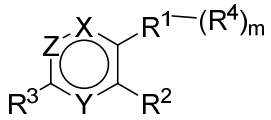
(allopurinol/febuxostat). RDEA3170 is derived from lesinurad, which is currently in a phase II clinical trials. In addition to the abovementioned drugs, losartan, fenofibrate, atorvastatin and others also have a uric acid-lowering effect, but their mechanisms have not been fully elucidated. Therefore, it is of great significance to find new drugs to treat hyperuricemia

[009] Novel compounds and pharmaceutical compositions, certain of which have been found to inhibit GLUT9 have been discovered, together with methods of synthesizing and using the compounds including methods for the treatment of GLUT9-mediated diseases in a patient by administering the compounds.

SUMMARY

[010] Compounds disclosed herein may possess useful GLUT9 inhibiting activity and may be used in the treatment or prophylaxis of a disease or condition in which GLUT9 plays an active role.

[011] In one aspect, described herein is a compound of Formula (I'):



Formula (I')

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

X is selected from CH and N;

Y is selected from CH, S, O, and N;

Z is selected from a bond and CR^7;

R^1 is selected from aryl and heteroaryl;

R^2 is a mono- or bi-cyclic heterocycloalkyl or a mono- or bi-cyclic heteroaryl, either of which may be optionally substituted with one or more R^6;

R^3 is selected from:

alkyl optionally substituted with SO_2-alkyl,

alkoxyalkyl,

alkoxyalkoxyalkyl,

haloalkyl,

haloalkoxyalkyl,

cycloalkylalkyl, and

cycloalkoxyalkyl;

each R^4 is independently selected from:

alkoxy optionally substituted with R^5,

alkylamino optionally substituted with R^5,

dialkylamino optionally substituted with R^5,

SO_2R^{8a},

alkylthio,

haloalkoxy,

cycloalkoxy,

cycloalkylalkoxy,

halo,

alkyl, and

haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more alkyl, halo, oxo, alkoxy, or alkoxyalkyl;

each R^5 is independently selected from hydroxyl, alkoxy, amino, alkylamino, dialkylamino, haloalkoxy, and alkoxyalkoxy;

each R^6 is independently selected from hydroxyl, hydroxyalkoxy, carboxyl, methylcarboxyl, carboxylalkyl, carboxylalkoxy, halo, alkyl, alkoxy, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, cyano, and tetrazolyl;

R^7 is selected from hydrogen and halo; and

R^{8a} and R^{8b} are each independently selected from alkyl, amino, alkylamino, dialkylamino;

wherein X and Y are not both CH.

[012] In another aspect, also described herein are pharmaceutical compositions comprising a compound described herein, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient. In some examples, the pharmaceutical composition is formulated for administration to a mammal by intravenous administration, subcutaneous administration, oral administration, inhalation, nasal administration, dermal administration, or ophthalmic administration. In some examples, the pharmaceutical composition is formulated for administration to a mammal by oral administration. In some examples, the pharmaceutical composition is in the form of a tablet, a pill, a capsule, a liquid, a suspension, a gel, a dispersion, a solution, an emulsion, an ointment, or a lotion. In

some examples, the pharmaceutical composition is in the form of a tablet, a pill, or a capsule.

In another aspect, the present disclosure refers to use of a compound described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a condition selected from hyperuricemia and gout.

In another aspect, the present disclosure refers to use of a compound described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for preventing or treating a disease or condition ameliorated by the inhibition of GLUT9.

In another aspect, the present disclosure refers to an *ex vivo* method of inhibition of GLUT9 comprising contacting GLUT9 *ex vivo* with a compound described herein, or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure refers to use of a compound described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for lowering blood uric acid levels in a mammal.

[013] In any of the aforementioned examples are further examples in which the effective amount of the compound described herein, or a pharmaceutically acceptable salt thereof, is: (a) systemically administered to the mammal; and/or (b) administered orally to the mammal; and/or (c) intravenously administered to the mammal; and/or (d) administered by inhalation; and/or (e) administered by nasal administration; or and/or (f) administered by injection to the mammal; and/or (g) administered topically to the mammal; and/or (h) administered by ophthalmic administration; and/or (i) administered rectally to the mammal; and/or (j) administered non-systemically or locally to the mammal.

[014] In any of the aforementioned examples are further examples comprising single administrations of the effective amount of the compound, including further examples in which the compound is administered once a day to the mammal or the compound is administered to the mammal multiple times over the span of one day. In some examples, the compound is administered on a continuous dosing schedule. In some examples, the compound is administered on a continuous daily dosing schedule.

[015] In any of the examples disclosed herein, the mammal is a human.

[016] In some examples, compounds provided herein are orally administered to a human.

[017] Also described herein, in some examples, is a compound described herein, or a pharmaceutically acceptable salt thereof, for use as a medicament.

[018] Also described herein, in some examples, is a compound described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition selected from hyperuricemia and gout.

[019] Also described herein, in some examples, is a compound described herein, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for the prevention or treatment of a disease or condition ameliorated by the inhibition of GLUT9.

[020] Also described herein, in some examples, is a method of inhibition of GLUT9 comprising contacting GLUT9 with a compound described herein, or a pharmaceutically acceptable salt thereof

[021] Also described herein, in some examples, is a method of treatment of a GLUT9-mediated disease comprising the administration of a therapeutically effective amount of a compound described herein, or a pharmaceutically acceptable salt thereof, to a patient in

need thereof. In some examples, said disease is selected from hyperuricemia, gout, and uncontrolled gout including comorbidities and associated diseases.

[022] Also described herein, in some examples, is a method of treatment of a GLUT9-mediated disease comprising the administration of: a therapeutically effective amount of a compound described herein, or a pharmaceutically acceptable salt thereof; and another therapeutic agent. In some examples, said other agent is selected from inhibitors of uric acid synthesis, uricosurics, and uric acid catabolizing agents. In some such examples, said uricosuric is selected from probenecid, lesinurad, benzbromarone, and sulfinpyrazone. In some such examples, said inhibitor of uric acid synthesis is selected from allopurinol and febuxostat. In some such examples, said uric acid catabolizing agent is pegloticase. In some other examples, said other agent is colchichine.

[023] Also described herein, in some examples, is a method for lowering blood uric acid levels in a patient comprising the administration of a therapeutically effective amount of a compound described herein, or a pharmaceutically acceptable salt thereof, to a patient

[024] Articles of manufacture, which include packaging material, a compound described herein, or a pharmaceutically acceptable salt thereof, within the packaging material, and a label that indicates that the compound or composition, or pharmaceutically acceptable salt, tautomers, pharmaceutically acceptable N-oxide, pharmaceutically active metabolite, pharmaceutically acceptable prodrug, or pharmaceutically acceptable solvate thereof, is used for inhibiting GLUT9, or for the treatment, prevention or amelioration of one or more symptoms of a disease or condition that would benefit from inhibiting GLUT9, are provided.

[025] Other objects, features and advantages of the compounds, methods and compositions described herein will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific examples, are given by way of illustration only, since various changes and modifications within the spirit and scope of the instant disclosure will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

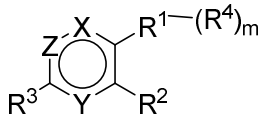
[026] **Figure 1** shows the nucleic acid sequence of human GLUT9B/GLUT9 variant 2/Q96S37-2/Glut9 Isoform2 (SEQ ID NO: 3).

[027] **Figure 2** shows the amino acid sequence of human GLUT9B/GLUT9 variant 2/Q96S37-2/Glut9 Isoform2 (SEQ ID NO: 4).

CLAIMS

What is claimed is:

1. A compound of Formula (I'):



Formula (I')

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

X is selected from CH and N;

Y is selected from CH, S, O, and N;

Z is selected from a bond and CR^7;

R^1 is selected from aryl and heteroaryl;

R^2 is a mono- or bi-cyclic heterocycloalkyl or a mono- or bi-cyclic heteroaryl, either of which may be optionally substituted with one or more R^6;

R^3 is selected from:

alkyl optionally substituted with SO_2-alkyl,

alkoxyalkyl,

alkoxyalkoxyalkyl,

haloalkyl,

haloalkoxyalkyl,

cycloalkylalkyl, and

cycloalkoxyalkyl;

each R^4 is independently selected from:

alkoxy optionally substituted with R^5,

alkylamino optionally substituted with R^5,

dialkylamino optionally substituted with R^5,

SO_2R^{8a},

alkylthio,

haloalkoxy,

cycloalkoxy,

cycloalkylalkoxy,

halo,

alkyl, and

haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more alkyl, halo, oxo, alkoxy, or alkoxyalkyl;

each R^5 is independently selected from hydroxyl, alkoxy, amino, alkylamino, dialkylamino, haloalkoxy, and alkoxyalkoxy;

each R^6 is independently selected from hydroxyl, hydroxyalkoxy, carboxyl, methylcarboxyl, carboxylalkyl, carboxylalkoxy, halo, alkyl, alkoxy, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, cyano, and tetrazolyl;

R^7 is selected from hydrogen and halo; and

R^{8a} and R^{8b} are each independently selected from alkyl, amino, alkylamino, dialkylamino;

wherein X and Y are not both CH.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

X is selected from CH and N;

Y is selected from CH and N; and

Z is CH.

3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, wherein:

X is CH; Y is N; and Z is CH;

or X is N; Y is CH; and Z is CH;

or X is N; Y is N; and Z is CH.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

X is N; Y is N; and Z is CH.

5. The compound any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is phenyl, monocyclic heteroaryl, or bicyclic heteroaryl.

6. The compound any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is phenyl.

7. The compound any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is bicyclic heteroaryl.

8. The compound any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein:

each R^4 is independently selected from alkoxy optionally substituted with R^5, SO_2R^{8a}, haloalkoxy, cycloalkoxy, cycloalkylalkoxy, halo, alkyl, and haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more alkyl, halo, oxo, alkoxy, or alkoxyalkyl;

each R^5 is independently selected from hydroxyl, alkoxy, amino, alkylamino, dialkylamino, and haloalkoxy; and

m is an integer from 0 to 3.

9. The compound any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein:

each R^4 is independently selected from alkoxy, haloalkoxy, and halo;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl; and

m is an integer from 0 to 3.

10. The compound any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from alkyl optionally substituted with SO_2-alkyl, alkoxyalkyl, haloalkyl, haloalkoxyalkyl, cycloalkylalkyl, and cycloalkoxyalkyl.

11. The compound any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from alkyl, alkoxyalkyl, haloalkyl, and haloalkoxyalkyl.

12. The compound any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from alkyl and alkoxyalkyl.

13. The compound any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is alkoxyalkyl.

14. The compound any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is a mono- or bi-cyclic heterocycloalkyl, which is substituted with one or more R^6;

each R^6 is independently selected from hydroxyl, carboxyl, carboxylalkyl, carboxylalkoxy, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, and tetrazolyl; and

R^{8b} is selected from alkyl, amino, alkylamino, dialkylamino.

15. The compound any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is a mono-cyclic heterocycloalkyl, which is substituted with one R^6;

R^6 is selected from carboxyl, carboxylalkyl, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, and tetrazolyl; and

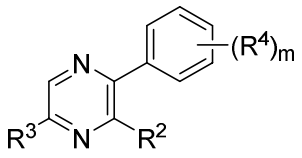
R^{8b} is selected from alkyl, amino, alkylamino, dialkylamino.

16. The compound any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is a piperidinyl, which is substituted with one R^6; and

R^6 is selected from carboxyl, carboxylalkyl, and heterocycloalkyl.

17. The compound of claim 1, wherein the compound is a compound of Formula (IV):



Formula (IV)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 3;

R^2 is a mono- or bi-cyclic heterocycloalkyl, which is substituted with one or more R^6;

R^3 is selected from alkyl optionally substituted with SO_2-alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, haloalkyl, haloalkoxyalkyl, cycloalkylalkyl, and cycloalkoxyalkyl;

each R^4 is independently selected from alkoxy optionally substituted with R^5, SO_2R^{8a}, haloalkoxy, cycloalkoxy, cycloalkylalkoxy, halo, alkyl, and haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more alkyl, halo, oxo, alkoxy, or alkoxyalkyl;

each R^5 is independently selected from hydroxyl, alkoxy, amino, alkylamino, dialkylamino, and haloalkoxy;

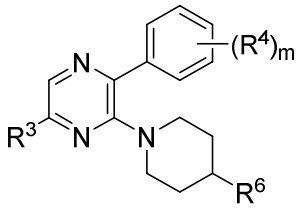
each R^6 is independently selected from hydroxyl, carboxyl, carboxylalkyl, carboxylalkoxy, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, and tetrazolyl; and

R^{8b} is selected from alkyl, amino, alkylamino, dialkylamino.

18. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is a mono-cyclic heterocycloalkyl, which is substituted with one R^6.

19. The compound of claim 17 or claim 18, wherein the compound is a compound of Formula (V), or a pharmaceutically acceptable salt thereof:



Formula (V).

20. The compound of any one of claims 17-19, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from alkyl, alkoxyalkyl, haloalkyl, and haloalkoxyalkyl;

each R^4 is independently selected from alkoxy, haloalkoxy, and halo;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl;

R^6 is selected from carboxyl, carboxylalkyl, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, and tetrazolyl; and

R^{8b} is selected from alkyl, amino, alkylamino, dialkylamino.

21. The compound of any one of claims 17-19, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from alkyl and alkoxyalkyl;

each R^4 is independently selected from alkoxy, haloalkoxy, and halo;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together form a fused heterocycloalkyl or a fused heteroaryl; and

R^6 is selected from carboxyl, carboxylalkyl, and heterocycloalkyl.

22. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

X is selected from CH and N;

Y is selected from CH, S, O, and N;

Z is selected from a bond and CR^7;

R^1 is selected from aryl and heteroaryl,

R^2 is a mono- or bi-cyclic heterocycloalkyl or a mono- or bi-cyclic heteroaryl, either of which may be optionally substituted with one or more R^6;

R^3 is selected from: alkyl optionally substituted with SO_2-alkyl, haloalkyl, haloalkoxyalkyl, cycloalkylalkyl, and cycloalkoxyalkyl;

each R^4 is independently selected from: alkoxy optionally substituted with R^5, SO_2R^{8a}, haloalkoxy, cycloalkoxy, cycloalkylalkoxy, and halo;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more alkyl, halo, oxo, alkoxy, or alkoxyalkyl;

each R^5 is independently selected from hydroxyl, alkoxy, amino, alkylamino, dialkylamino, and haloalkoxy;

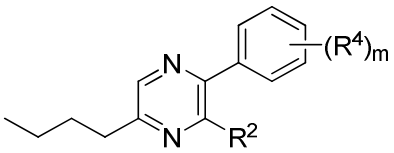
each R^6 is independently selected from hydroxyl, hydroxyalkoxy, carboxyl, methylcarboxyl, carboxylalkyl, carboxylalkoxy, halo, alkyl, alkoxy, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, heterocycloalkyl, cyano, and tetrazolyl;

R^7 is selected from hydrogen and halo; and

R^{8a} and R^{8b} are each independently selected from alkyl, amino, alkylamino, dialkylamino;

wherein X and Y are not both CH.

23. The compound of claim 22, wherein the compound is a compound of Formula (II):



Formula (II)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 3;

R^2 is a mono- or bi-cyclic heterocycloalkyl, optionally substituted with one or more R^6;

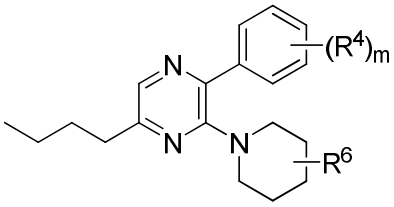
each R^4 is independently selected from alkoxy optionally substituted with R^5, SO_2R^{8a}, and halo, or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl;

R^5 is selected from alkoxy, amino, alkylamino, and dialkylamino;

each R^6 is independently selected from carboxyl, carboxylalkyl, halo, alkyl, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, and tetrazolyl; and

R^{8a} and R^{8b} are each independently selected from alkyl, amino, alkylamino, dialkylamino.

24. The compound of claim 23, wherein the compound is a compound of Formula (III):



Formula (III)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 3;

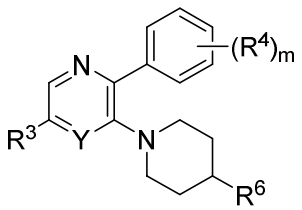
each R^4 is independently selected from alkoxy optionally substituted with R^5, SO_2R^{8a}, and halo, or two R^1 substituents taken together form a fused heterocycloalkyl or a fused heteroaryl;

R^5 is selected from alkoxy, amino, alkylamino, and dialkylamino;

R^6 is selected from carboxyl, carboxylalkyl, halo, alkyl, SO_2R^{8b}, $C(=O)NHSO_2R^{8b}$, and tetrazolyl; and

R^{8a} and R^{8b} are each independently selected from alkyl, amino, alkylamino, dialkylamino.

25. The compound of claim 1, wherein the compound is a compound of Formula (VI):



Formula (VI)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

Y is N or CH;

R^3 is selected from:

C_1-C_6alkyl optionally substituted with SO_2-(C_1-C_6alkyl),

(C_1-C_6alkoxy)-C_1-C_6alkyl,

(C_1-C_6alkoxy)-(C_1-C_6alkoxy)-C_1-C_6alkyl,

C_1-C_6haloalkyl,

(C_1-C_6haloalkoxy)-C_1-C_6alkyl,

(C_3-C_6cycloalkyl)-C_1-C_6alkyl, and

(C_3-C_6cycloalkoxy)-C_1-C_6alkyl;

each R^4 is independently selected from:

C_1-C_6alkoxy optionally substituted with R^5,

C_1-C_6alkylamino optionally substituted with R^5,

di-(C_1-C_6alkyl)-amino optionally substituted with R^5,

SO_2R^{8a},

C_1-C_6alkylthio,

C_1-C_6haloalkoxy,

C_3-C_6cycloalkoxy,

(C_3-C_6cycloalkyl)-C_1-C_6alkoxy,

halo,

C_1-C_6alkyl, and

C_1-C_6haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more C_1-C_6alkyl, halo, oxo, C_1-C_6alkoxy, or (C_1-C_6alkoxy)-C_1-C_6alkyl;

each R^5 is independently selected from hydroxyl, C_1-C_6alkoxy, amino, C_1-C_6alkylamino, di-C_1-C_6alkylamino, C_1-C_6haloalkoxy, and (C_1-C_6alkoxy)-C_1-C_6alkoxy;

R^6 is selected from -C(=O)OH, -CH_2C(=O)OH, -C(=O)O-C_1-C_6alkyl, -C(=O)NHSO_2R^{8b}, heterocycloalkyl, and tetrazolyl;

R^{8a} and R^{8b} are each independently selected from C_1-C_6alkyl, amino, C_1-C_6alkylamino, di-(C_1-C_6alkyl)-amino.

26. The compound of claim 25, or a pharmaceutically acceptable salt thereof:

m is an integer from 0 to 4;

Y is N or CH;

R^3 is selected from: C_1-C_6alkyl, (C_1-C_4alkoxy)-C_1-C_6alkyl, C_1-C_6haloalkyl, (C_1-C_4haloalkoxy)-C_1-C_6alkyl, (C_3-C_6cycloalkyl)-C_1-C_6alkyl, and (C_3-C_6cycloalkoxy)-C_1-C_6alkyl;

each R^4 is independently selected from: C_1-C_6alkoxy optionally substituted with R^5, C_1-C_4alkylamino optionally substituted with R^5, di-(C_1-C_4alkyl)-amino optionally substituted with R^5, SO_2R^{8a}, C_1-C_6haloalkoxy, C_3-C_6cycloalkoxy, (C_3-C_6cycloalkyl)-C_1-C_6alkoxy, halo, C_1-C_6alkyl, and C_1-C_6haloalkyl;

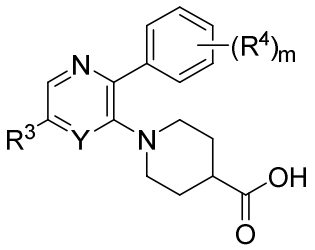
or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused heterocycloalkyl or a fused heteroaryl, either of which may be optionally substituted with one or more C_1-C_6alkyl, halo, oxo, C_1-C_6alkoxy, or (C_1-C_4alkoxy)-C_1-C_6alkyl;

each R^5 is independently selected from hydroxyl, C_1-C_6alkoxy, amino, C_1-C_4alkylamino, di-(C_1-C_4alkyl)-amino, C_1-C_6haloalkoxy, and (C_1-C_4alkoxy)-C_1-C_6alkoxy;

R^6 is selected from -C(=O)OH, -CH_2C(=O)OH, -C(=O)O-C_1-C_4alkyl, -C(=O)$NHSO_2R^{8b}$, and tetrazolyl;

R^{8a} and R^{8b} are each independently selected from C_1-C_6alkyl, amino, C_1-C_4alkylamino, di-(C_1-C_4alkyl)-amino.

27. The compound of claim 25, wherein the compound is a compound of Formula (VI-1):



Formula (VI-1)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

Y is N or CH;

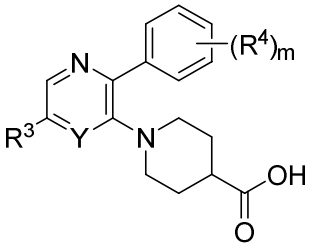
R^3 is selected from: C_1-C_6alkyl, (C_1-C_4alkoxy)-C_1-C_6alkyl, C_1-C_6haloalkyl, (C_1-C_4haloalkoxy)-C_1-C_6alkyl, (C_3-C_6cycloalkyl)-C_1-C_6alkyl, and (C_3-C_6cycloalkoxy)-C_1-C_6alkyl;

each R^4 is independently selected from: C_1-C_6alkoxy optionally substituted with R^5, C_1-C_4alkylamino optionally substituted with R^5, di-(C_1-C_4alkyl)-amino optionally substituted with R^5, C_1-C_6haloalkoxy, C_3-C_6cycloalkoxy, (C_3-C_6cycloalkyl)-C_1-C_6alkoxy, halo, C_1-C_6alkyl, and C_1-C_6haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused 5-membered heterocycloalkyl or a fused 5-membered heteroaryl, either of which may be optionally substituted with one or more C_1-C_6alkyl, halo, oxo, C_1-C_6alkoxy, or (C_1-C_4alkoxy)-C_1-C_6alkyl; and

each R^5 is independently selected from hydroxyl, C_1-C_6alkoxy, amino, C_1-C_4alkylamino, di-(C_1-C_4alkyl)-amino, C_1-C_6haloalkoxy, and (C_1-C_4alkoxy)-C_1-C_6alkoxy.

28. The compound of claim 25, wherein the compound is a compound of Formula (VI-2):



Formula (VI-2)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 4;

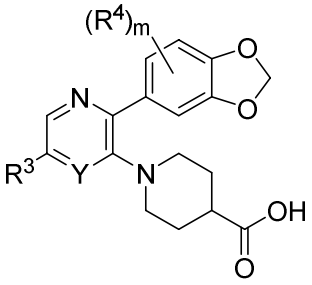
Y is N or CH;

R^3 is selected from: C_1-C_6alkyl, (C_1-C_4alkoxy)-C_1-C_6alkyl, C_1-C_6haloalkyl, and (C_1-C_4haloalkoxy)-C_1-C_6alkyl;

each R^4 is independently selected from: C_1-C_6alkoxy, C_1-C_4haloalkoxy, halo, C_1-C_4alkyl, and C_1-C_4haloalkyl;

or two R^4 substituents on adjacent carbon atoms of R^1 are taken together to form a fused 5-membered heterocycloalkyl comprising 1 or 2 O atoms or a fused 5-membered heteroaryl comprising 1 O atom and 0 or 1 N atoms, either of which may be optionally substituted with one or more C_1-C_4alkyl, halo, C_1-C_4alkoxy or (C_1-C_4alkoxy)-C_1-C_4alkyl.

29. The compound of claim 25, wherein the compound is a compound of Formula (VI-3):



Formula (VI-3)

or a pharmaceutically acceptable salt thereof, wherein:

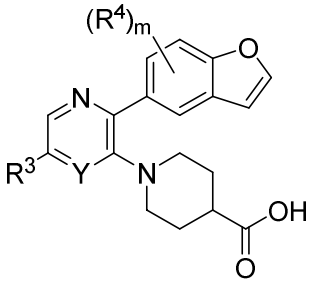
m is an integer from 0 to 2;

Y is N or CH;

R^3 is selected from: C_1-C_6alkyl, (C_1-C_4alkoxy)-C_1-C_6alkyl, C_1-C_6haloalkyl, and (C_1-C_4haloalkoxy)-C_1-C_6alkyl; and

each R^4 is independently selected from: C_1-C_6alkoxy, C_1-C_4haloalkoxy, halo, C_1-C_4alkyl, and C_1-C_4haloalkyl.

30. The compound of claim 25, wherein the compound is a compound of Formula (VI-4):



Formula (VI-4)

or a pharmaceutically acceptable salt thereof, wherein:

m is an integer from 0 to 2;

Y is N or CH;

R^3 is selected from: C_1-C_6alkyl, (C_1-C_4alkoxy)-C_1-C_6alkyl, C_1-C_6haloalkyl, and (C_1-C_4haloalkoxy)-C_1-C_6alkyl; and

each R^4 is independently selected from: C_1-C_6alkoxy, C_1-C_4haloalkoxy, halo, C_1-C_4alkyl, and C_1-C_4haloalkyl.

