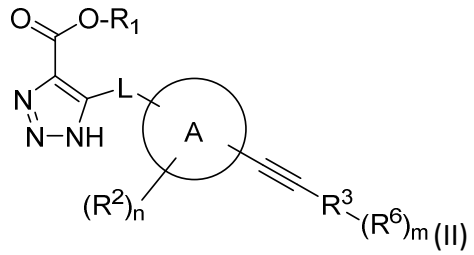
CLAIMS

What is claimed is:

1. A compound of structural Formula II



(II)

or a salt, polymorph, or tautomer thereof, wherein:

R^1 is chosen from hydrogen, C_1–C_6 alkyl, and C_1–C_6 cycloalkyl;

L is chosen from O, S, CH_2, NH, NR^4, S(O), SO_2, and CR^4=CR^5;

A is chosen from monocyclic or bicyclic aryl, and monocyclic or bicyclic heteroaryl;

each R^2 is independently chosen from 5-10-membered heteroaryl, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 alkylthio, C_1–C_6 haloalkoxy, C_1–C_6 haloalkyl, C_6–C_{10} aryl, cyano, and halogen;

n is 0, 1, or 2;

R^3 is chosen from 3-10-membered heterocycloalkyl, 5-10-membered heteroaryl, C_1–C_6 alkyl, C_1–C_6 sulfonyl, C_3–C_6 cycloalkyl, C_3–C_6 cycloalkylalkyl, C_6–C_{10} aryl, and C_6–C_{10} arylalkyl;

R^4 and R^5 are each independently chosen from hydrogen and C_1–C_6 alkyl, or R^4 and R^5, together with the atoms to which they are attached, form a cycloalkenyl; and

each R^6 is independently chosen from 4-6-membered heterocycloalkyl, 5-10-membered heteroaryl, amino, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 haloalkyl, C_3–C_6 cycloalkyl, C_3–C_6 cycloalkylalkyl, carboxyl, cyano, halogen, hydroxyl, methyl-4-6-membered heterocycloalkyl, and phenyl; and

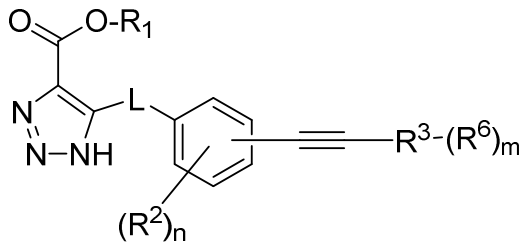
m is 0, 1, 2, or 3.

2. The compound of claim 1, wherein A is chosen from indazolyl, indolyl, naphthalenyl, oxazolyl, oxodihydropyridinyl, phenyl, pyridazinyl, pyridinyl, and thiazolyl.

3. The compound of claim 1, wherein A is monocyclic aryl.

4. The compound of claim 3, wherein A is phenyl.

5. A compound of claim 1, having structural Formula III,



(III)

or a salt, polymorph, or tautomer thereof, wherein:

R^1 is chosen from hydrogen, C_1–C_6 alkyl, and C_1–C_6 cycloalkyl;

L is chosen from O, S, CH_2, NH, NR^4, S(O), SO_2, and CR^4=CR^5;

each R^2 is independently chosen from 5-10-membered heteroaryl, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 alkylthio, C_1–C_6 haloalkoxy, C_1–C_6 haloalkyl, C_6–C_{10} aryl, cyano, and halogen;

n is 0, 1, or 2;

R^3 is chosen from 3-10-membered heterocycloalkyl, 5-10-membered heteroaryl, C_1–C_6 alkyl, C_1–C_6 sulfonyl, C_3–C_6 cycloalkyl, C_3–C_6 cycloalkylalkyl, C_6–C_{10} aryl, and C_6–C_{10} arylalkyl;

R^4 and R^5 are each independently chosen from hydrogen and C_1–C_6 alkyl, or R^4 and R^5, together with the atoms to which they are attached, form a cycloalkenyl; and

each R^6 is independently chosen from 4-6-membered heterocycloalkyl, 5-10-membered heteroaryl, amino, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 haloalkyl, C_3–C_6 cycloalkyl, C_3–C_6 cycloalkylalkyl, carboxyl, cyano, halogen, hydroxyl, methyl-4-6-membered heterocycloalkyl, and phenyl; and

m is 0, 1, 2, or 3.

