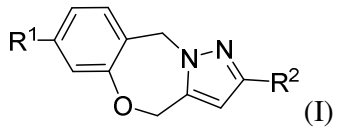
**WHAT IS CLAIMED IS:**

1. A compound of formula (I):




(I)

or a prodrug thereof, or a pharmaceutically acceptable salt thereof, wherein:

$R^1$ is $-NR^aR^b$ or a 5-10 membered heteroaryl that is optionally substituted with one or more groups $R^c$;

$R^2$ is a 6-10 membered aryl that is optionally substituted with one or more groups $R^r$; or $R^2$ is a 5-10 membered heteroaryl that is that is optionally substituted with one or more groups $R^s$; or $R^2$ is a 3-10 membered heterocycle that is that is optionally substituted with one or more groups $R^z$;

$R^a$ is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkynylcarbonyl, 3-6 membered heterocycle, or a 5-6 membered heteroaryl that is optionally substituted with one or more groups $R^f$; wherein each $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkynylcarbonyl, and 3-6 membered heterocycle is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, cyano, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $C(=O)NR^mR^n$, and $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more groups independently selected form the group consisting of halo, hydroxy, cyano, $-NR^mR^n$, and $-C(=O)NR^mR^n$;

$R^b$ is H or $(C_1\text{-}C_6)$alkyl;

each $R^c$ is independently selected from the group consisting of cyano, $-NR^dR^e$, $-C(=O)NR^dR^e$, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, and $(C_1\text{-}C_6)$alkanoyl, wherein each $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and $(C_1\text{-}C_6)$alkanoyl is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, and cyano;

$R^d$ and $R^e$ are each independently selected from the group consisting of H and $(C_1\text{-}C_6)$alkyl; or $R^d$ and $R^e$ taken together with the nitrogen to which they are attached form a 3-6 membered heterocyclic ring that is optionally substituted with one or more groups independently selected from the group consisting of halo and $(C_1\text{-}C_6)$alkyl;

each $R^f$ is independently selected from the group consisting of halo, hydroxy, cyano, $-NR^gR^h$, $-C(=O)NR^gR^h$, and $(C_1-C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, $-NR^gR^h$, $-C(=O)NR^gR^h$, and cyano;

$R^g$ and $R^h$ are each independently selected from the group consisting of H and $(C_1-C_6)$alkyl; or $R^g$ and $R^h$ taken together with the nitrogen to which they are attached form a 3-6 membered heterocyclic ring that is optionally substituted with one or more groups independently selected from the group consisting of halo and $(C_1-C_6)$alkyl;

$R^m$ is H or $(C_1-C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, cyano, and oxo;

$R^n$ is H or $(C_1-C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, cyano, and oxo;

each $R^r$ is independently selected from the group consisting of halo, hydroxy, cyano, $-NR^tR^u$, $-C(=O)NR^tR^u$, $-S(O)_2NR^tR^u$, $(C_1-C_6)$alkyl, $(C_3-C_6)$cycloalkyl, $(C_1-C_6)$alkoxy, $(C_1-C_6)$alkylthio, $-N(H)S(O)_2R^x$, $-S(O)_2R^x$, $(C_2-C_6)$alkenyl, and $(C_2-C_6)$alkynyl, wherein each $(C_1-C_6)$alkyl, $(C_3-C_6)$cycloalkyl, $(C_1-C_6)$alkoxy, $(C_1-C_6)$alkylthio, $(C_2-C_6)$alkenyl, and $(C_2-C_6)$alkynyl is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, $-NR^tR^u$, $-C(=O)NR^tR^u$, $-S(O)_2NR^tR^u$, $-S(O)_2R^x$, and cyano;

each $R^s$ is independently selected from the group consisting of halo, cyano, $-NR^vR^w$, $-C(=O)NR^vR^w$, $-S(O)_2NR^vR^w$, $(C_1-C_6)$alkyl, $(C_3-C_6)$cycloalkyl, $(C_1-C_6)$alkoxy, $(C_1-C_6)$alkanoyl, $(C_1-C_6)$alkylthio, 3-6 membered heterocycle, and $-S(O)_2R^y$, wherein each $(C_1-C_6)$alkyl, $(C_3-C_6)$cycloalkyl, $(C_1-C_6)$alkoxy, $(C_1-C_6)$alkanoyl, 3-6 membered heterocycle, and $(C_1-C_6)$alkylthio, is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, $-NR^tR^u$, $-C(=O)NR^tR^u$, $S(O)_2NR^vR^w$, $-S(O)_2R^y$, and cyano;

$R^t$ and $R^u$ are each independently selected from the group consisting of H, $(C_1-C_6)$alkyl, $(C_1-C_6)$alkanoyl, and $(C_2-C_6)$alkynylcarbonyl; or $R^t$ and $R^u$ taken together with the nitrogen to which they are attached form a 3-6 membered heterocyclic ring that is optionally substituted with one or more groups independently selected from the group consisting of halo and $(C_1-C_6)$alkyl;

$R^v$ and $R^w$ are each independently selected from the group consisting of H, $(C_1-C_6)$alkyl, and $(C_1-C_6)$alkanoyl; or $R^v$ and $R^w$ taken together with the nitrogen to which they are attached

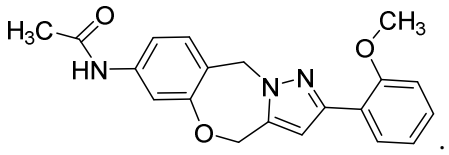
form a 3-6 membered heterocyclic ring that is optionally substituted with one or more groups independently selected from the group consisting of halo and $(C_1\text{-}C_6)$alkyl;

$R^x$ is H or $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, cyano, and oxo;

$R^y$ is H or $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, cyano, and oxo; and

each $R^z$ is independently selected from the group consisting of oxo, halo, hydroxy, and $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy, carboxy, $-NR^tR^u$, $-C(=O)NR^tR^u$, $S(O)_2NR^vR^w$, $-S(O)_2R^y$, cyano, and oxo;

provided the compound is not:



2. The compound of claim 1, wherein:

$R^1$ is $-NR^aR^b$ or a 5-10 membered heteroaryl that is optionally substituted with one or more groups $R^c$;

$R^2$ is a phenyl that is optionally substituted with one or more groups $R^r$; or $R^2$ is a 5- 9 membered heteroaryl that is that is optionally substituted with one or more groups $R^s$; or $R^2$ is a 9-membered heterocycle that is that is optionally substituted with one or more groups $R^z$;

$R^a$ is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_2\text{-}C_6)$alkynylcarbonyl, 3-6 membered heterocycle, or a 5-membered heteroaryl that is optionally substituted with one or more groups $R^f$; wherein each $(C_1\text{-}C_6)$alkyl and $(C_3\text{-}C_6)$cycloalkyl is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, $(C_2\text{-}C_6)$alkynyl, $C(=O)NR^mR^n$, and $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more hydroxy;

$R^b$ is H or $(C_1\text{-}C_6)$alkyl;

each $R^c$ is independently selected from the group consisting of cyano, $-NR^dR^e$, and $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more cyano;

$R^d$ and $R^e$ are each H;

each $R^f$ is independently selected from the group consisting of halo, hydroxy, cyano, -C(=O)$NR^gR^h$, and ($C_1$-$C_6$)alkyl that is optionally substituted with one or more groups independently selected from the group consisting of halo, hydroxy and carboxy;

$R^g$ and $R^h$ are each H;

$R^m$ is H;

$R^n$ is H;

each $R^r$ is independently selected from the group consisting of halo, hydroxy, cyano, -$NR^tR^u$, -C(=O)$NR^tR^u$, -$S(O)_2NR^tR^u$, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, -N(H)$S(O)_2R^x$, -$S(O)_2R^x$, and ($C_2$-$C_6$)alkynyl, wherein each ($C_1$-$C_6$)alkyl and ($C_2$-$C_6$)alkynyl, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, -$NR^tR^u$, -C(=O)$NR^tR^u$, and cyano;

each $R^s$ is independently selected from the group consisting of halo, cyano, -$NR^vR^w$, -C(=O)$NR^vR^w$, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkylthio, 3-6 membered heterocycle, and -$S(O)_2R^y$, wherein each ($C_1$-$C_6$)alkyl is optionally substituted with one or more groups independently selected from the group consisting of halo and -$NR^tR^u$;

$R^t$ and $R^u$ are each independently selected from the group consisting of H, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkanoyl, and ($C_2$-$C_6$)alkynylcarbonyl; or $R^t$ and $R^u$ taken together with the nitrogen to which they are attached form a 3-6 membered heterocyclic ring that is optionally substituted with one or more groups independently selected from the group consisting of halo and ($C_1$-$C_6$)alkyl;

$R^v$ and $R^w$ are each independently selected from the group consisting of H, ($C_1$-$C_6$)alkyl, and ($C_1$-$C_6$)alkanoyl;

$R^x$ is ($C_1$-$C_6$)alkyl;