31. The compound of claim 29 or claim 30, or a pharmaceutically acceptable salt thereof, wherein:

m is 0 or 1; and

R^4 is selected from: C_1-C_6alkoxy, C_1-C_4haloalkoxy, and halo.

32. The compound of any one of claims 25-31, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from: C_3-C_6alkyl, (C_1-C_4alkoxy)-C_3-C_6alkyl, C_3-C_6haloalkyl, and (C_1-C_4haloalkoxy)-C_3-C_6alkyl.

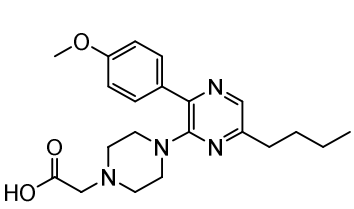
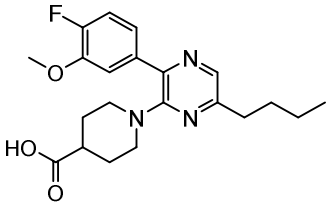
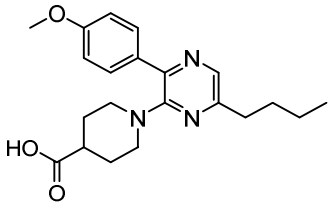
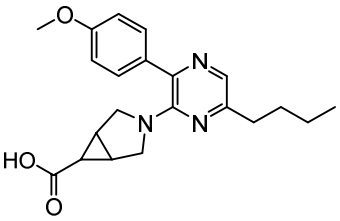
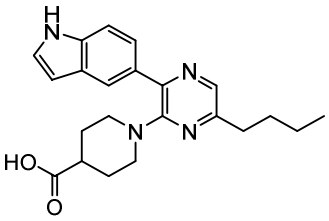
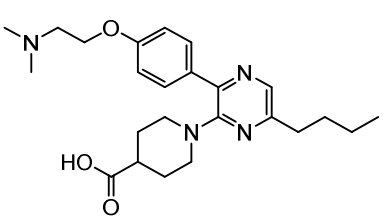
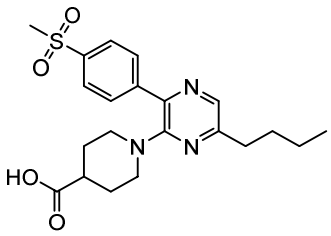
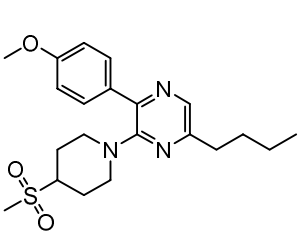
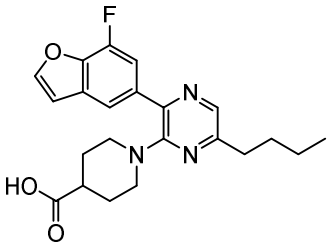
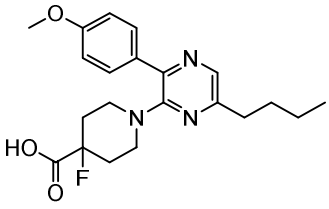
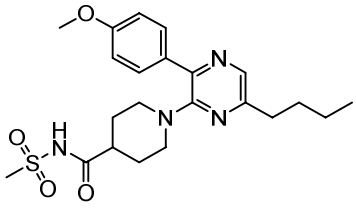
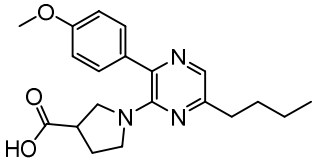
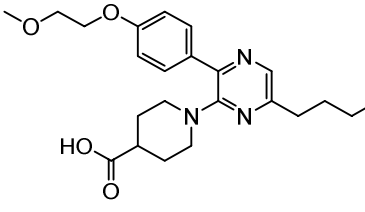
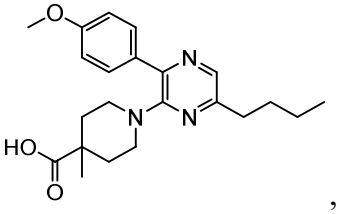
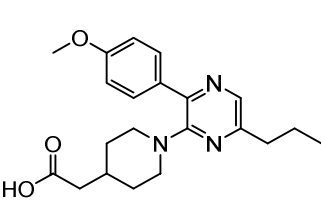
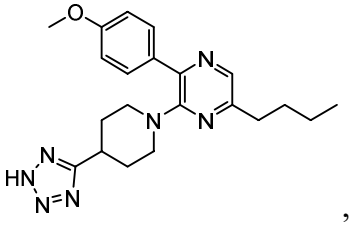
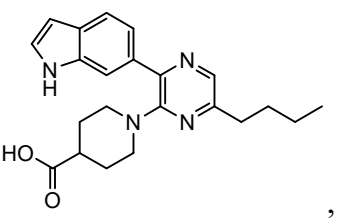
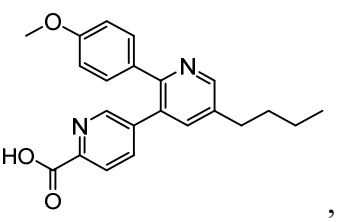
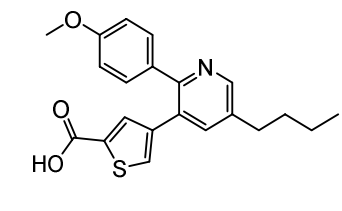
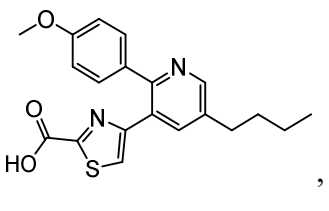
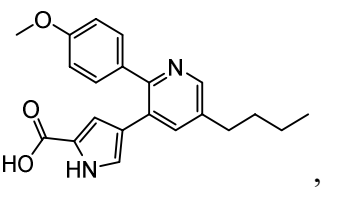
33. The compound of any one of claims 25-31, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from: (C_1-C_4alkoxy)-C_3-C_6alkyl and (C_1-C_4haloalkoxy)-C_3-C_6alkyl.

34. The compound of any one of claims 25-33, or a pharmaceutically acceptable salt thereof, wherein:

Y is N.

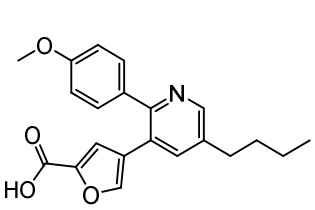
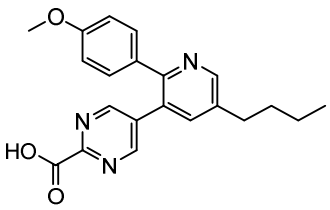
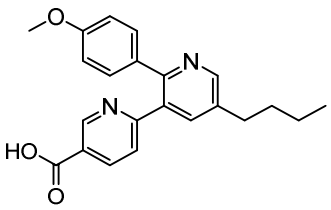
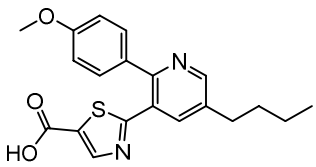
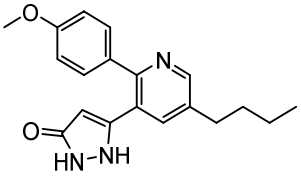
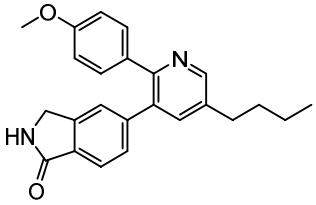
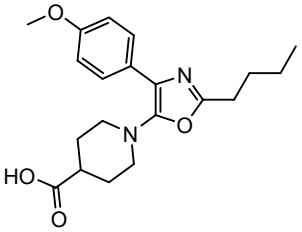
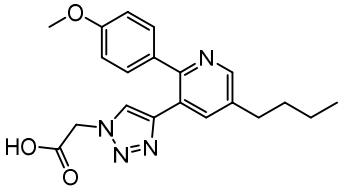
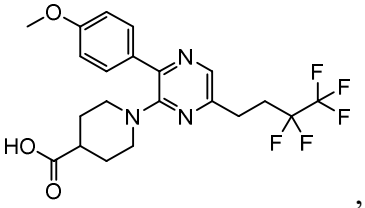
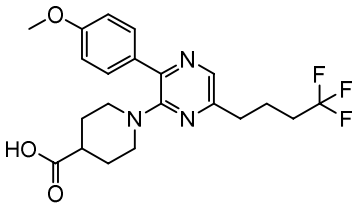
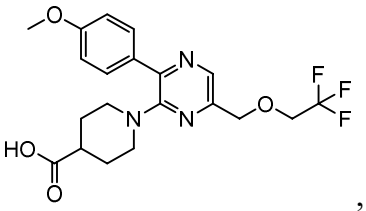
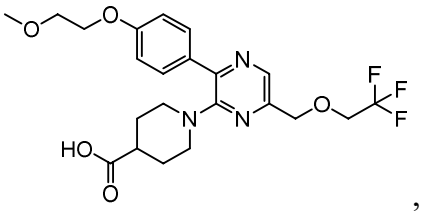
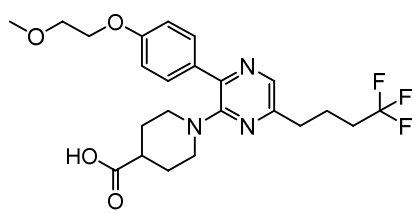
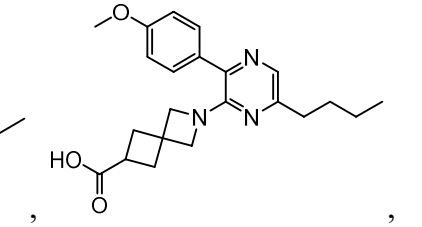
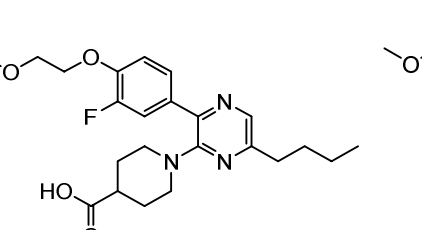
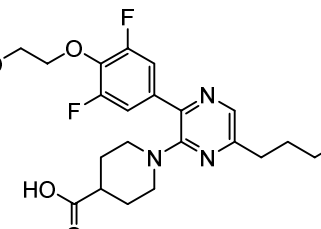
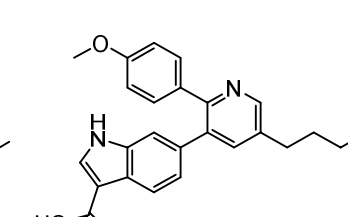
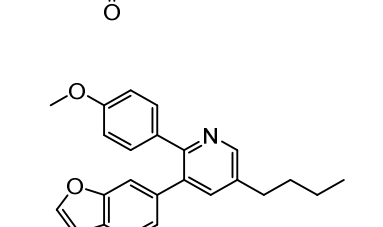
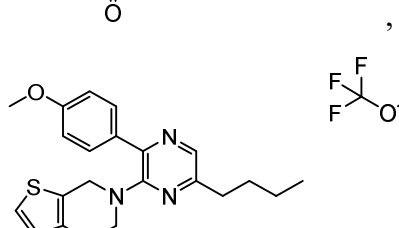
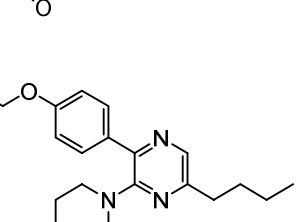
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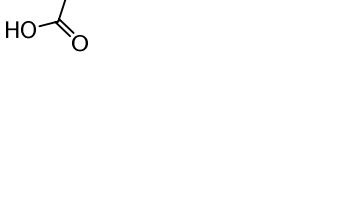
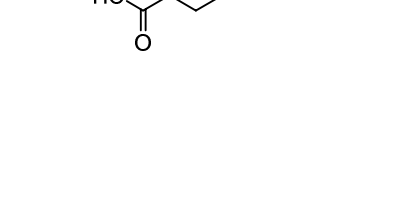