6. The compound of any one of claims 1 to 5, wherein R^3 is chosen from methyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, tetrahydrofuranyl, cyclohexyl, tetrahydropyranyl, piperidinyl, dihydropyranyl, indazolyl, benzodioxolyl, phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, benzoxazolyl, oxodihydropyridinyl, thiazolyl, tetrazolyl, cyclopropylmethyl, cyclobutylmethyl,

cyclopentylmethyl, cyclohexylmethyl, benzyl, dioxaspirodecanyl, oxocyclohexyl, and bicyclo[1.1.1]pentyl, any of which is optionally substituted with 1, 2, or 3 R^6 groups.

7. The compound of any one of claims 1 to 5, wherein R^3 is chosen from C_1–C_6 alkyl, C_3–C_6 cycloalkyl, and C_3–C_6 cycloalkylalkyl, any of which is optionally substituted with 1, 2, or 3 R^6 groups.

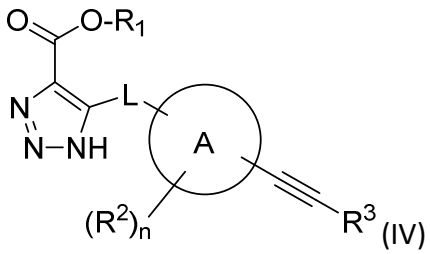
8. The compound of any one of claims 1 to 5, wherein R^3 is chosen from propyl and cyclopropylmethyl.

9. The compound of any one of claims 1 to 8, wherein R^6 is chosen from methyl, hydroxyl, amino, dimethylamino, propyl, cyclopropylmethyl, indazolyl, benzodioxolyl, cyclopropyl, tetrahydrofuranyl, cyclohexyl, tetrahydropyranyl, piperidinyl, methylpiperidinyl, phenyl, fluoro, chloro, methylsulfonyl, cyano, trifluoromethyl, methoxy, carboxyl, and fluoromethyl.

10. The compound of claim 9, wherein R^6 is chosen from chloro, methyl, cyano, fluoro, methylsulfonyl, methoxy, carboxyl, trifluoromethyl.

11. The compound of any one of claims 1 to 10, wherein m is 0.

12. A compound of claim 1, having structural Formula IV,



(IV)

or a salt, polymorph, or tautomer thereof, wherein:

R^1 is chosen from hydrogen, C_1–C_6 alkyl, and C_1–C_6 cycloalkyl;

L is chosen from O, S, CH_2, NH, NR^4, S(O), SO_2, and CR^4=CR^5;

A is chosen from monocyclic or bicyclic aryl, and monocyclic or bicyclic heteroaryl;

each R^2 is independently chosen from 5-10-membered heteroaryl, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 alkylthio, C_1–C_6 haloalkoxy, C_1–C_6 haloalkyl, C_6–C_{10} aryl, cyano,

and halogen;

n is 0, 1, or 2;

R^3 is chosen from C_1–C_6 alkyl, C_3–C_6 cycloalkyl, and C_3–C_6 cycloalkylalkyl; and

R^4 and R^5 are each independently chosen from hydrogen and C_1–C_6 alkyl, or R^4 and R^5, together with the atoms to which they are attached, form a cycloalkenyl.

13. The compound of any one of claims 1 to 12, wherein L is chosen from O, S, CH_2, and NH.

14. The compound of claim 13, wherein L is O or S.

15. The compound of claim 12, wherein A is chosen from indazolyl, indolyl, naphthalenyl, oxazolyl, oxodihydropyridinyl, phenyl, pyridazinyl, pyridinyl, and thiazolyl.

16. The compound of claim 15, wherein A is monocyclic aryl.

17. The compound of claim 16, wherein A is phenyl.

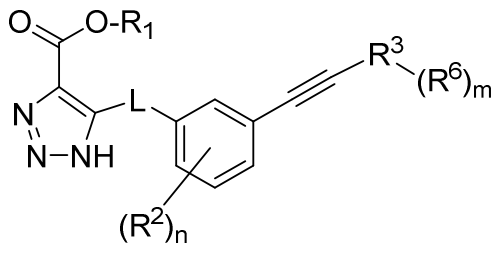
18. The compound of any one of claims 1 to 17, wherein each R^2 is independently chosen from fluoro, chloro, methyl, methoxy, trifluoromethyl, methylthio, methylsulfonyl, trifluoromethoxy, trifluoroethoxy, phenyl, and pyrazolyl.