$R^y$ is ($C_1$-$C_6$)alkyl; and

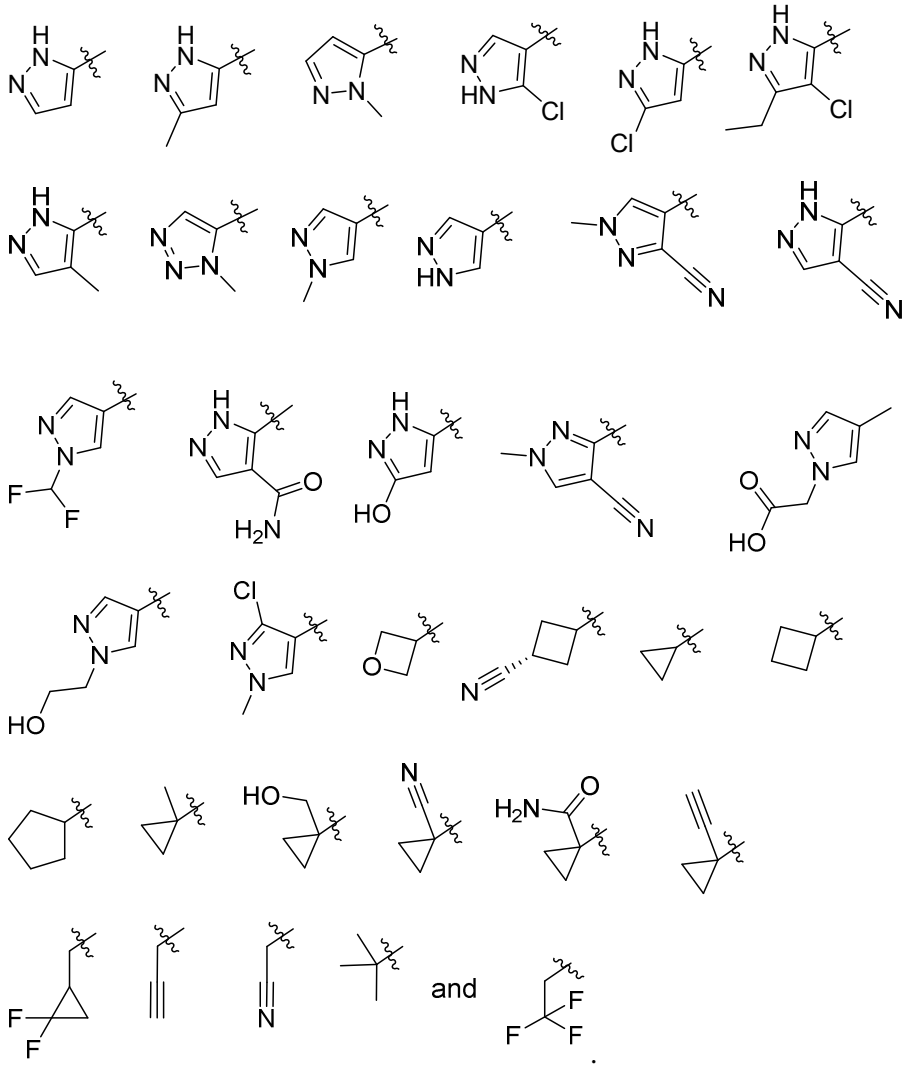
each $R^z$ is independently selected from the group consisting of oxo and ($C_1$-$C_6$)alkyl;

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

3. The compound, prodrug, or pharmaceutically acceptable salt of claim 1 or 2, wherein $R^1$ is -$NR^aR^b$.

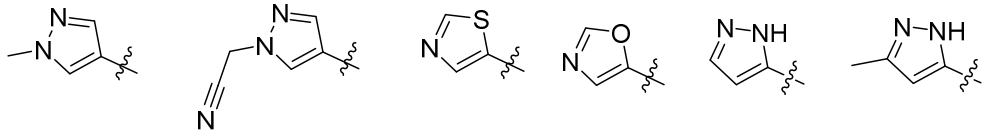
4. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-3, wherein $R^a$ is acetyl.

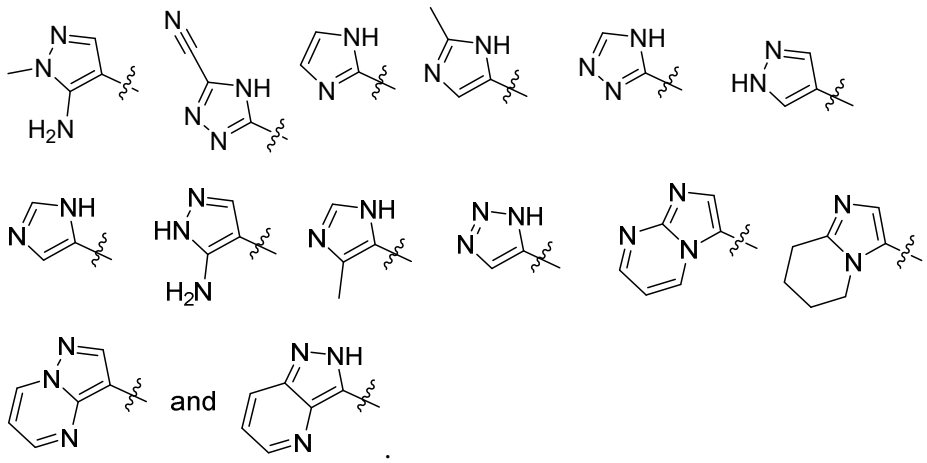
5. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-3, wherein $R^a$ is selected from the group consisting of:




6. The compound, prodrug, or pharmaceutically acceptable salt of claim 1 or 2, wherein $R^1$ is a 5-membered heteroaryl that is optionally substituted with one or more groups $R^c$.

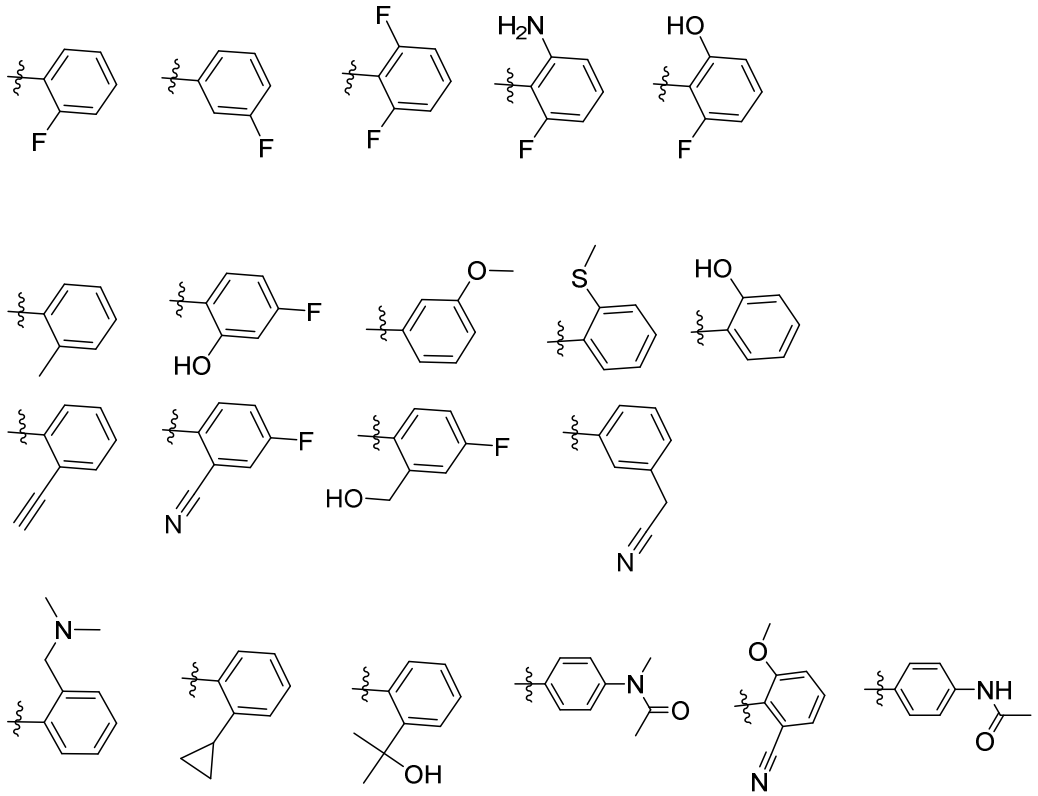
7. The compound, prodrug, or pharmaceutically acceptable salt of claim 1 or 2 wherein $R^1$ is selected from the group consisting of:

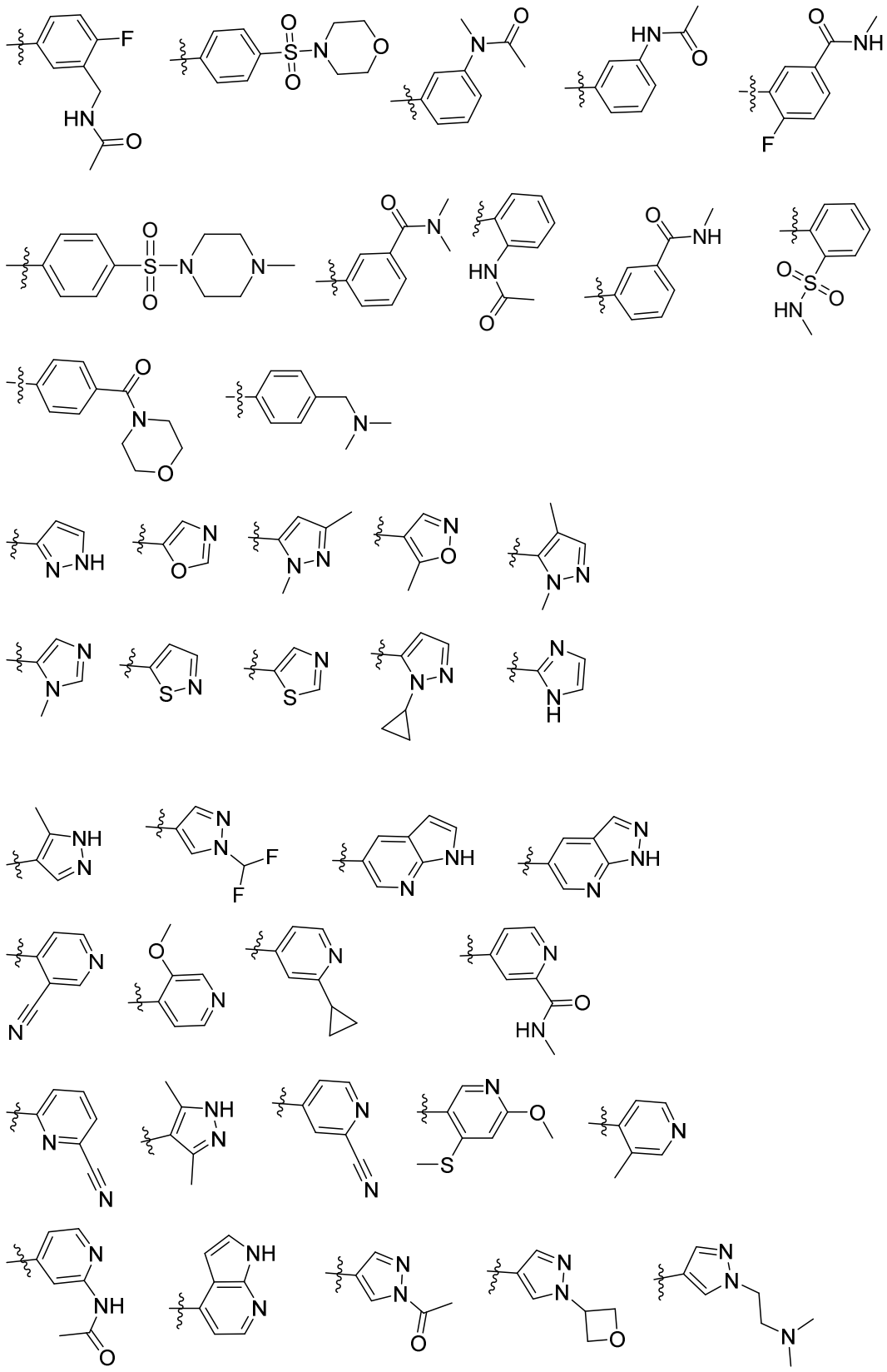


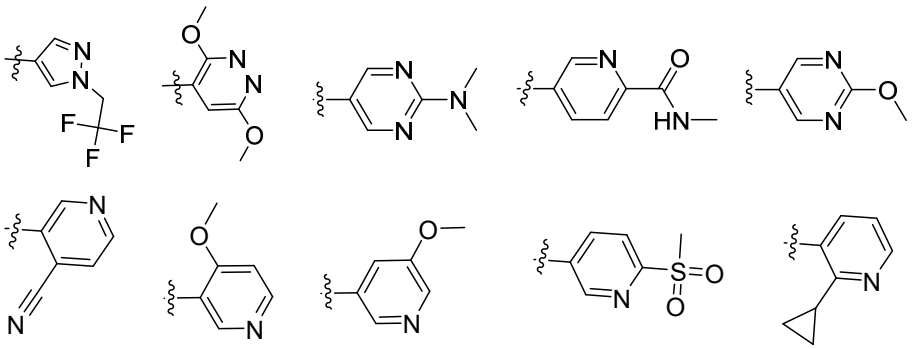


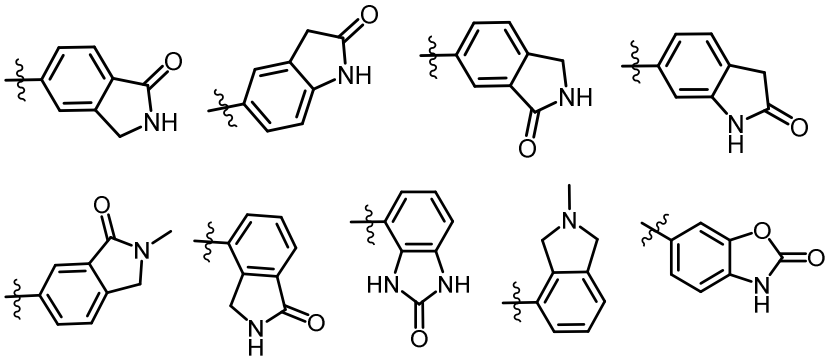

8. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-7, wherein $R^2$ is a 5-9 membered heteroaryl that is optionally substituted with one or more groups $R^s$, or phenyl that is optionally substituted with one or more groups $R^r$.

9. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-7, wherein $R^2$ is selected from the group consisting of:







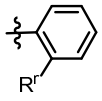






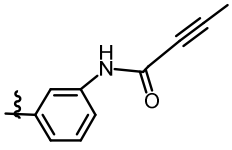
and .

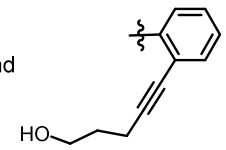
10. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-7, wherein $R^2$ is:

;

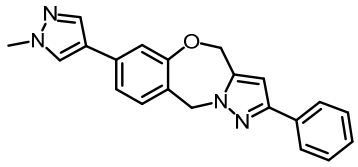
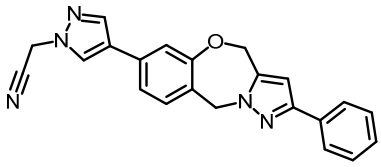
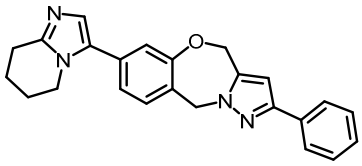
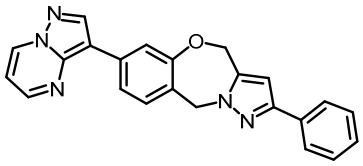
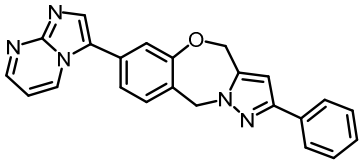
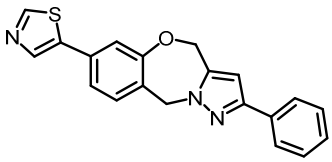
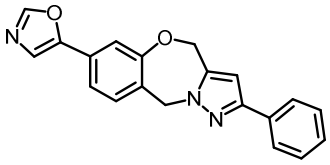
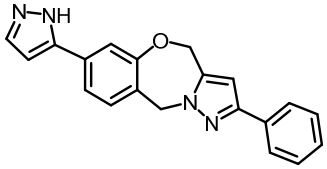
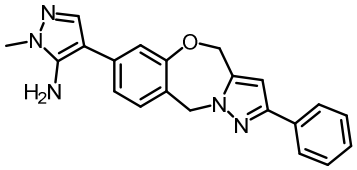
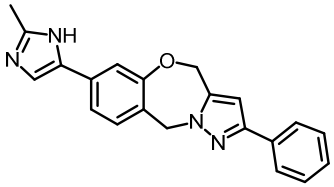
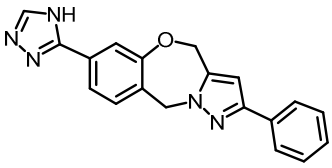
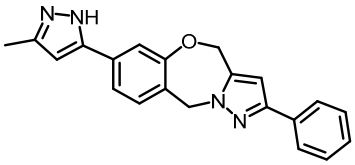
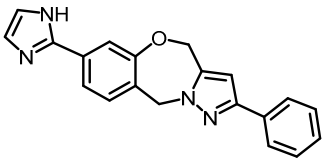
and $R^r$ $(C_2\text{-}C_6)$alkynyl that is substituted with hydroxy.

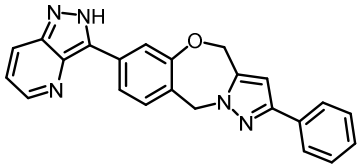
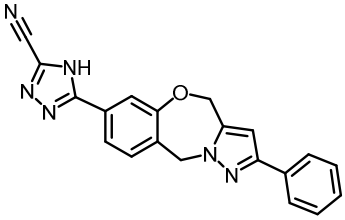
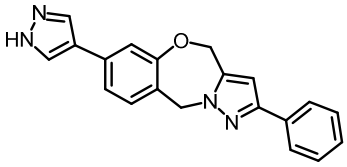
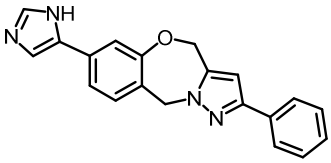
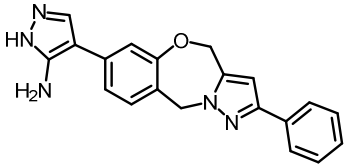
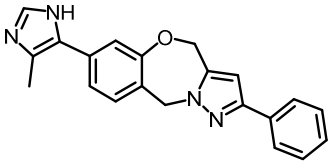
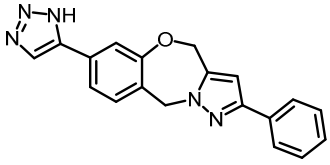
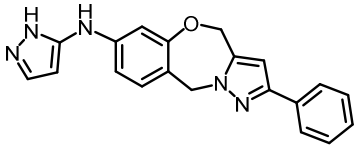
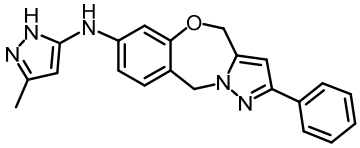
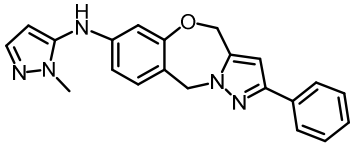
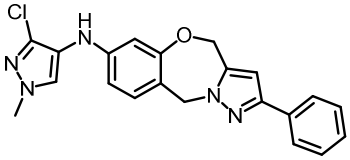
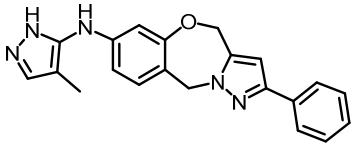
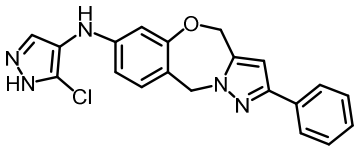
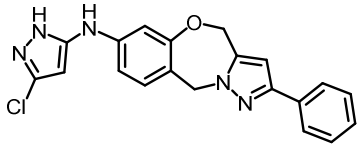
11. The compound, prodrug, or pharmaceutically acceptable salt of any one of claims 1-7, wherein $R^2$ is selected from the group consisting of:

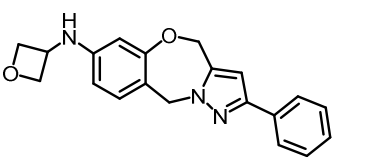


and .