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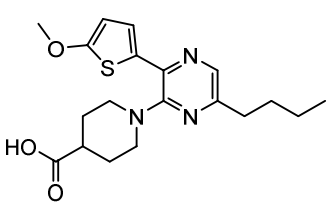
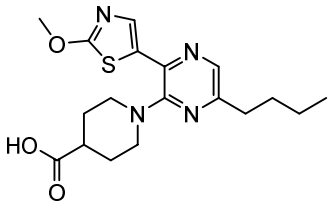
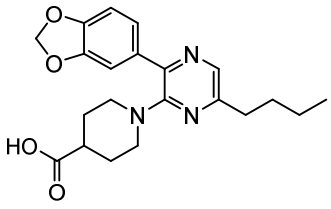
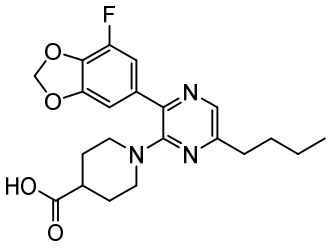
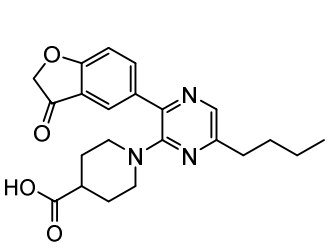
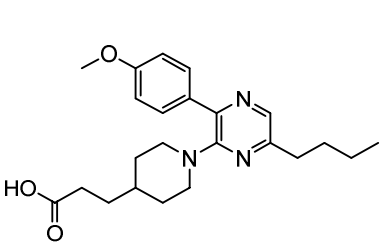
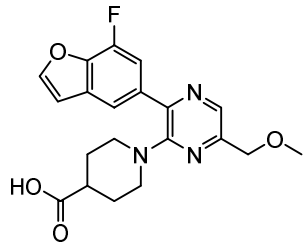
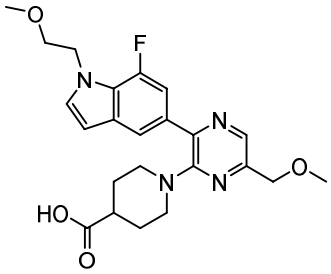
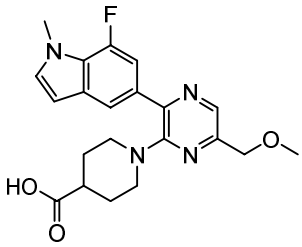
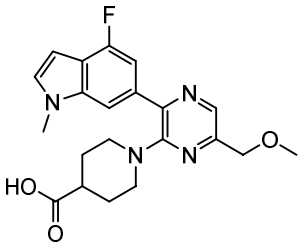
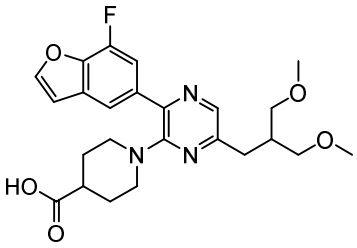
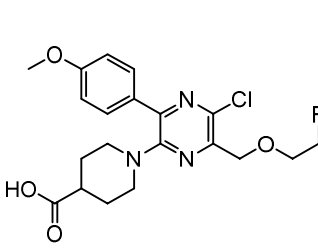
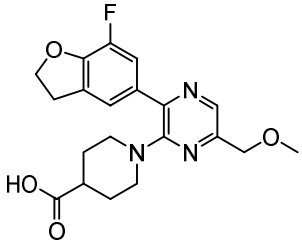
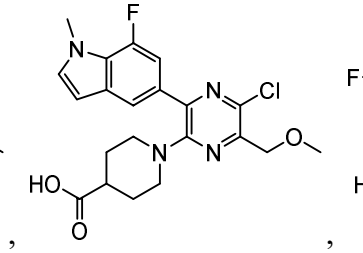
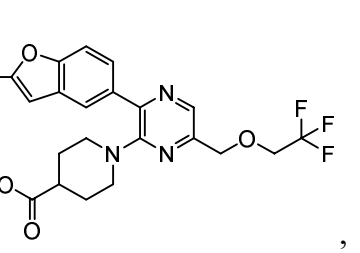
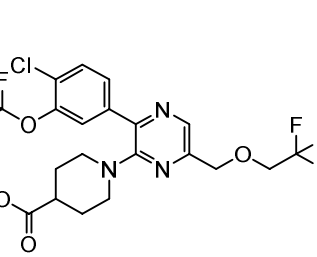
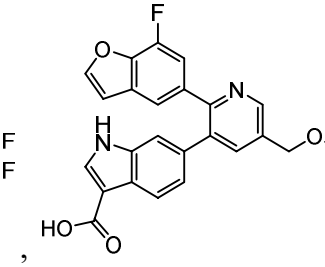
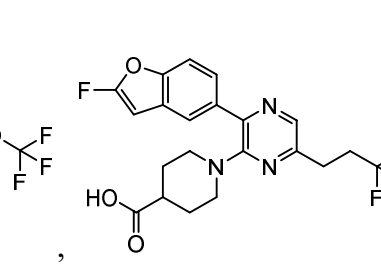
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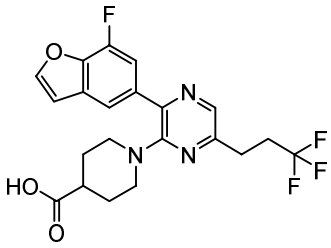
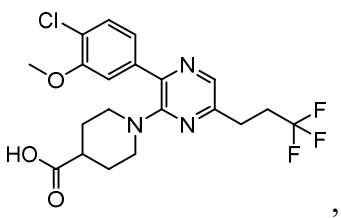
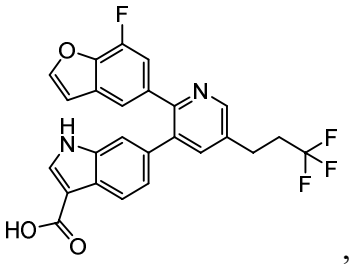
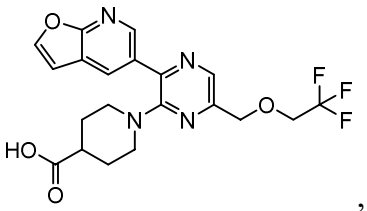
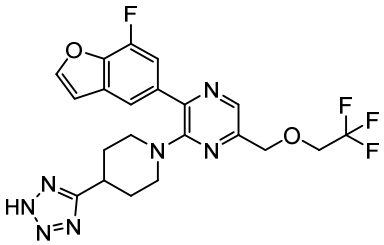
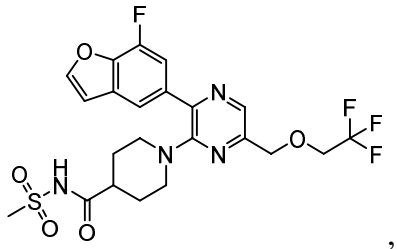
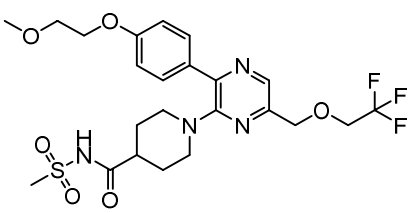
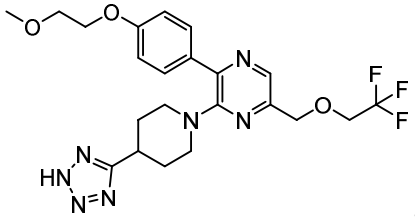
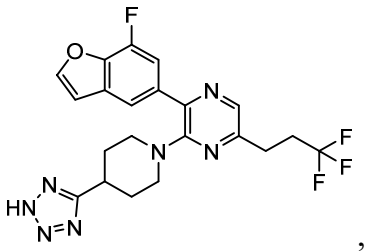
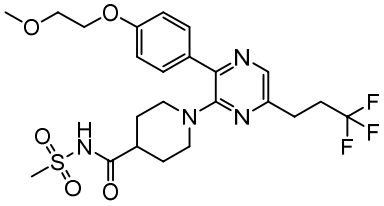
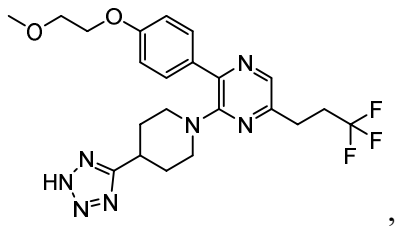
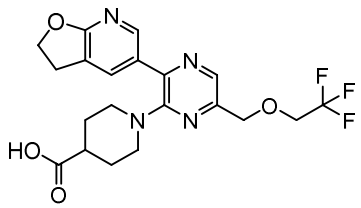
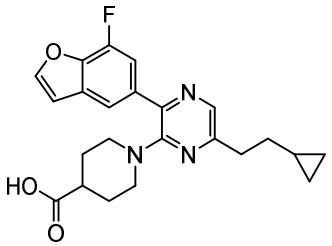
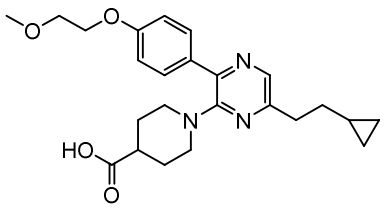
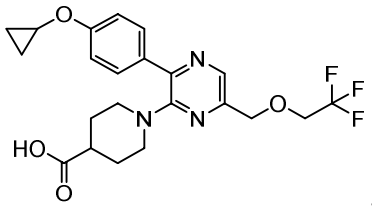
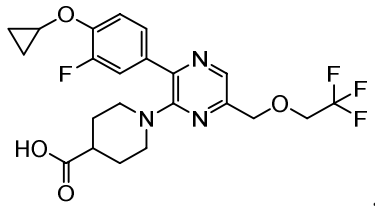
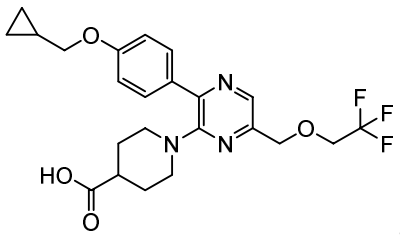
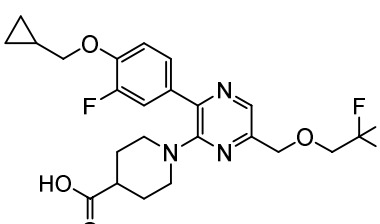
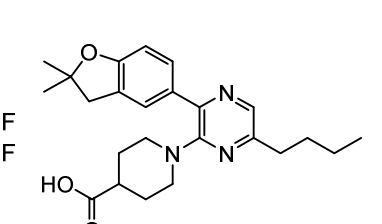
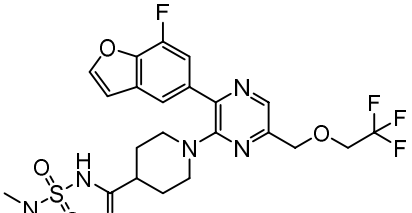
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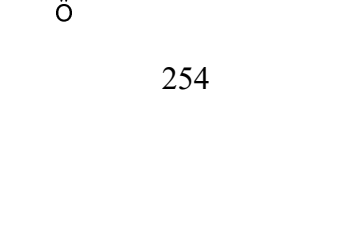