19. The compound of claim 18, wherein each R^2 is independently chosen from fluoro, chloro, methyl, trifluoromethyl, methylsulfonyl, and methoxy.

20. The compound of any one of claims 1 to 19, wherein n is 0.

21. The compound of any one of claims 12 to 20, wherein R^3 is chosen from isobutyl and cyclopropylmethyl.

22. A compound of claim 5, having structural Formula V,



(V)

or a salt, polymorph, or tautomer thereof, wherein:

R^1 is chosen from hydrogen, C_1–C_6 alkyl, and C_1–C_6 cycloalkyl;

L is chosen from O and S;

each R^2 is independently chosen from 5-10-membered heteroaryl, C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 alkylsulfonyl, C_1–C_6 alkylthio, C_1–C_6 haloalkoxy, C_1–C_6 haloalkyl, C_6–C_{10} aryl, cyano, and halogen;

n is 0, 1, or 2;

R^3 is chosen from C_2–C_6 alkyl, C_3–C_6 cycloalkyl, and C_3–C_6 cycloalkylalkyl;

and

each R^6 is C_1–C_6 alkoxy, C_1–C_6 alkyl, C_1–C_6 haloalkyl, C_3–C_6 cycloalkyl, cyano, halogen, and hydroxyl; and

m is 0, 1, 2, or 3.

23. The compound of claim 22, wherein R^1 is hydrogen.

24. The compound of claim 22 or 23, wherein n is 0.

25. The compound of any one of claims 22–24, wherein n is 0 or 1; and R^6 , if present, is halogen.

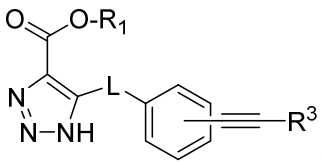
26. The compound of any one of claims 22–25, wherein R^3 is chosen from C_2–C_6 alkyl, C_3–C_6 cycloalkyl, and C_3–C_6 cycloalkylmethyl.