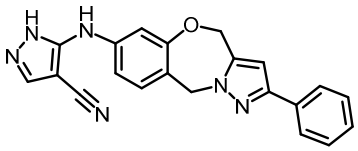
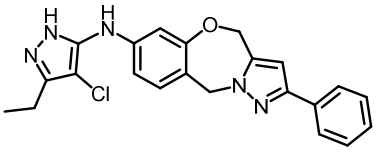
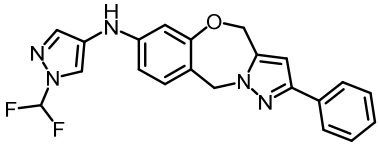
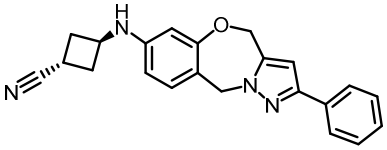
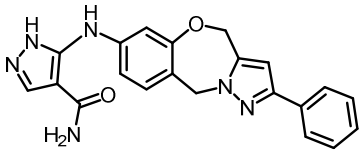
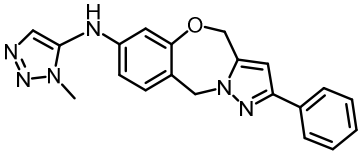
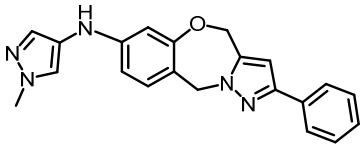
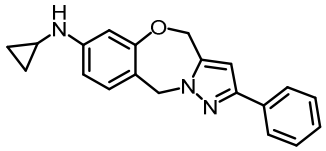
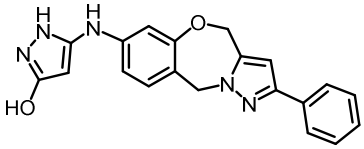
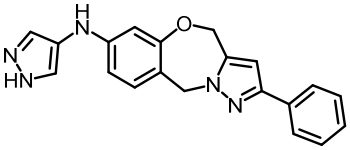
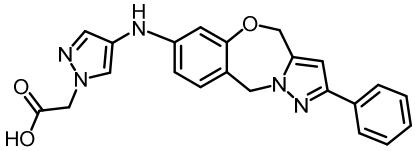
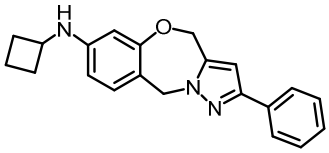
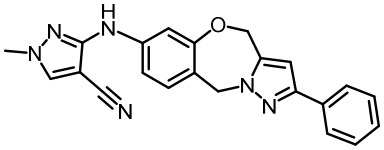
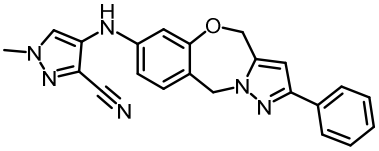
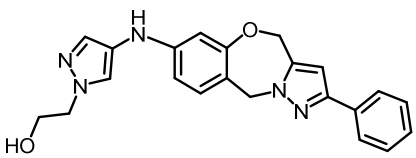
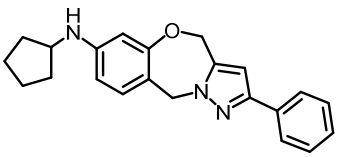
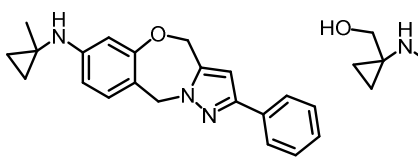
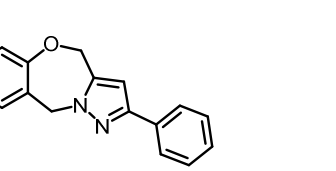
12. The compound, prodrug, or pharmaceutically acceptable salt of claim 1, which is selected from the group consisting of:

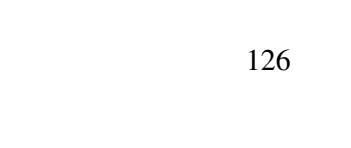














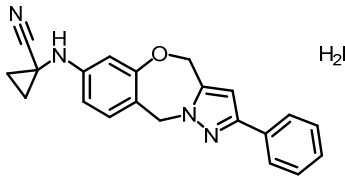
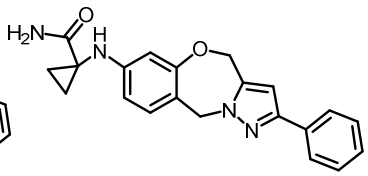