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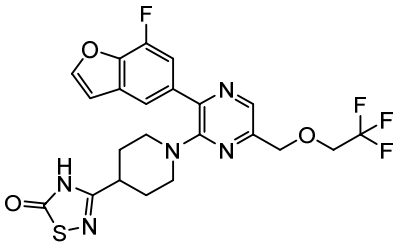
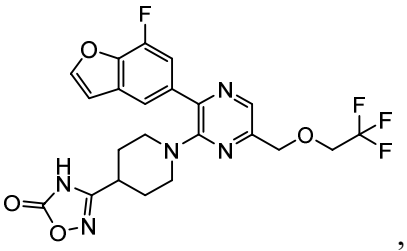
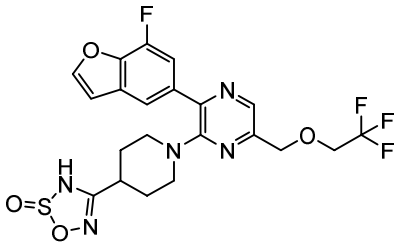
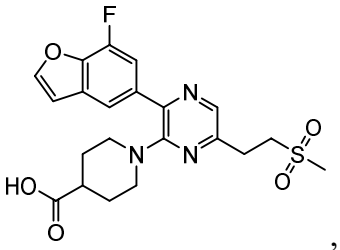
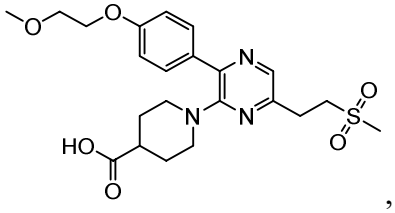
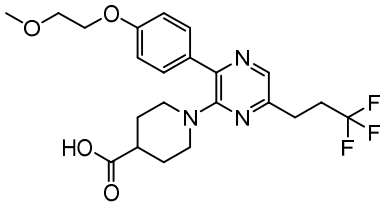
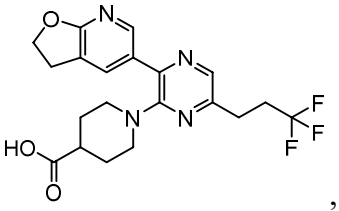
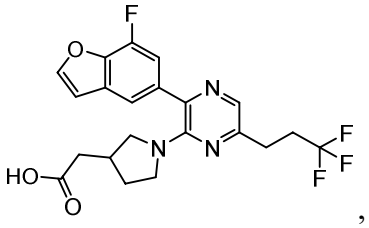
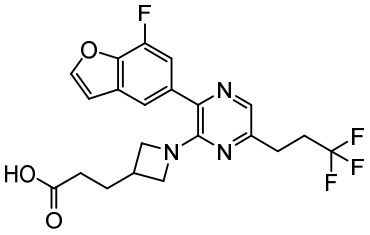
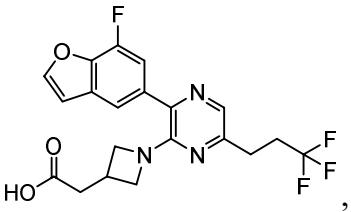
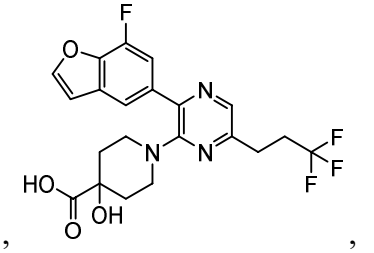
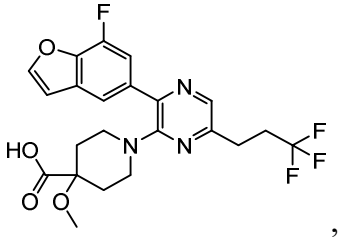
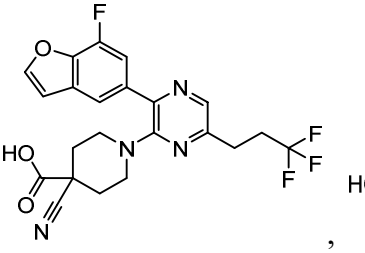
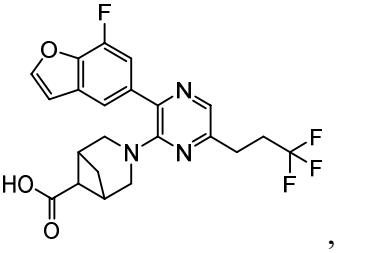
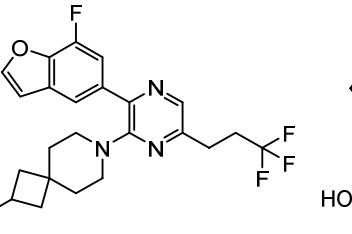
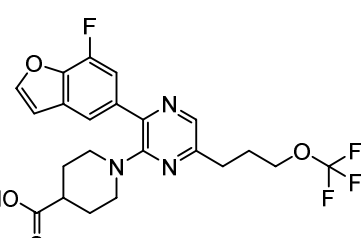
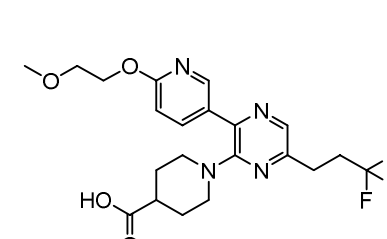
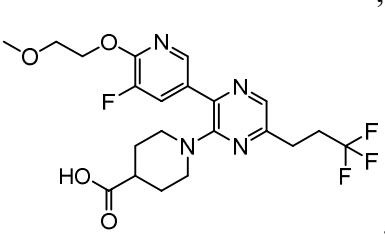
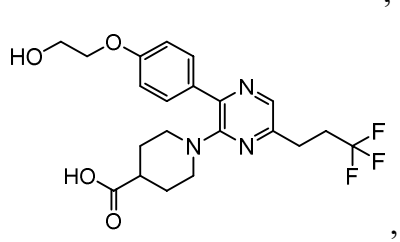
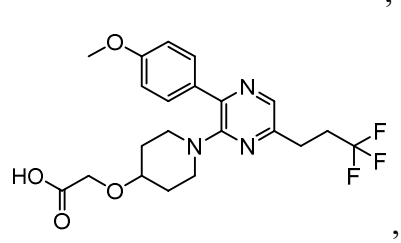
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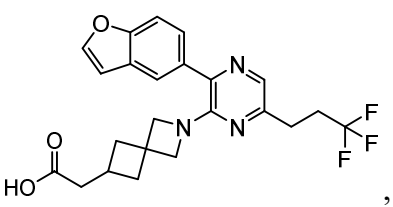
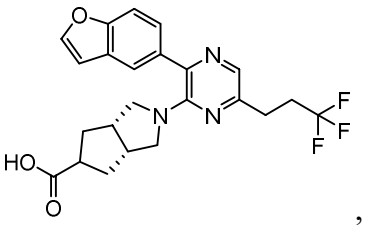
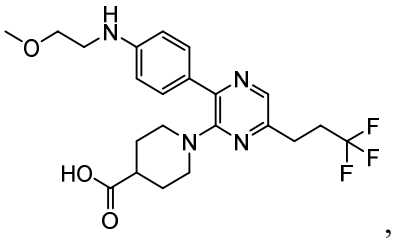
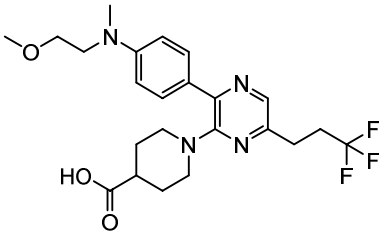
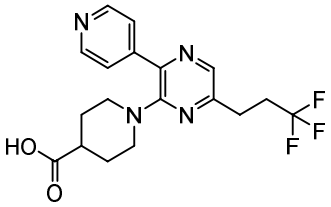
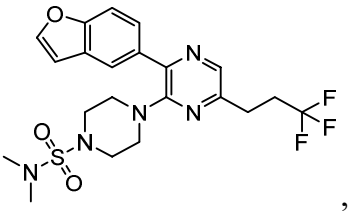
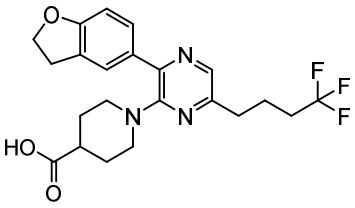
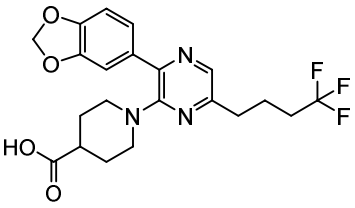
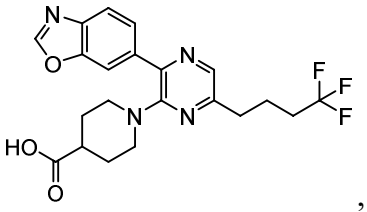
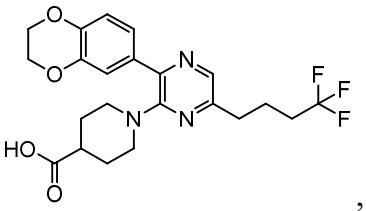
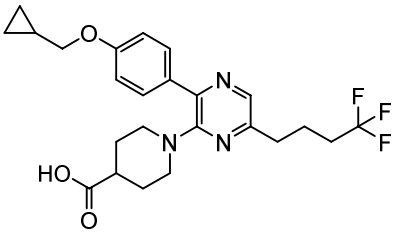
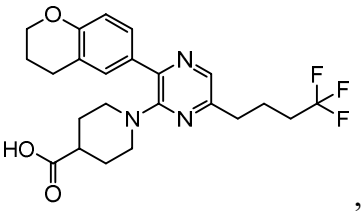
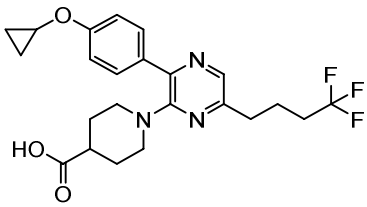
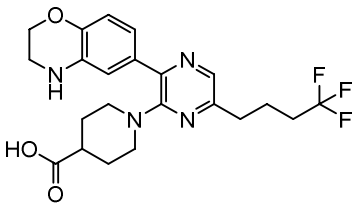
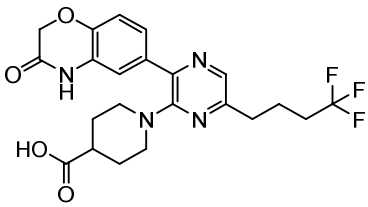
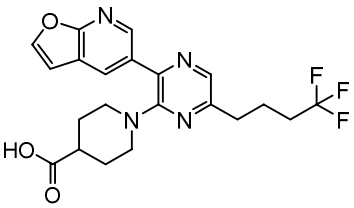
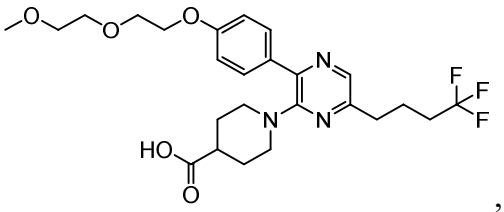
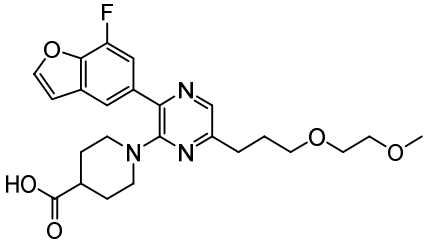
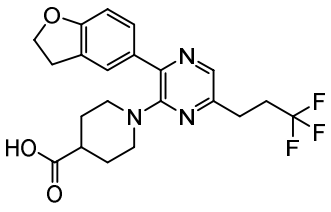
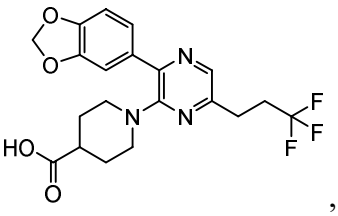
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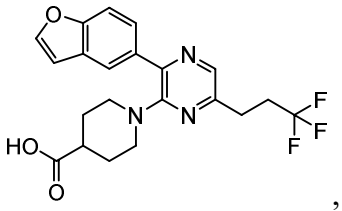
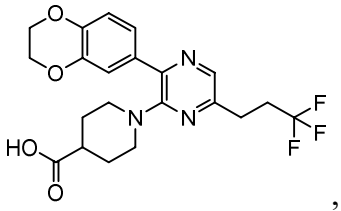
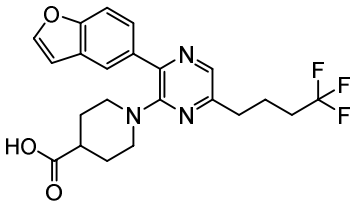
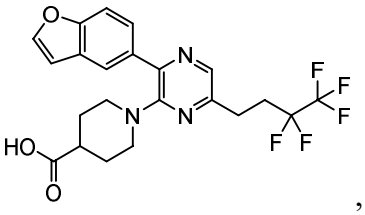
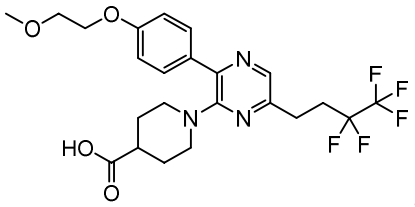
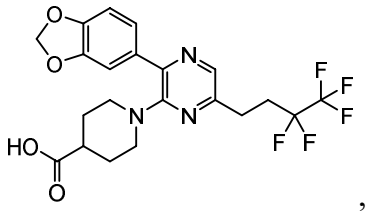
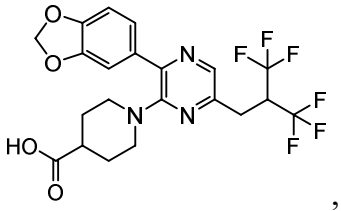
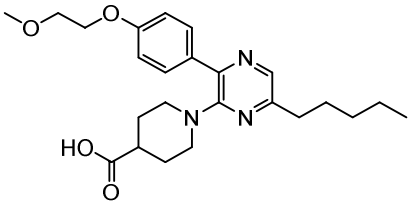
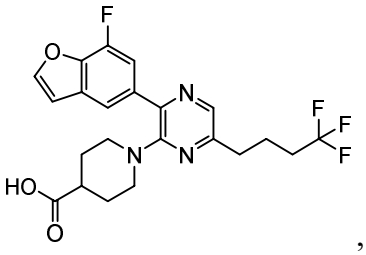
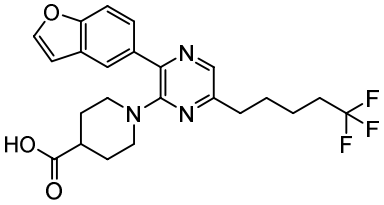
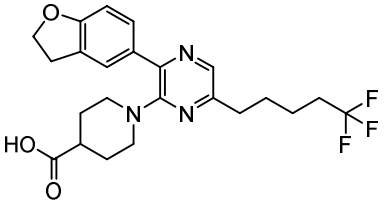
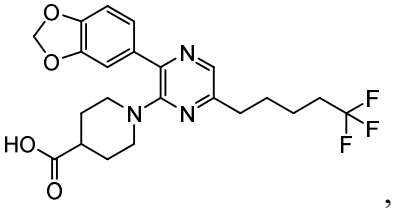
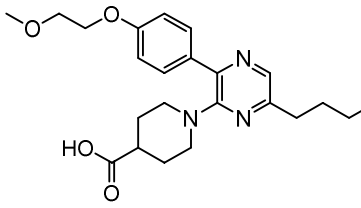
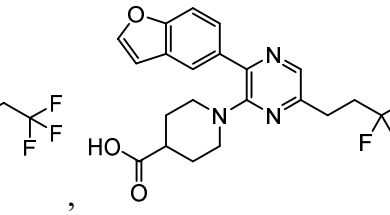
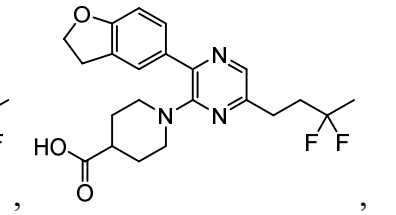
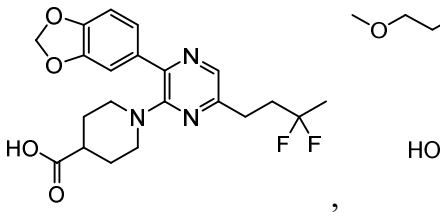