27. The compound of any of claims 22–26, wherein R^3 is chosen from ethyl, propyl, isopropyl, isobutyl, *sec*-butyl, *tert*-butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, and bicyclo[1.1.1]pentylmethyl.

28. The compound of any of claims 22–26, wherein R^3 is chosen from ethyl, propyl, isopropyl, isobutyl, *sec*-butyl, *tert*-butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, and cyclohexylmethyl.

29. The compound of claim 28, wherein R^3 is chosen from isobutyl and cyclopropylmethyl.

30. A compound of claim 12, having structural Formula VI,



(VI)

or a salt, polymorph, or tautomer thereof, wherein:

R^1 is chosen from hydrogen, C_1–C_6 alkyl, and C_1–C_6 cycloalkyl;

L is chosen from O, S, CH_2, and NH; and

R^3 is chosen from C_2–C_6 alkyl, C_3–C_6 cycloalkyl, and C_3–C_6 cycloalkylalkyl.

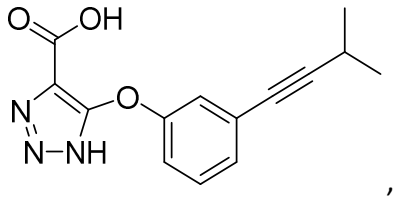
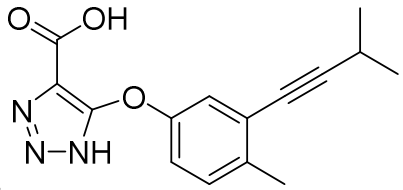
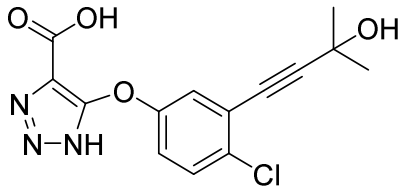
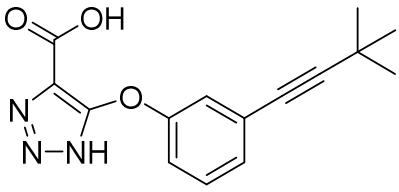
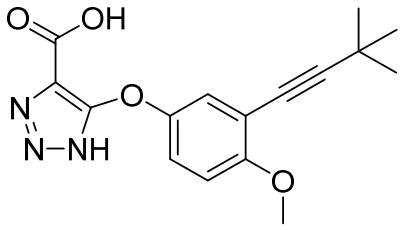
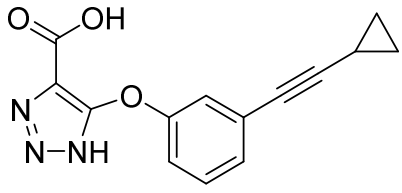
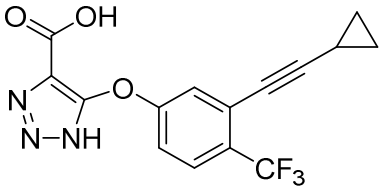
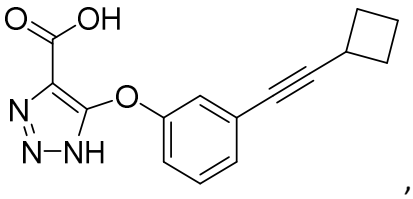
31. The compound of any one of claims 1 to 30, wherein R^1 is chosen from methyl, ethyl, isopropyl, t-butyl, and hydrogen.