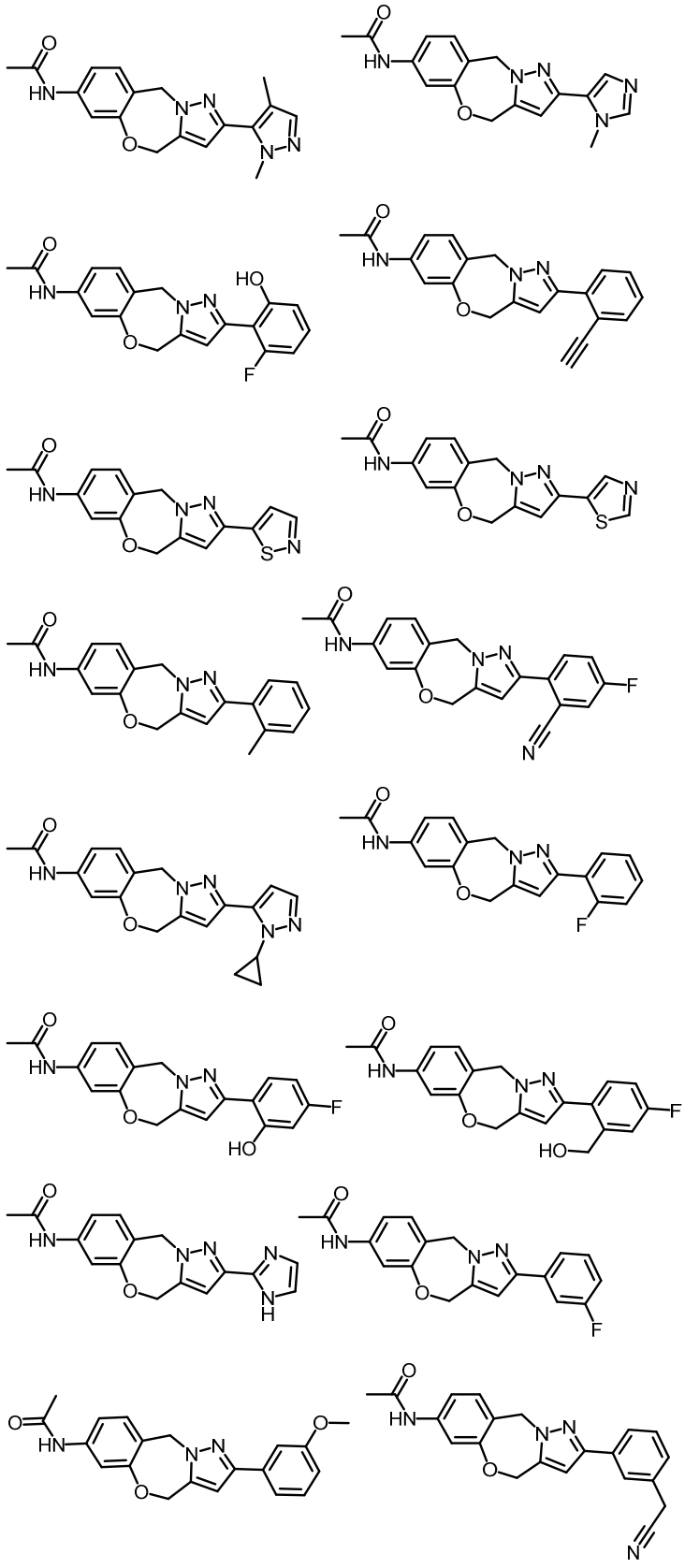


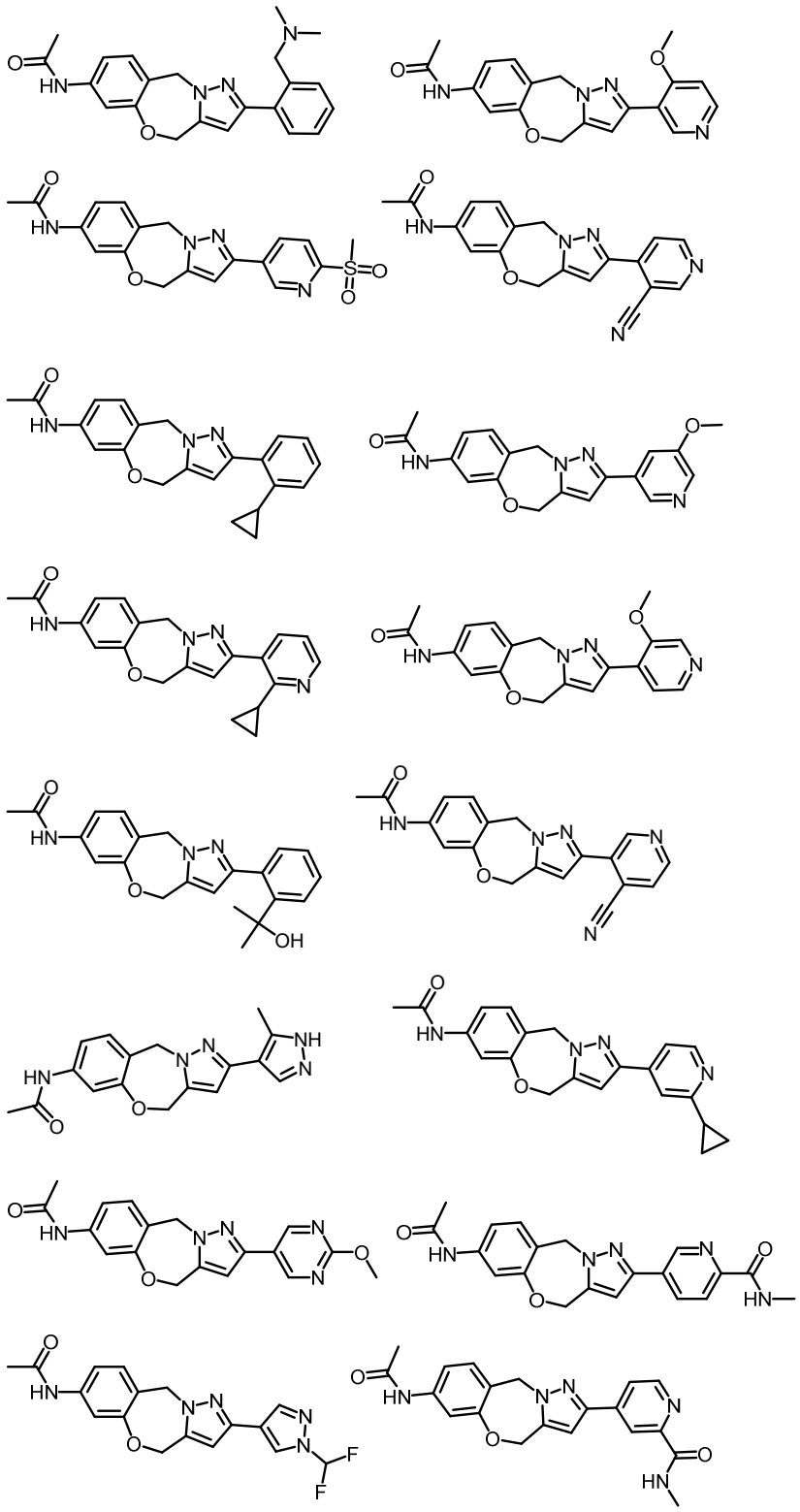


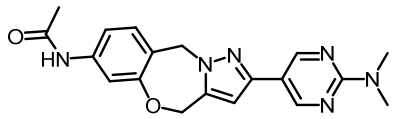
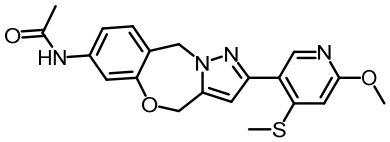



















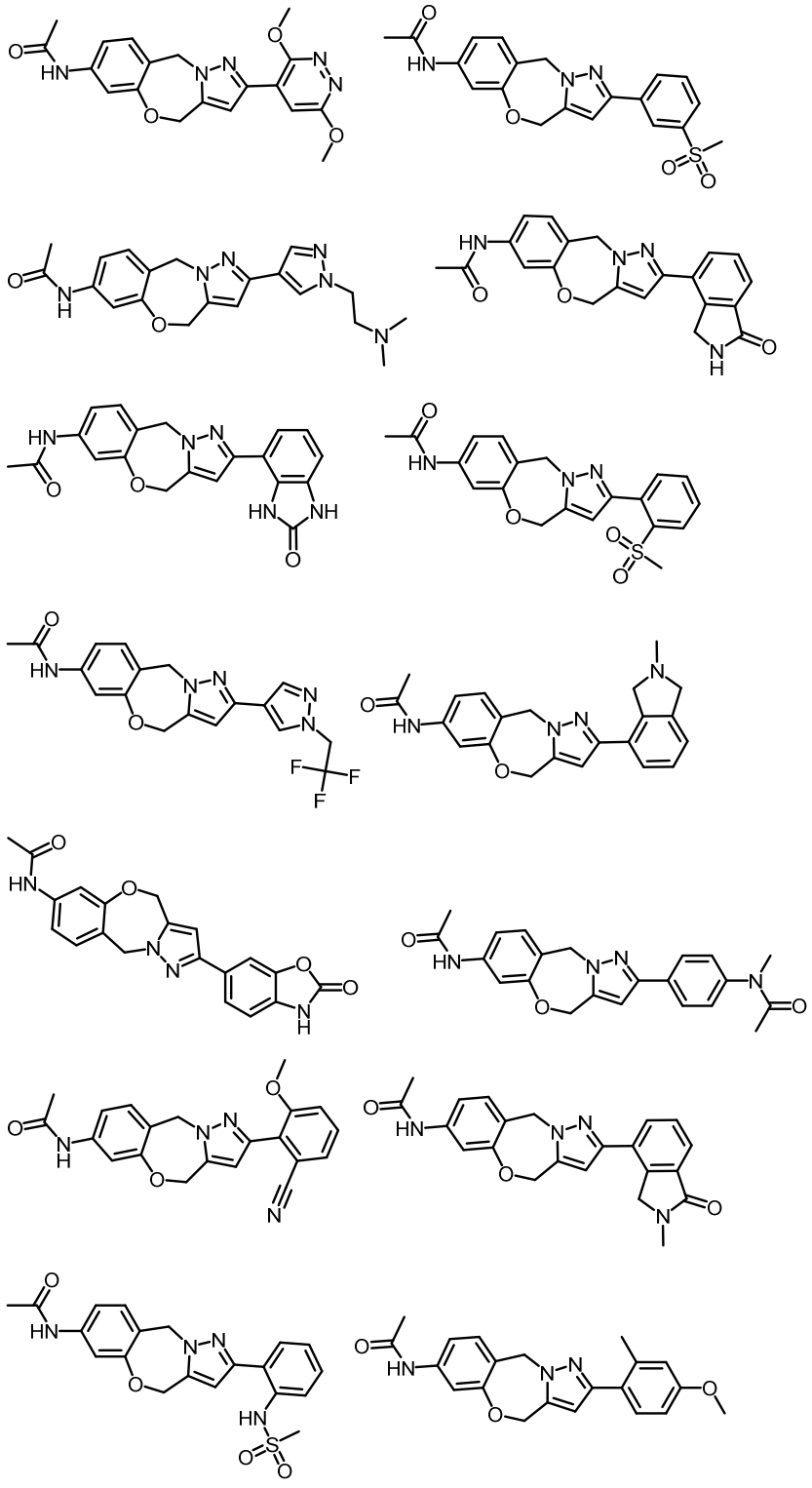


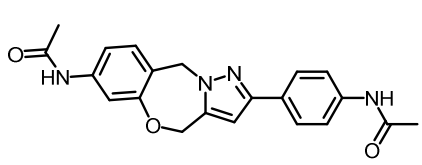
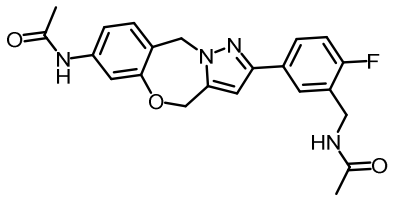
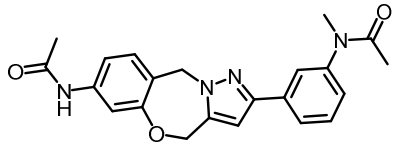
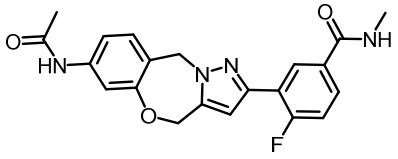
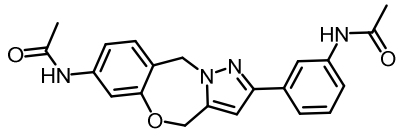
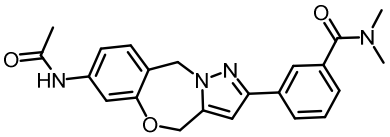
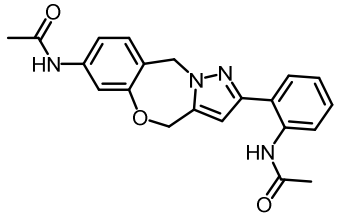
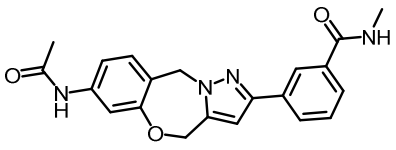
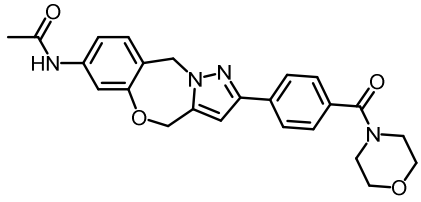
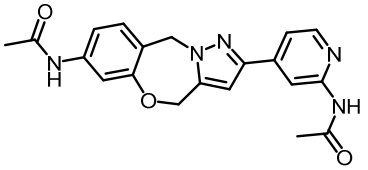
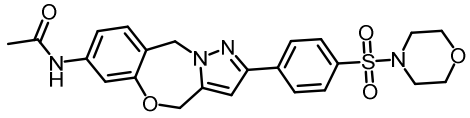
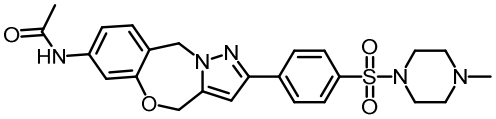
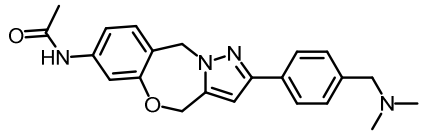
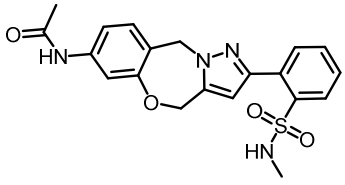
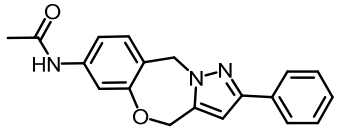
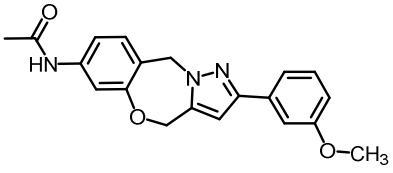