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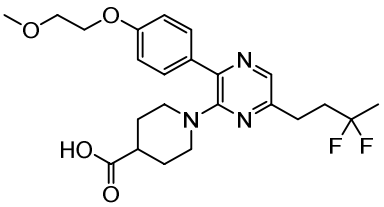
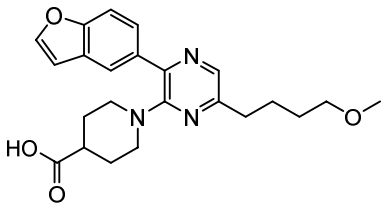
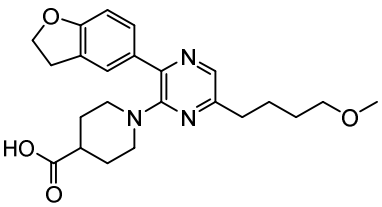
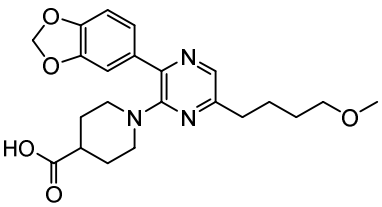
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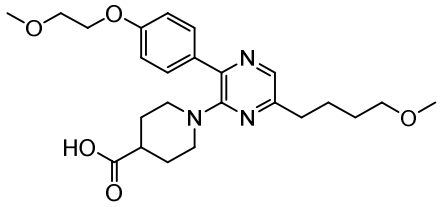
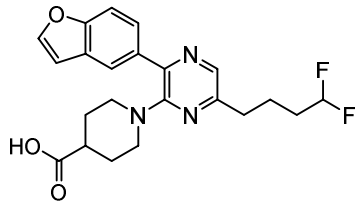
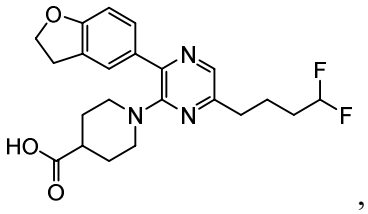
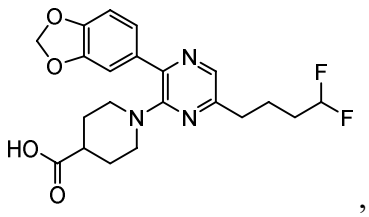
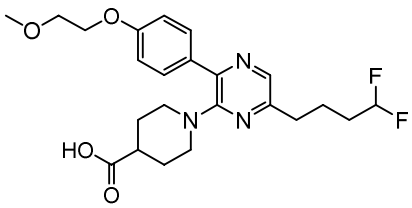
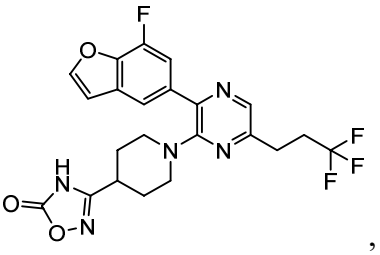
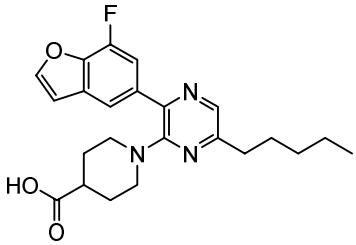
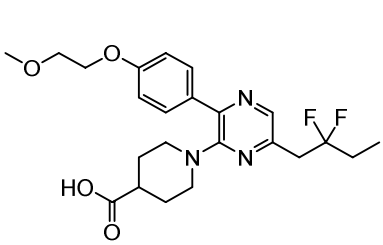
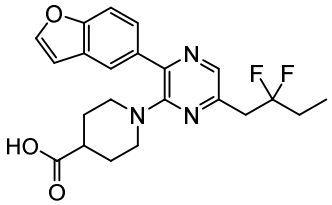
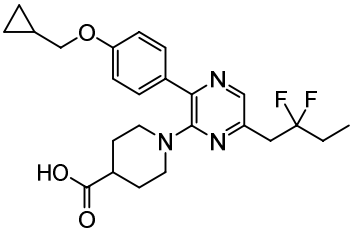
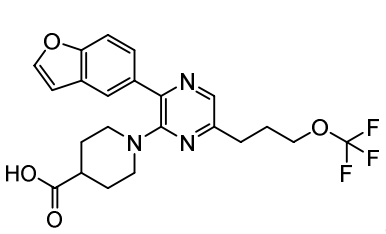
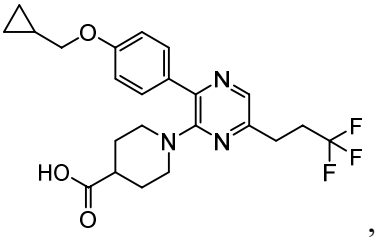
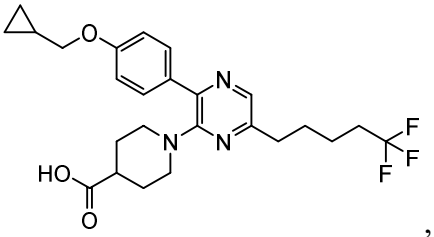
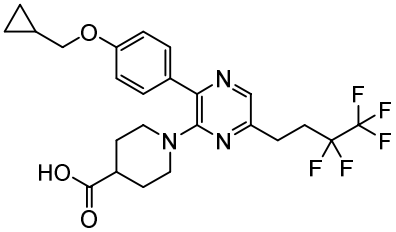
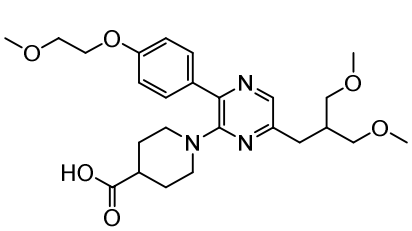
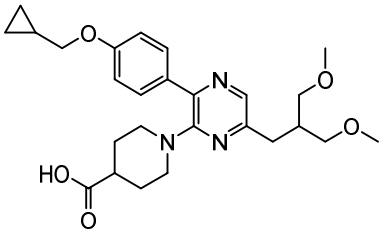
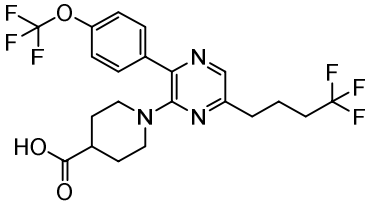
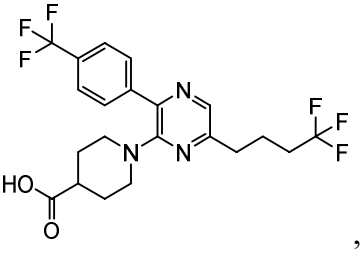
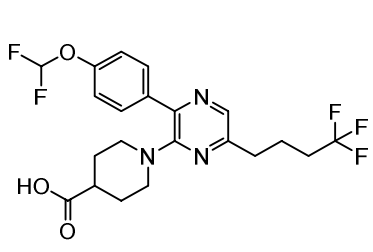
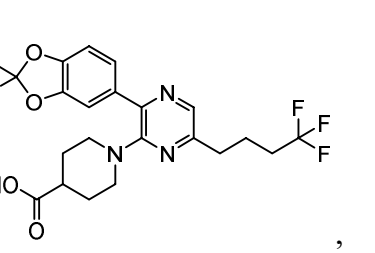