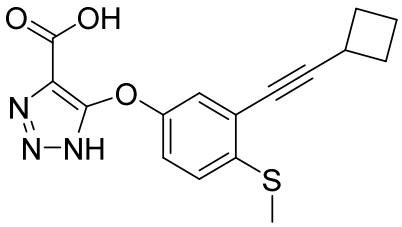
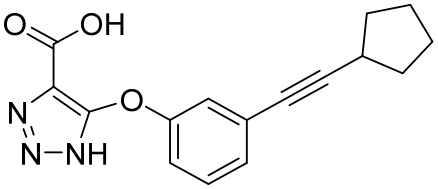
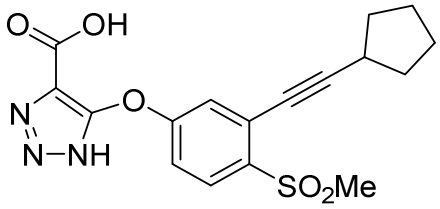
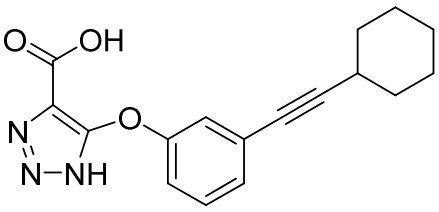
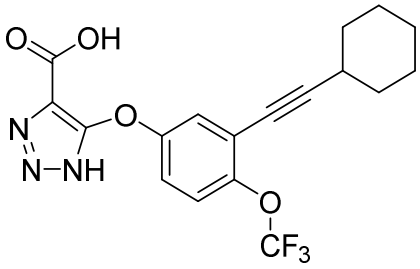
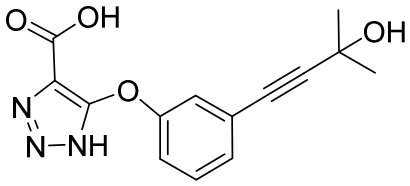
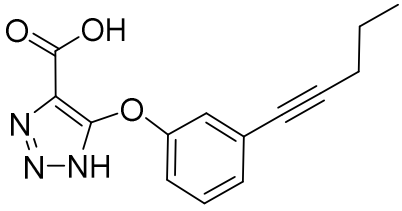
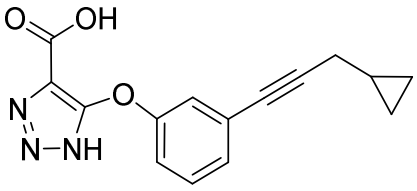
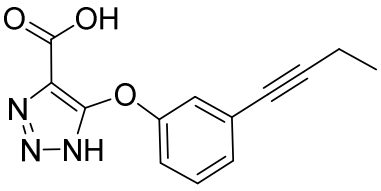
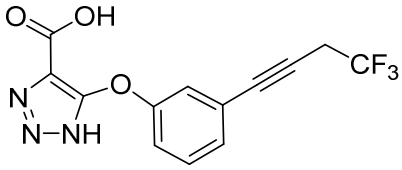
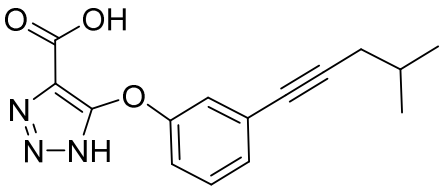
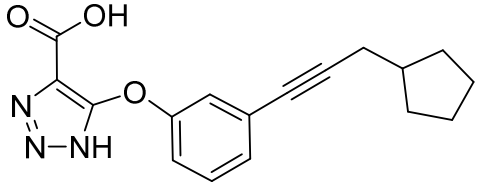
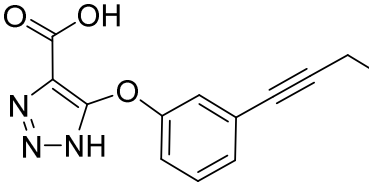
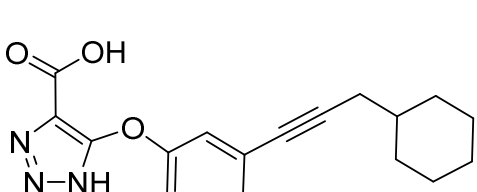
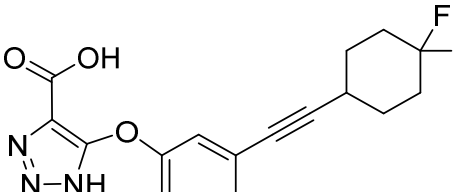
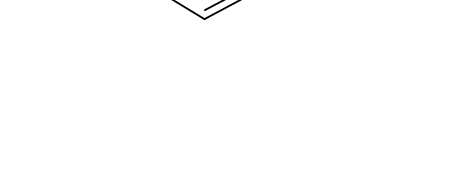
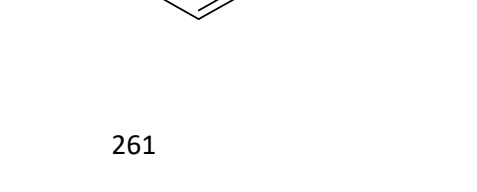
32. The compound of claim 31, wherein R^1 is hydrogen.