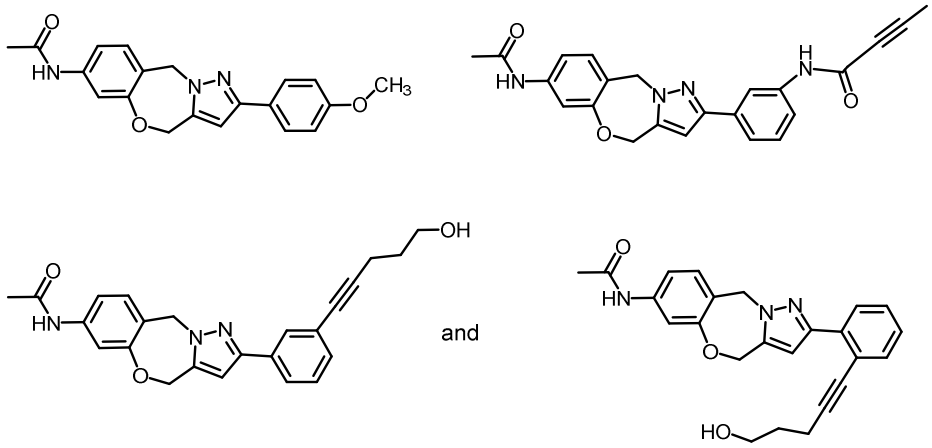






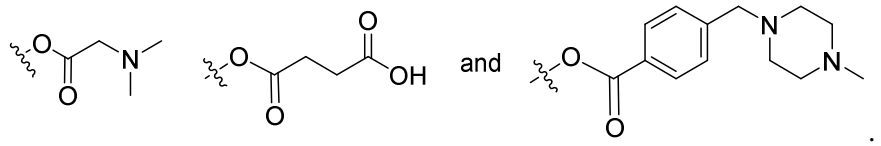




















and prodrugs and pharmaceutically acceptable salts thereof.

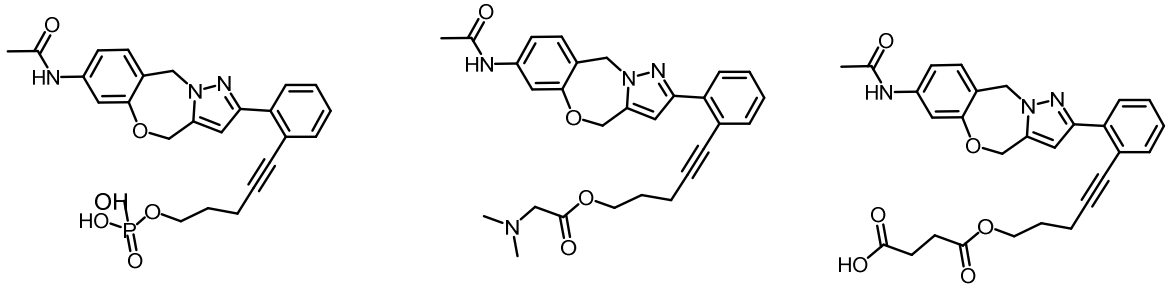
13. The prodrug of claim 1, which is a compound of formula (I) that comprises a hydroxy group that has been converted to a prodrug group that increases the aqueous solubility of the compound; or a pharmaceutically acceptable salt thereof.

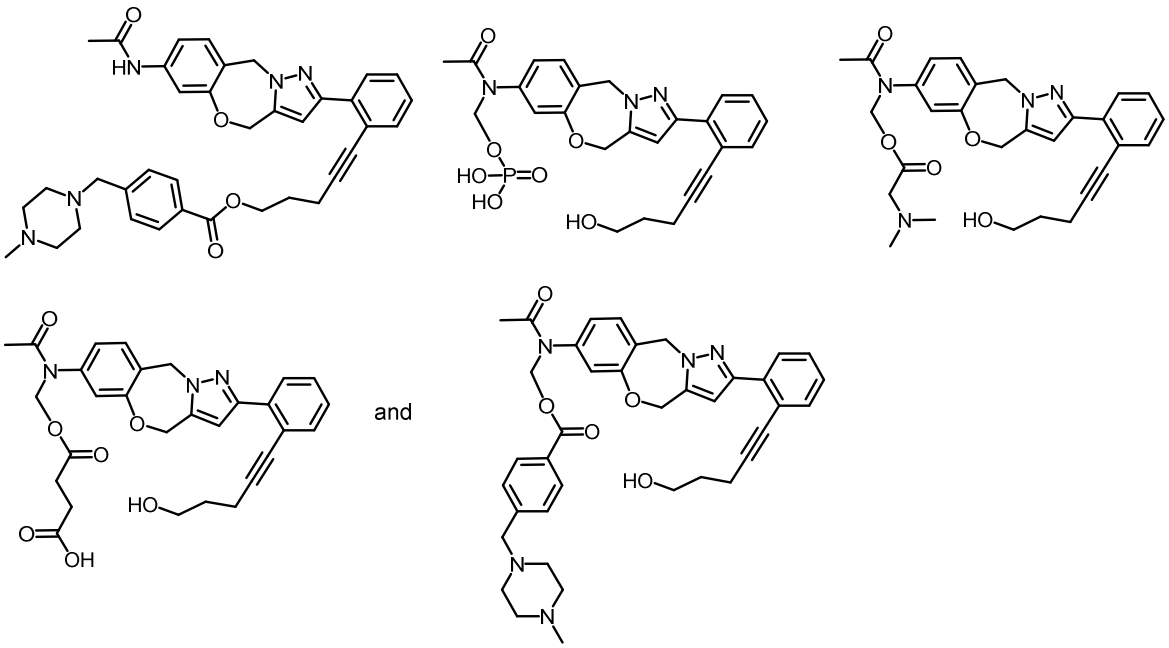
14. The prodrug or pharmaceutically acceptable salt of claim 13, wherein the hydroxy group has been converted to a prodrug group selected from the group consisting of: a phosphate,




.

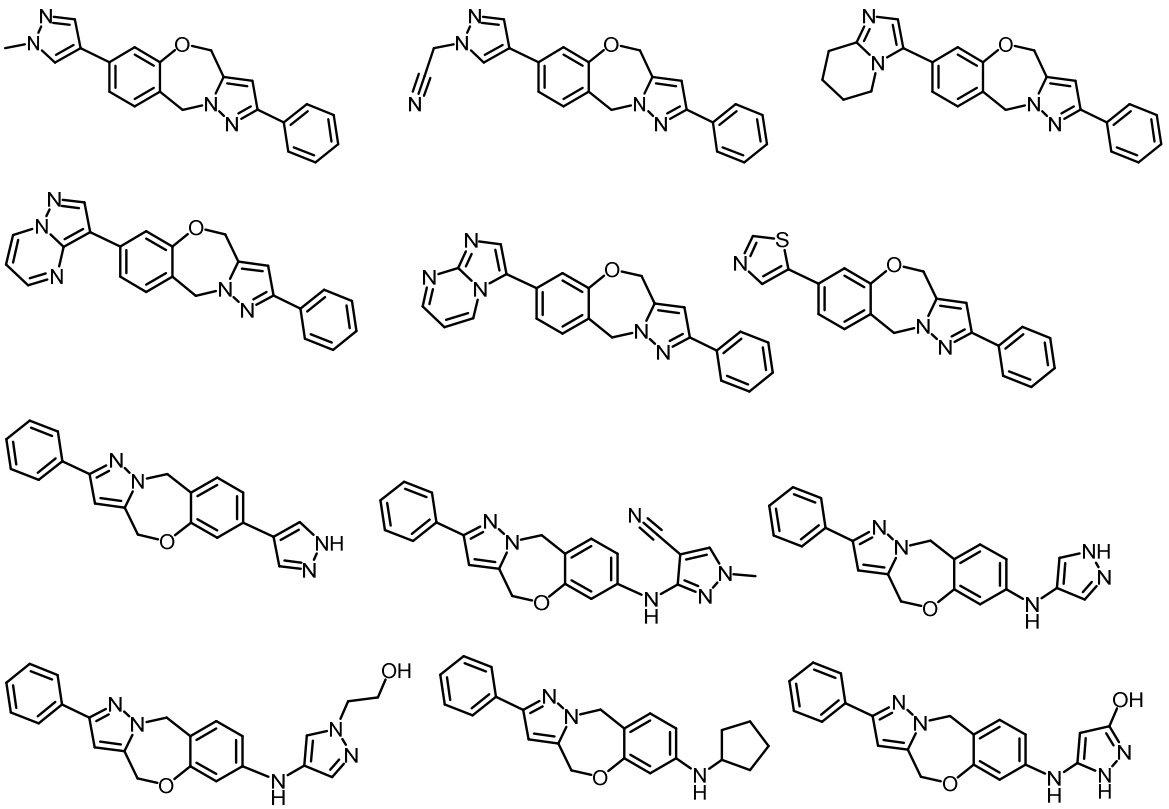
15. The prodrug or pharmaceutically acceptable salt of claim 1 that is selected from the group consisting of:

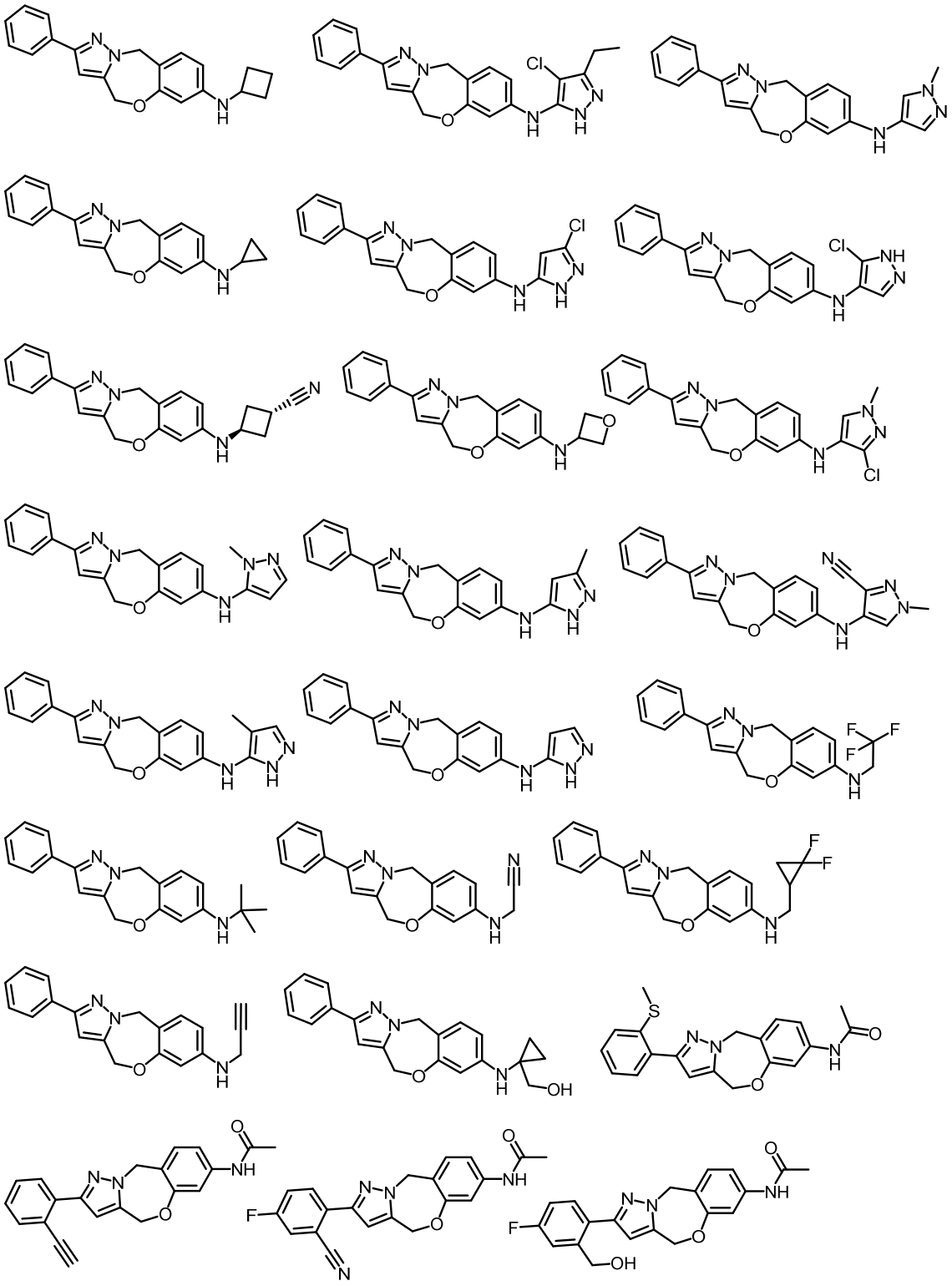


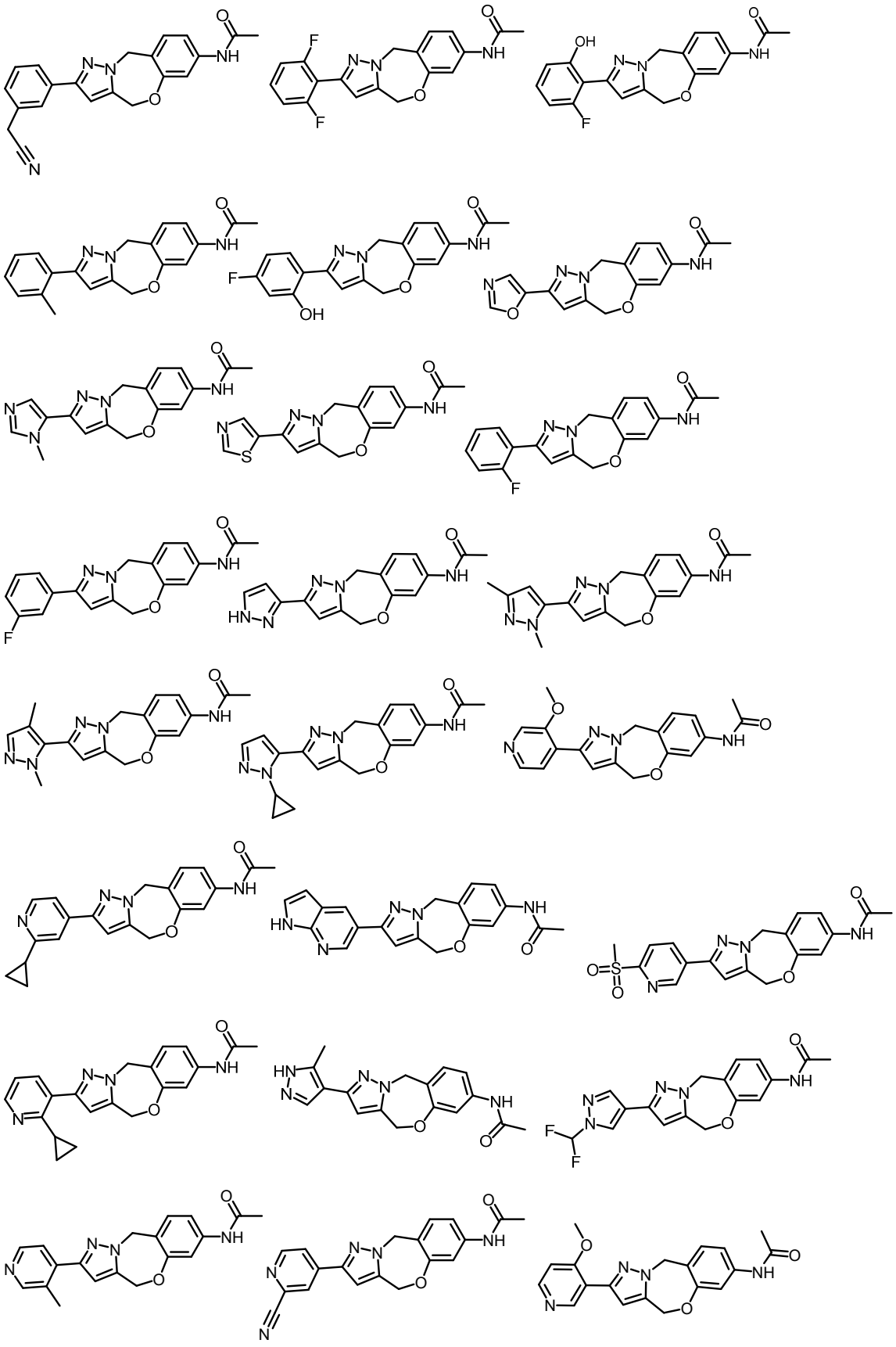


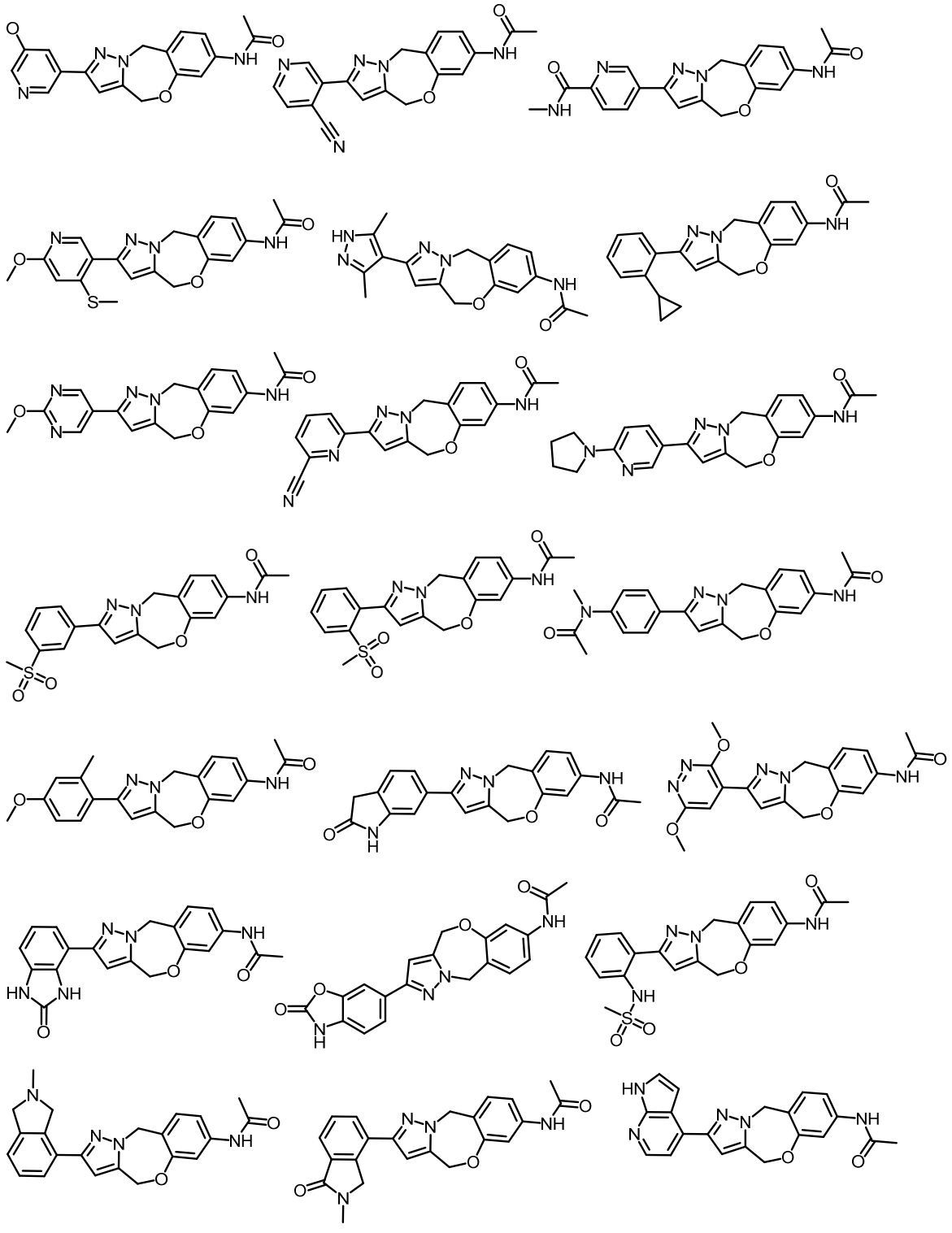

and pharmaceutically acceptable salts thereof.