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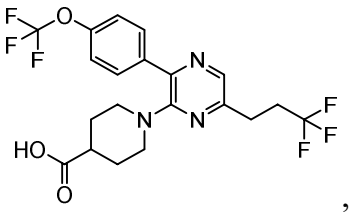
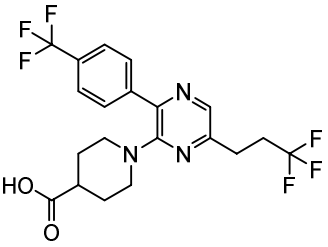
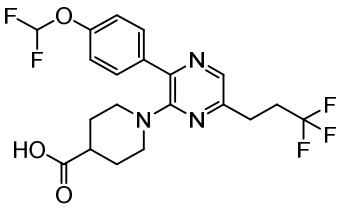
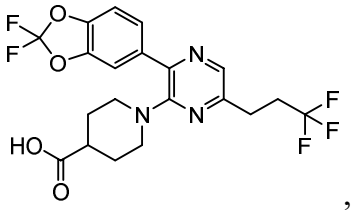
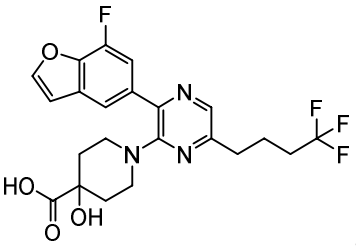
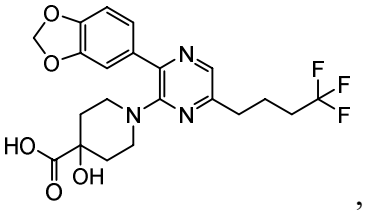
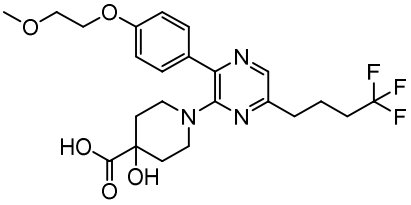
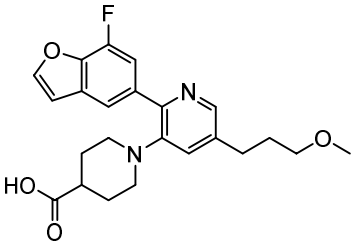
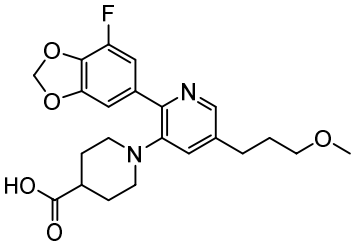
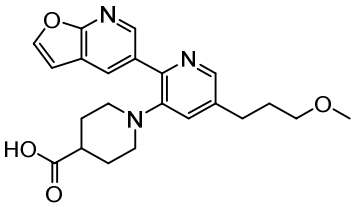
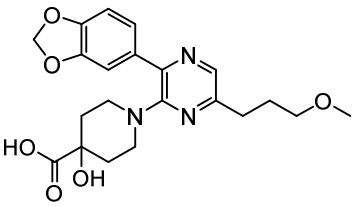
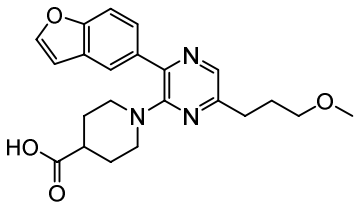
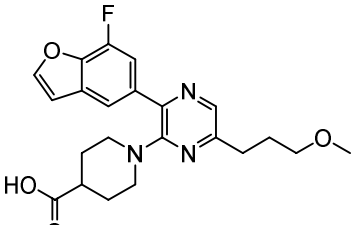
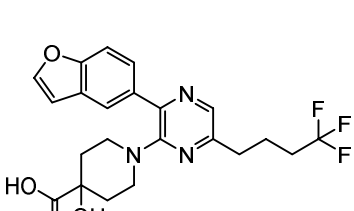
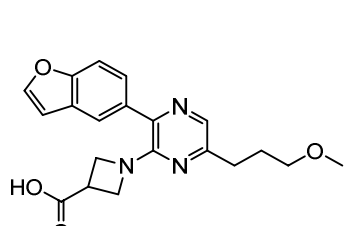
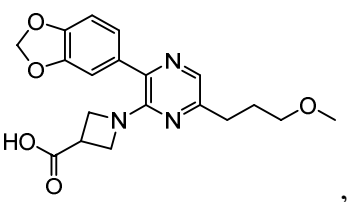
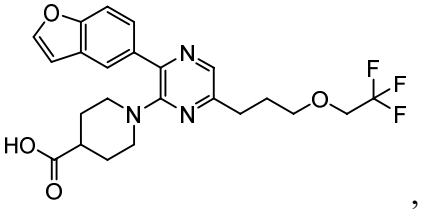
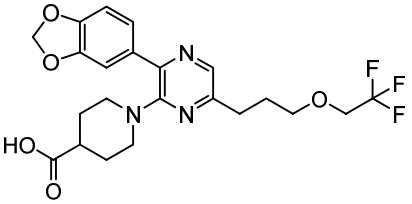
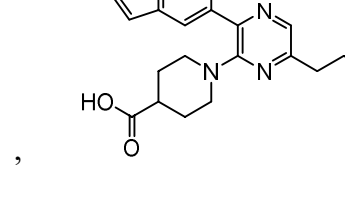
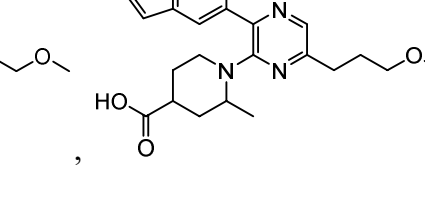
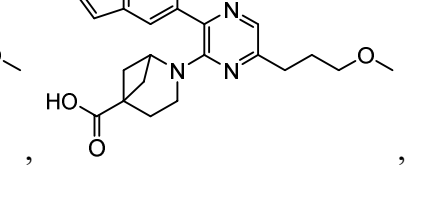
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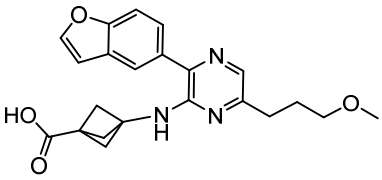
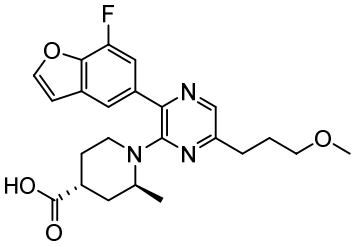
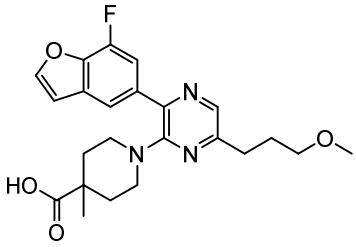
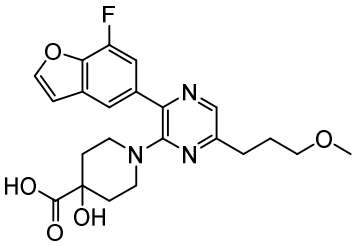
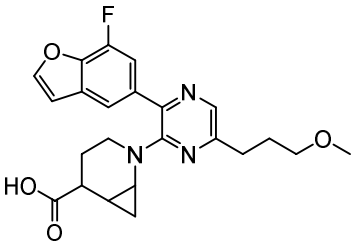
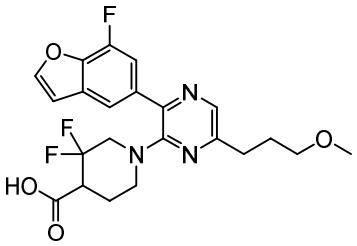
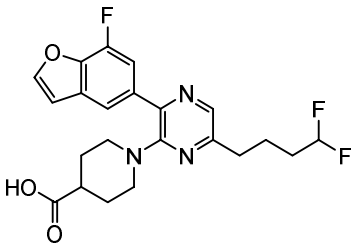
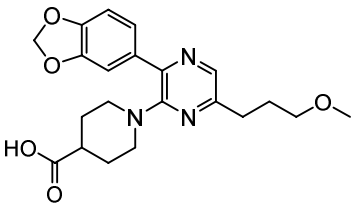
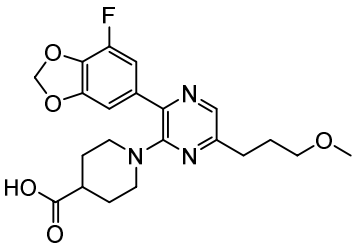
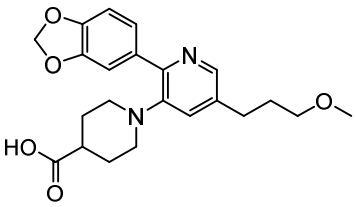
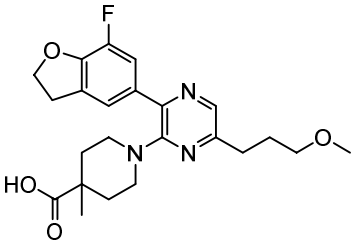
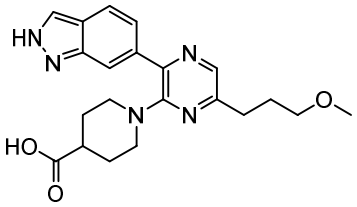
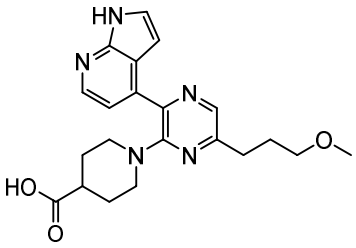
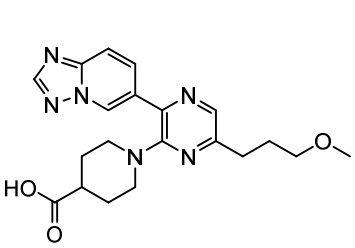
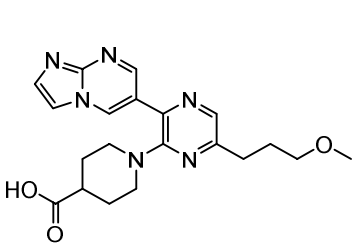
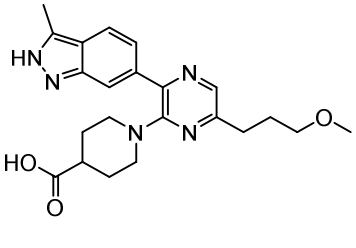
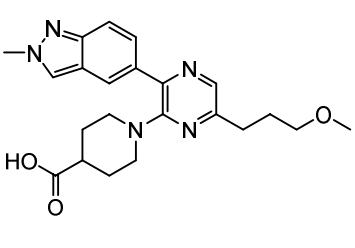
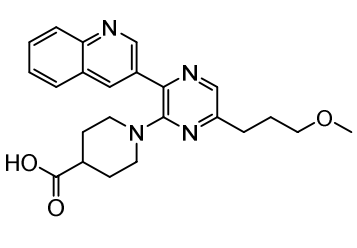
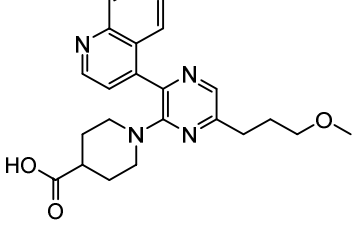
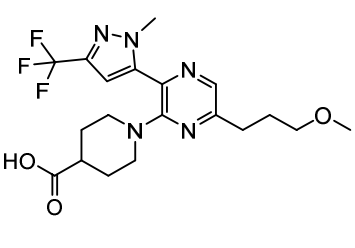
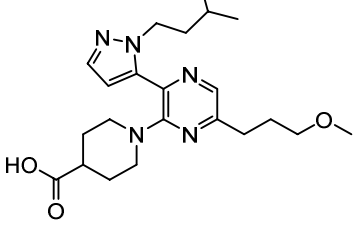
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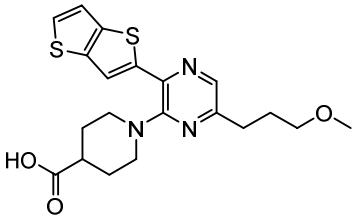
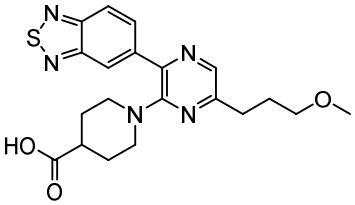
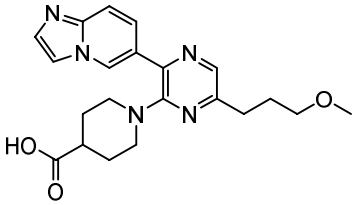
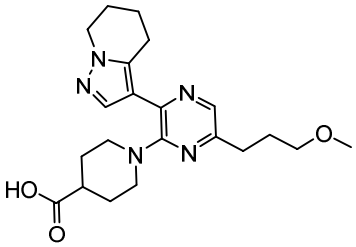
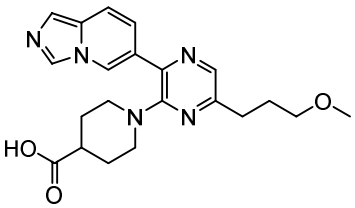
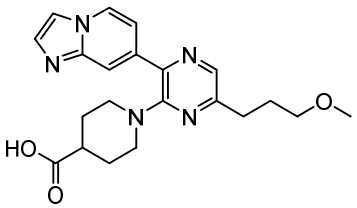
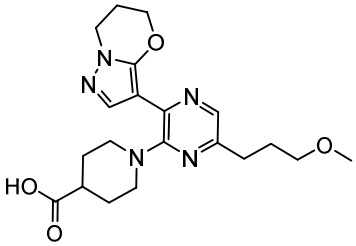
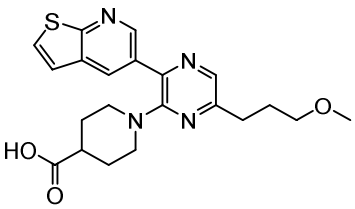
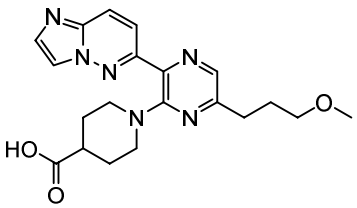
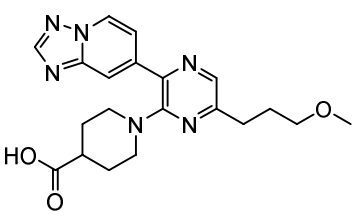
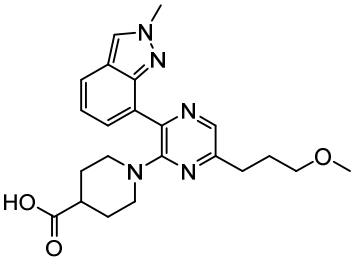
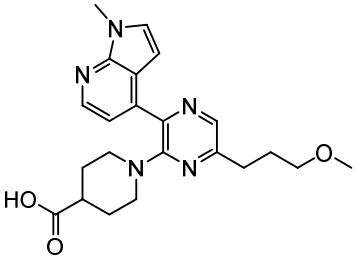
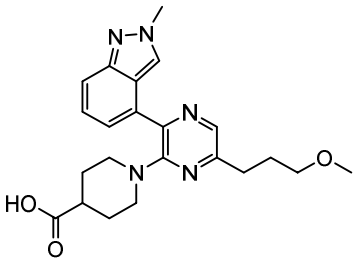
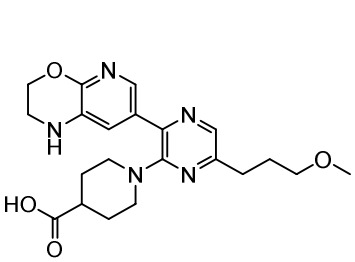
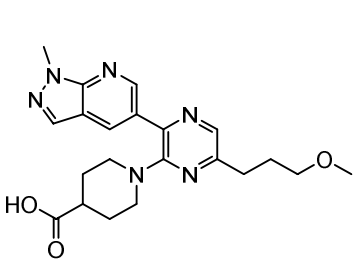
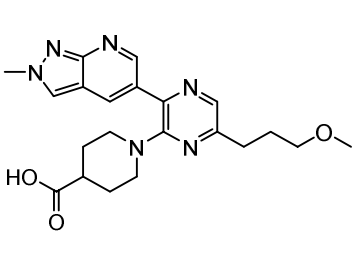
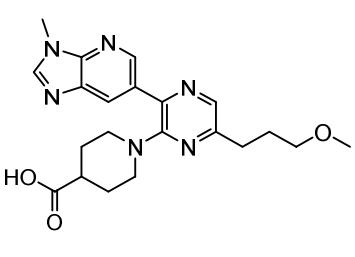
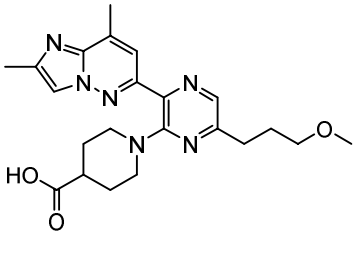
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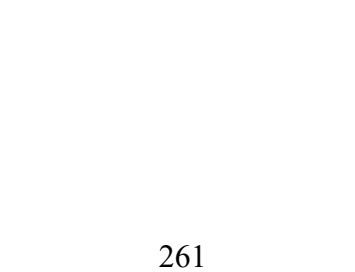