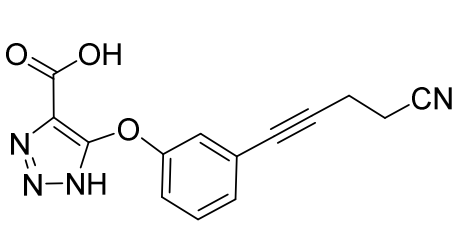
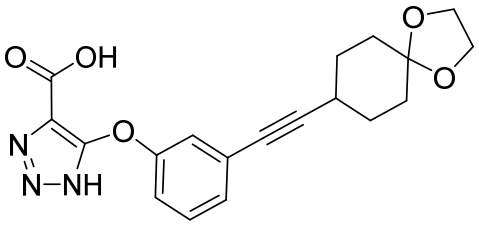
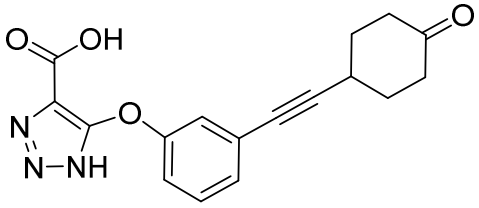
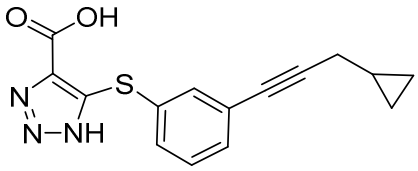
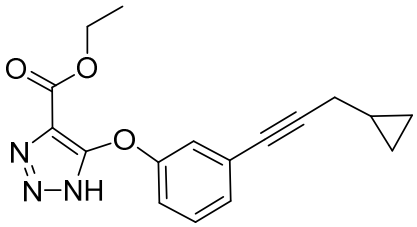
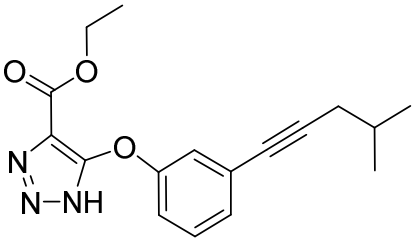
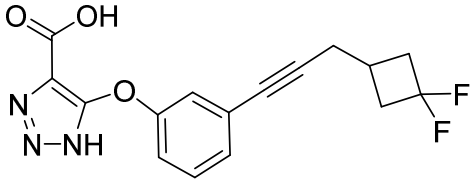
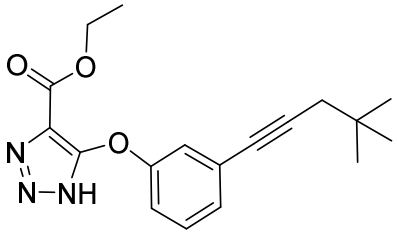
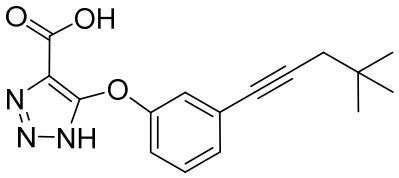
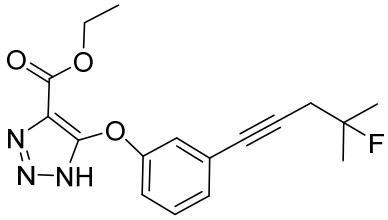
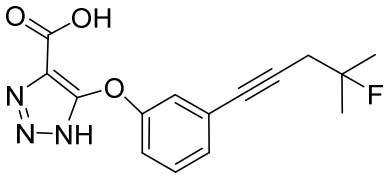
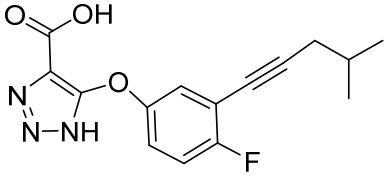
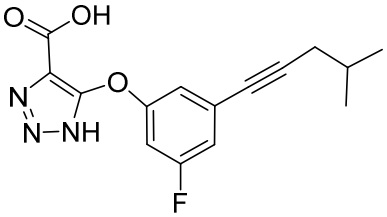
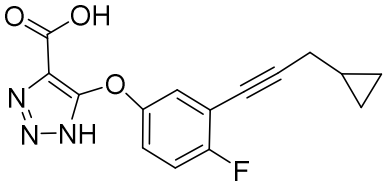
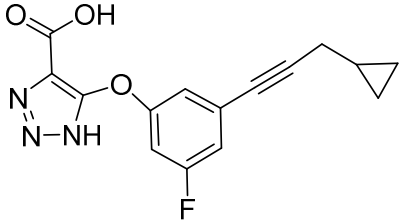
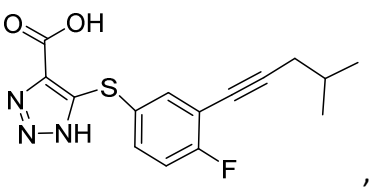
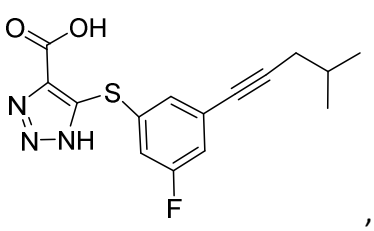
33. The compound of claim 30, wherein L is O or S.