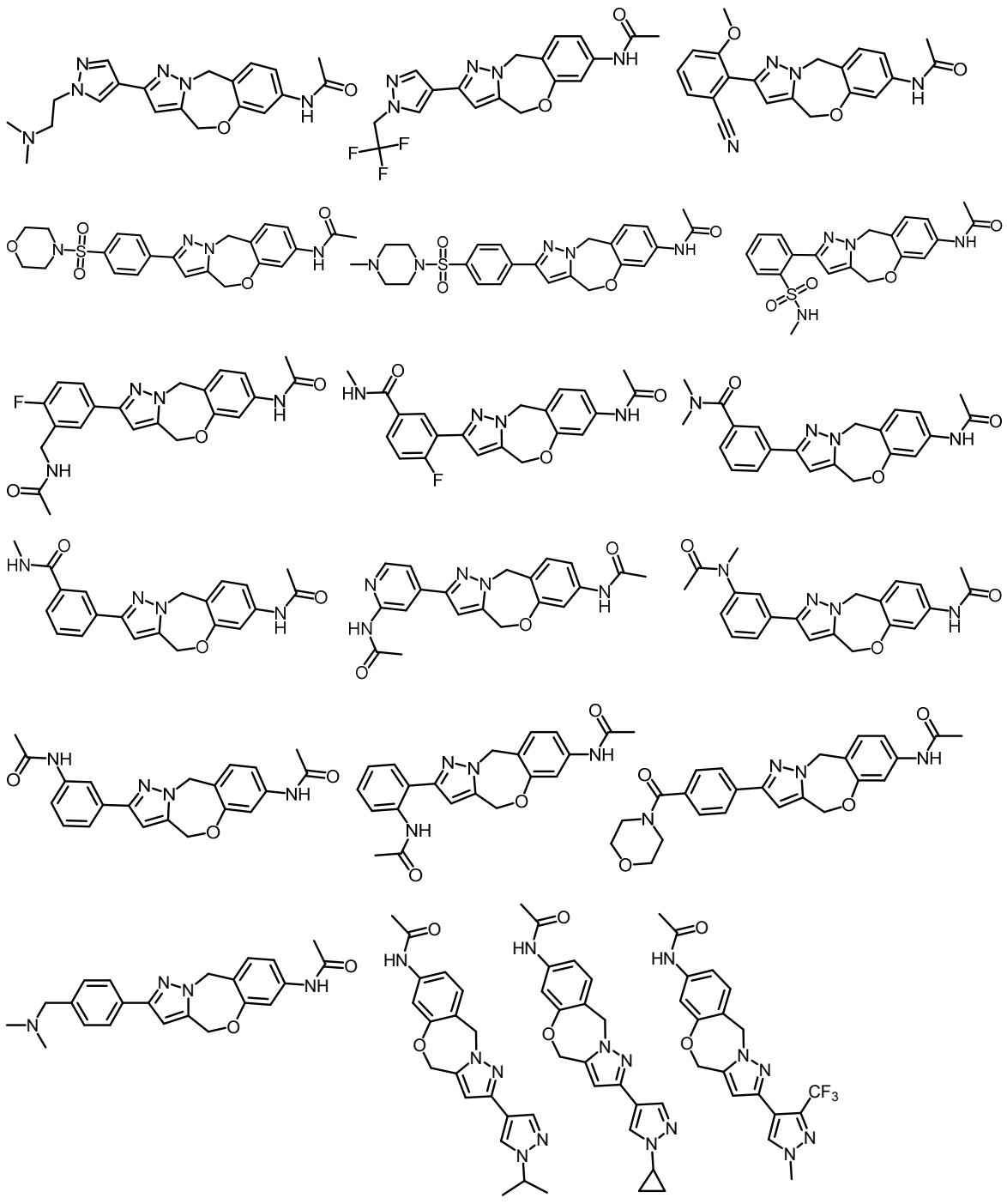
16. A compound selected from the group consisting of:

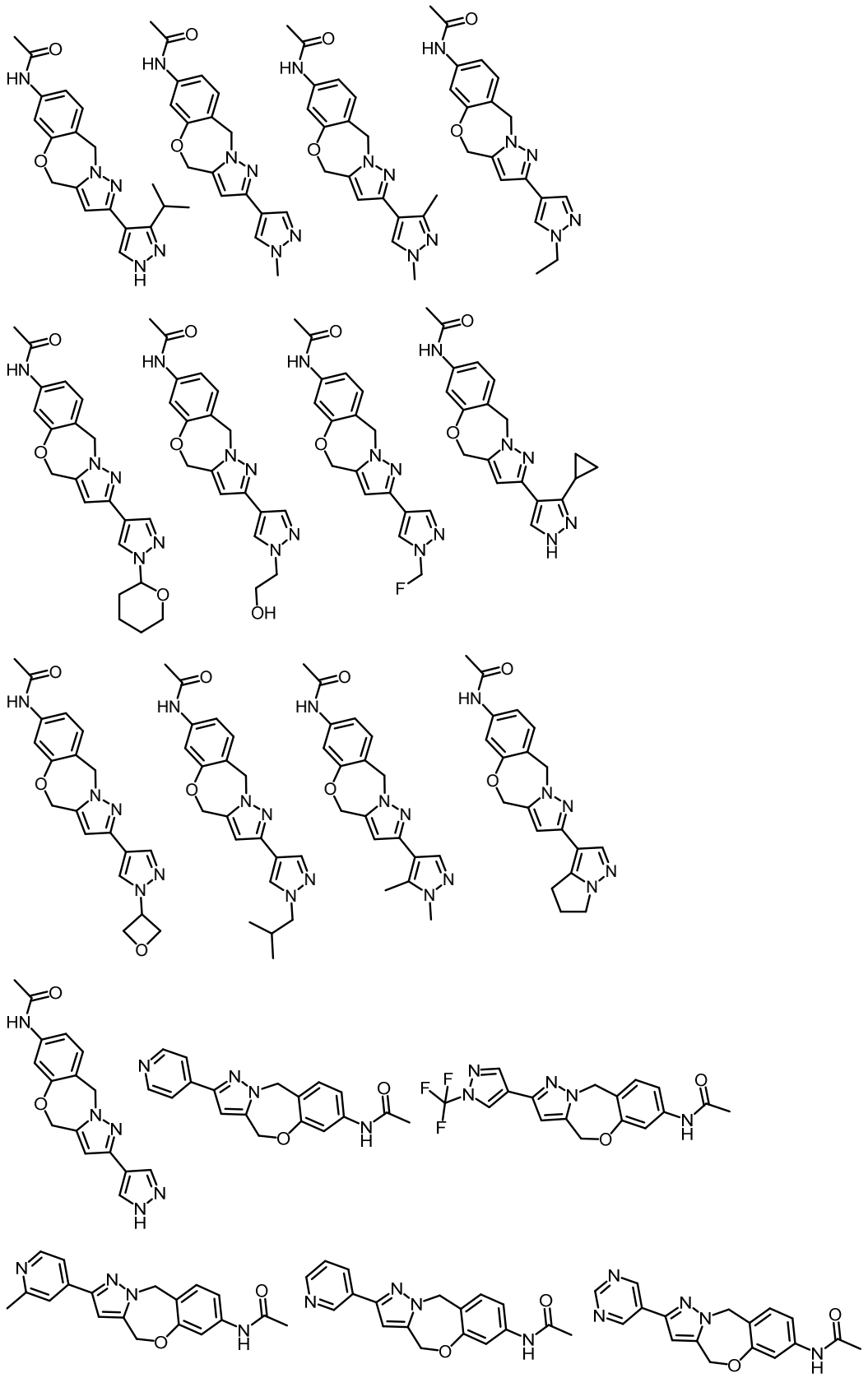


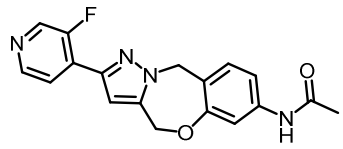










and 

or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising a compound, prodrug, or pharmaceutically acceptable salt as described in any one of claims 1-16 and a pharmaceutically acceptable excipient.

18. Use of a compound of formula (I) as described in any one of claims 1-16 or a prodrug thereof, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prophylactic or therapeutic treatment of a disease associated with the activity of glycolytic enzyme phosphofructokinase-1 liver type.

19. Use of a compound of formula (I) as described in any one of claims 1-16 or a prodrug thereof, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prophylactic or therapeutic treatment of cancer, diabetes, or a caspase-associated auto-inflammatory condition.

20. The use of claim 19, wherein the caspase-associated auto-inflammatory condition is sepsis or septic shock.

21. Use of a compound of formula (I) as described in any one of claims 1-16 or a prodrug thereof, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prophylactic or therapeutic treatment of a disease or condition selected from the group consisting of pulmonary disease, a systemic autoimmune disease, atherosclerosis, thrombosis, multiple sclerosis, Alzheimer's disease, psoriasis, and pulmonary fibrosis.

22. The use of claim 21, wherein the pulmonary disease is acute respiratory distress syndrome ARDS, chronic obstructive pulmonary disease COPD, bronchiectasis, or thrombosis.

23. The use of claim 19, wherein the cancer is selected from the group consisting of: brain, breast, lung, urinary bladder, cervical, skin, oral cavity, pharynx, colon, liver, cecum, stomach, pancreatic, prostate, oesophageal, hematologic, thyroid, uterine, and head and neck cancer.