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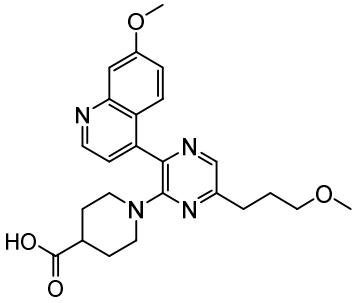
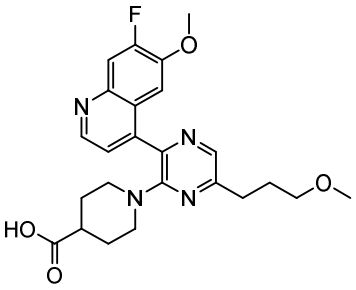
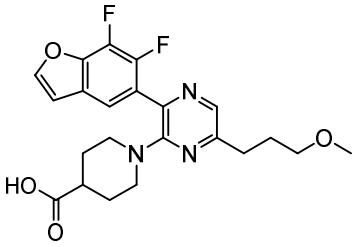
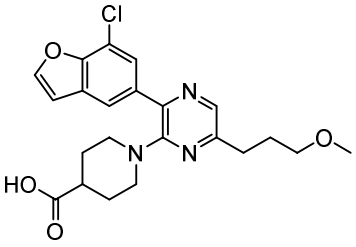
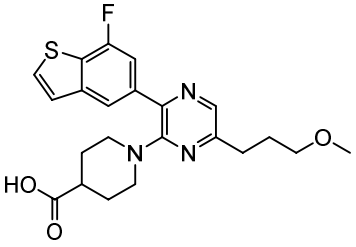
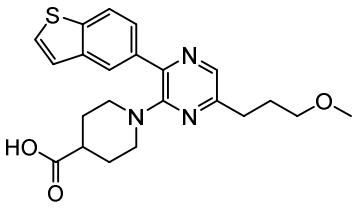
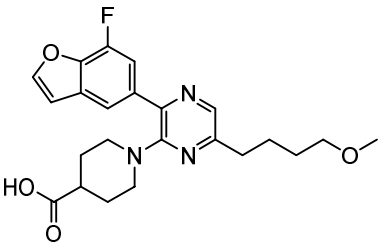
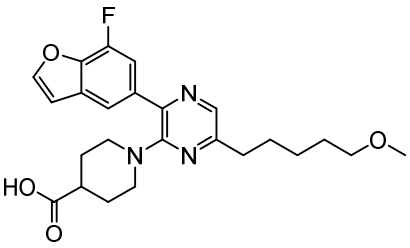
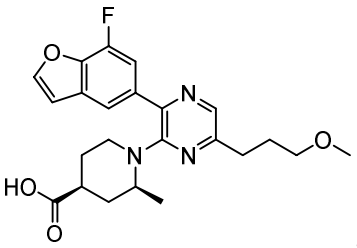
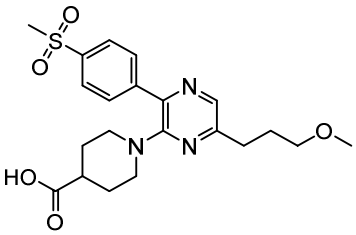
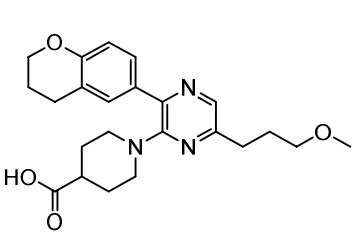
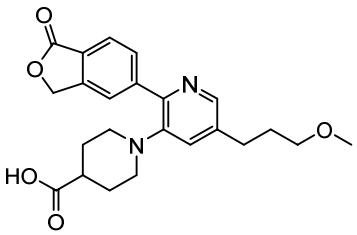
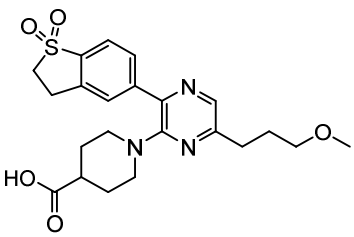
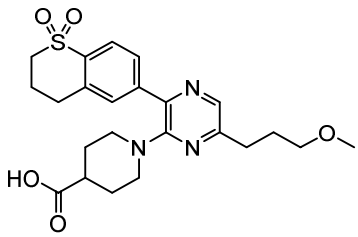
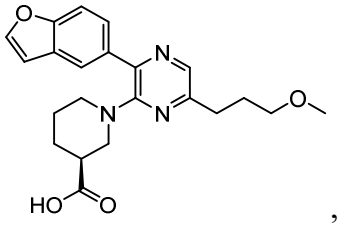
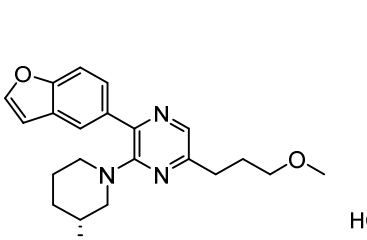
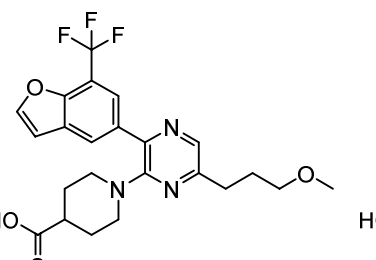
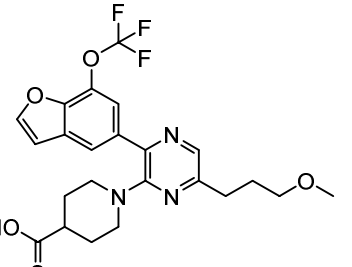
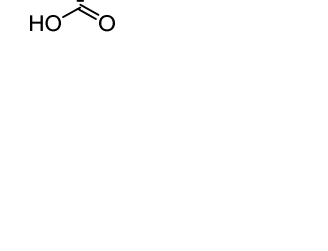
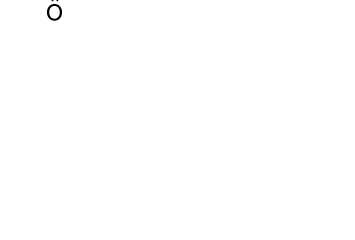
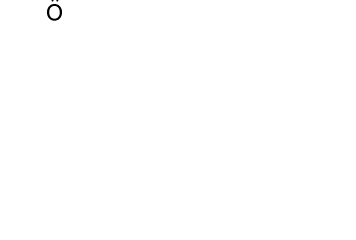
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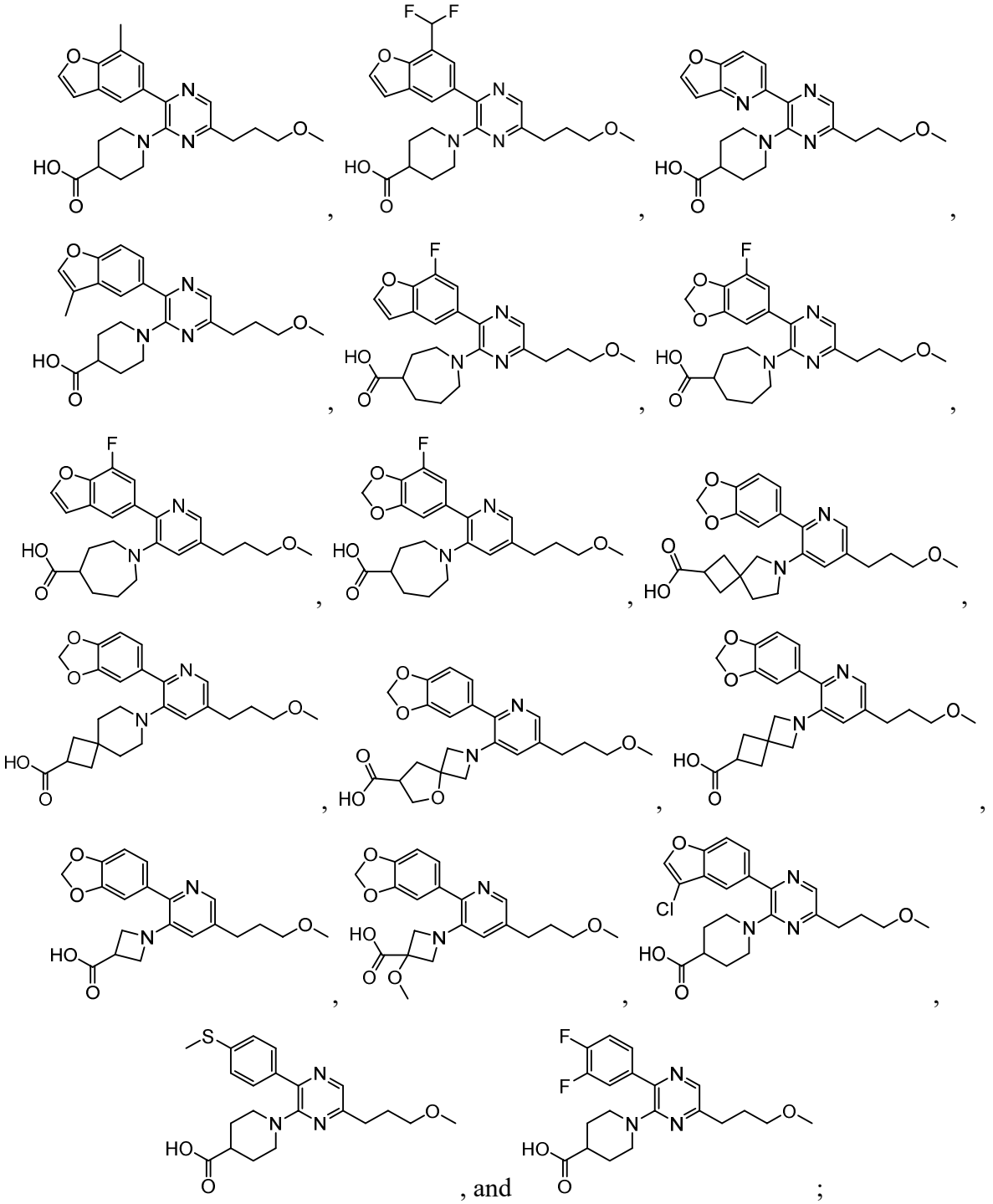
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or a pharmaceutically acceptable salt thereof.

36. A pharmaceutical composition comprising the compound of any one of claim 1-35, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

37. A compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof, for use as a medicament.

38. Use of a compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a condition selected from hyperuricemia and gout.
39. Use of a compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for preventing or treating a disease or condition ameliorated by the inhibition of GLUT9.
40. An *ex vivo* method of inhibition of GLUT9 comprising contacting GLUT9 *ex vivo* with a compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof.
41. The use of claim 39, wherein said disease is selected from hyperuricemia, gout, and uncontrolled gout including comorbidities and associated diseases.
42. The use of claim 39, for use in combination therapy with another agent, wherein the other agent is selected from inhibitors of uric acid synthesis, uricosurics, and uric acid catabolizing agents.
43. The use of claim 42, wherein said uricosuric is selected from probenecid, lesinurad, benzbromarone, and sulfinpyrazone.
44. The use of claim 42, wherein said inhibitor of uric acid synthesis is selected from allopurinol and febuxostat.
45. The use of claim 42, wherein said uric acid catabolizing agent is pegloticase.
46. The use or claim 39, for use in combination therapy with another agent, wherein the other agent is colchichine.
47. Use of a compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for lowering blood uric acid levels in a mammal.