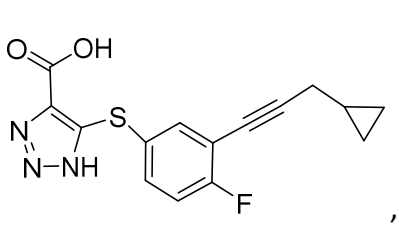
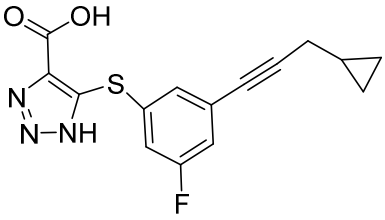
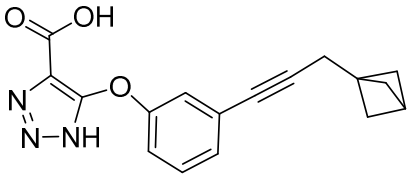
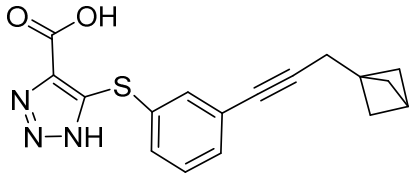
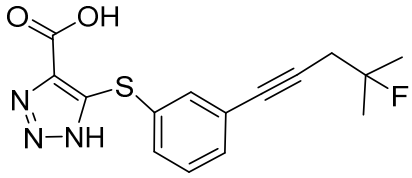
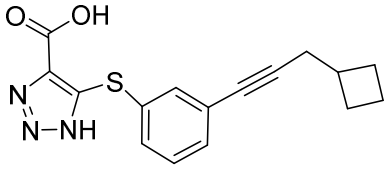
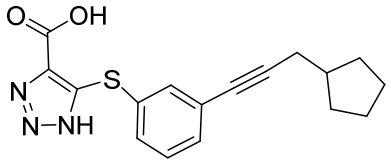
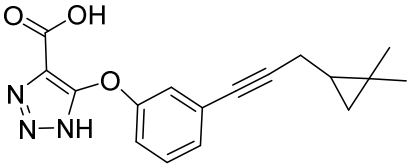
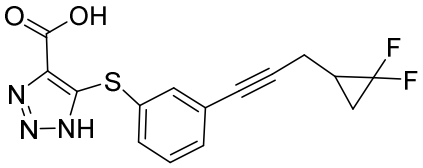
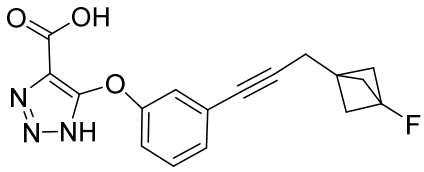
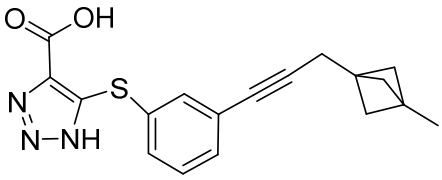
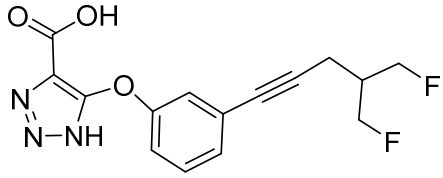
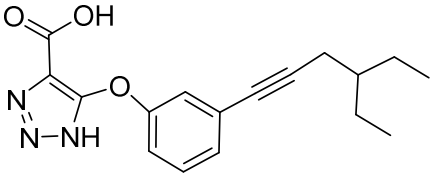
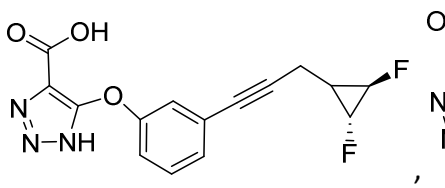
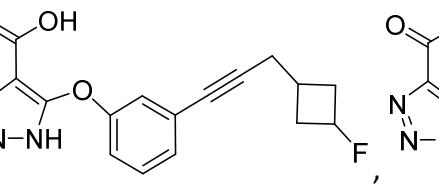
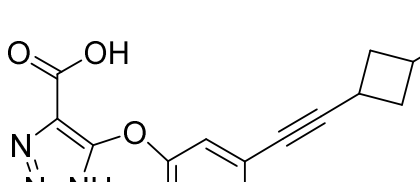
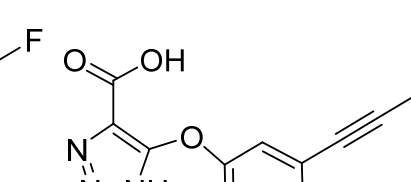
34. The compound of claim 30, wherein R^3 is chosen from isobutyl and cyclopropylmethyl.

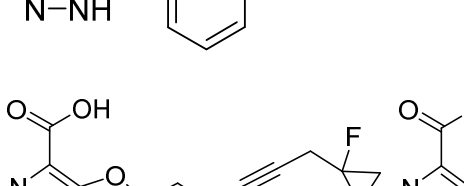
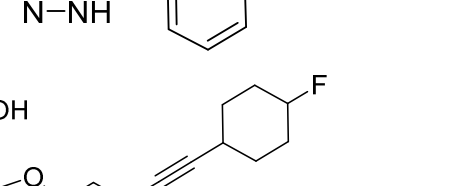
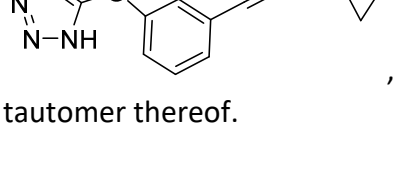
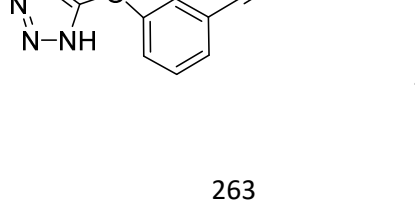
35. A compound chosen from Examples 3–414 or a salt, polymorph, or tautomer thereof.

36. A compound chosen from , , , , , , , ,


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, or a salt, polymorph, or tautomer thereof.

37. A compound of any of claims 1–36, or a salt, polymorph, or tautomer thereof, for use as a medicament.

38. A compound of any of claims 1–36, or a salt, polymorph, or tautomer thereof, for use in manufacturing a medicament for preventing or treating an oxalate-related disease.

39. A pharmaceutical composition comprising a compound of any of claims 1–36, or a salt, polymorph, or tautomer thereof together with a pharmaceutically acceptable carrier.

40. The pharmaceutical composition of any of claims 1–36, formulated for oral administration.

41. The pharmaceutical composition of any of claims 1–36, additionally comprising another therapeutic agent.

42. A method of inhibiting glycolate oxidase (GOX) activity in a biological sample comprising contacting the biological sample with a pharmaceutical composition as recited in any of claims 39–41, or a compound of any of claims 1–36, or a salt, polymorph, or tautomer thereof.

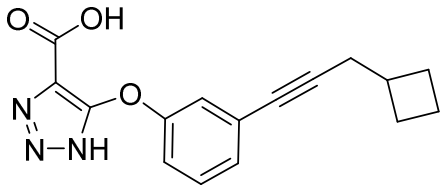
43. A pharmaceutical composition as recited in any of claims 39–41, or a compound of any of claims 1–36 or a salt, polymorph, or tautomer thereof, for use in human therapy.

44. A pharmaceutical composition as recited in any of claims 39–41, or a compound of any of claims 1–36 or a salt, polymorph, or tautomer thereof, for use in treating an oxalate-related disease.

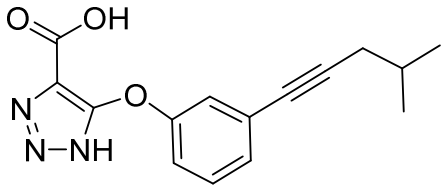
45. Use of a compound of any of claims 1–36 or a salt, polymorph, or tautomer thereof, for manufacturing a medicament to treat an oxalate-related disease.

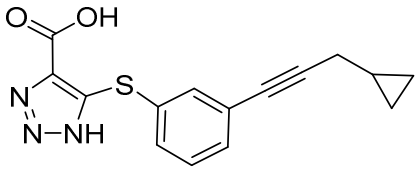
46. The use of claim 45, wherein the oxalate-related disease is hyperoxaluria, primary hyperoxaluria, enteric hyperoxaluria, calcium oxalate kidney stones, idiopathic calcium oxalate stone former (ICSF), calcium kidney stones after bariatric surgery, urolithiasis, or nephrolithiasis for a gastrointestinal disease.

47. The use of claim 46, wherein the gastrointestinal disease is Crohn's disease or ulcerative colitis.

48. A compound of structural formula 

, or a salt, polymorph, or tautomer thereof.

49. A compound of structural formula , or a salt, polymorph, or tautomer thereof.

50. A compound of structural formula , or a salt, polymorph, or tautomer thereof.

51. A pharmaceutical composition comprising a compound of any of claims 48-50, or a salt, polymorph, or tautomer thereof together with a pharmaceutically acceptable carrier.

52. Use of a pharmaceutical composition as recited in claim 51 or a compound of any of claims 48-50, or a salt, polymorph, or tautomer thereof, for manufacturing a medicament to treat an oxalate-related disease.

53. The use of claim 52, wherein the oxalate-related disease is hyperoxaluria, primary hyperoxaluria, enteric hyperoxaluria, calcium oxalate kidney stones, idiopathic calcium oxalate stone former (ICSF), calcium kidney stones after bariatric surgery, urolithiasis, or nephrolithiasis for a gastrointestinal disease.

54. The use of claim 53, wherein the gastrointestinal disease is Crohn’s disease or ulcerative colitis.