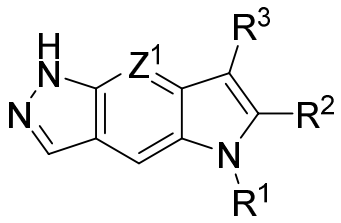
CLAIMS

1. A compound of Formula I:



(I),

a tautomer thereof, a deuterated derivative of that compound or tautomer, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

$\mathbf{Z^1}$ is chosen from C$\mathbf{R^Z}$ and N;

$\mathbf{R^Z}$ is chosen from hydrogen and halogen;

$\mathbf{R^1}$ is chosen from 5- to 6-membered aromatic rings and 5- to 6-membered heteroaromatic rings, each of which is substituted with 0-2 $\mathbf{R^A}$ groups;

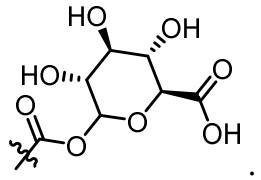
each $\mathbf{R^A}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, and C_1-C_6 haloalkoxy;

$\mathbf{R^2}$ is chosen from C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 $\mathbf{R^B}$ groups;

each $\mathbf{R^B}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkyl, and cyano groups;

$\mathbf{R^3}$ is chosen from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-3 $\mathbf{R^C}$ groups;

each $\mathbf{R^C}$ is independently chosen from $\mathbf{R^Y}$, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkyl, and carboxylic acid groups, wherein the C_1-C_6 alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two $\mathbf{R^C}$ groups taken together form a 3- to 6-membered cycloalkyl group; and

$\mathbf{R^Y}$ is 

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2. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein each $\mathbf{R^A}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkyl, and C_1-C_6 alkoxy.

3. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or claim 2, wherein $\mathbf{R^2}$ is chosen from C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 5- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 $\mathbf{R^B}$ groups.

4. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 3, wherein each $\mathbf{R^B}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkoxy, and cyano groups.

5. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 4, wherein each $\mathbf{R^C}$ is independently chosen from hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkyl, and carboxylic acid groups, wherein the C_1-C_6 alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two $\mathbf{R^C}$ groups taken together form a 3- to 6-membered cycloalkyl group.

6. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein:

$\mathbf{Z^1}$ is chosen from C$\mathbf{R^Z}$ and N;

$\mathbf{R^Z}$ is chosen from hydrogen and halogen;

$\mathbf{R^1}$ is chosen from 5- to 6-membered aromatic rings and 5- to 6-membered heteroaromatic rings, each of which is substituted with 0-2 $\mathbf{R^A}$ groups;

each $\mathbf{R^A}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

$\mathbf{R^2}$ is chosen from C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 5- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 $\mathbf{R^B}$ groups;

each $\mathbf{R^B}$ is independently chosen from halogen, hydroxy, C_1-C_6 alkoxy, and cyano groups;

$\mathbf{R^3}$ is chosen from C_1-C_6 alkyl, C_3-C_7 cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-3 $\mathbf{R^C}$ groups; and

each $\mathbf{R^C}$ is independently chosen from hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkyl, and carboxylic acid groups, wherein the C_1-C_6 alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two $\mathbf{R^C}$ groups taken together form a 3- to 6-membered cycloalkyl group.

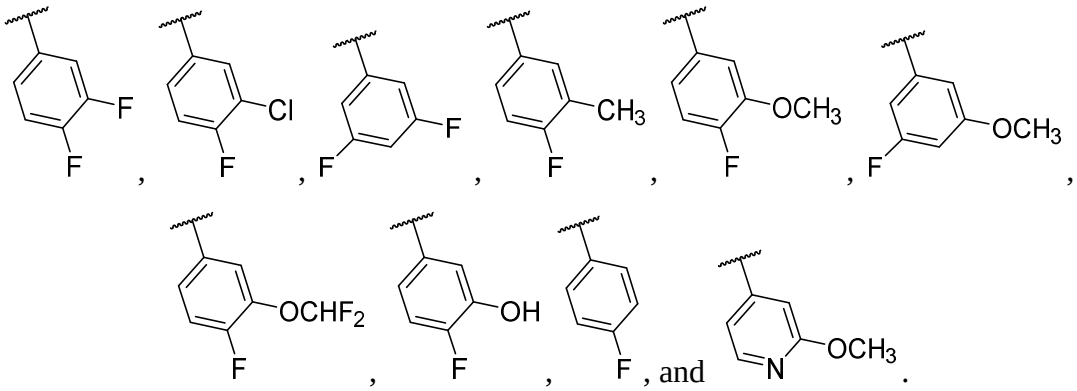
7. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein $\mathbf{R^1}$ is a C_6 aryl optionally substituted with halogen and/or C_1-C_6 alkoxy.

8. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein $\mathbf{R^1}$ is a C_6 heteroaryl optionally substituted with halogen and C_1-C_6 alkoxy.

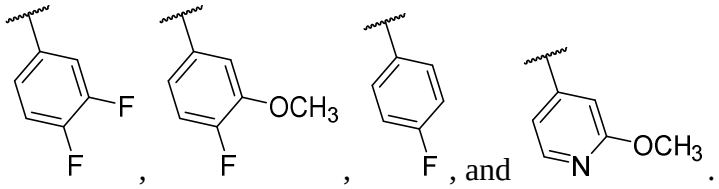
9. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6 or 8, wherein $\mathbf{R^1}$ is a C_6 heteroaryl substituted with 0-2 fluorine atoms.

10. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6 or 8, wherein $\mathbf{R^1}$ is a C_6 heteroaryl substituted with OMe and/or fluorine.

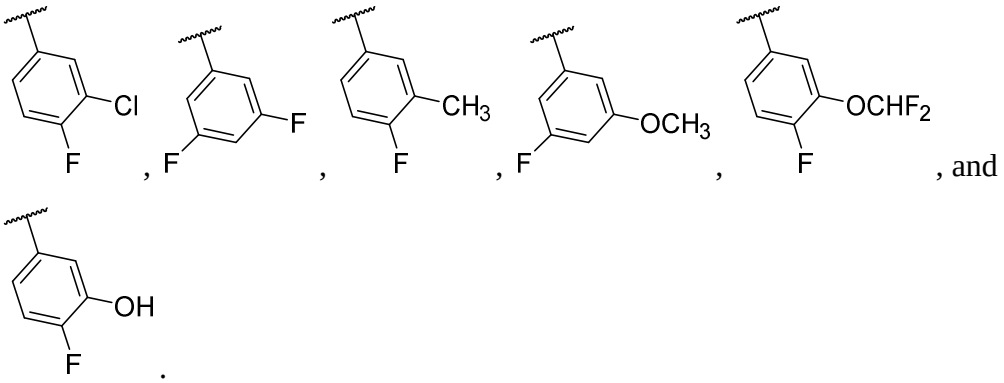
11. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or any one of claims 3 to 5, wherein $\mathbf{R^1}$ is chosen from:



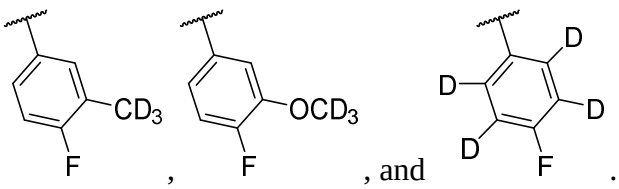
12. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein **R^1** is chosen from:



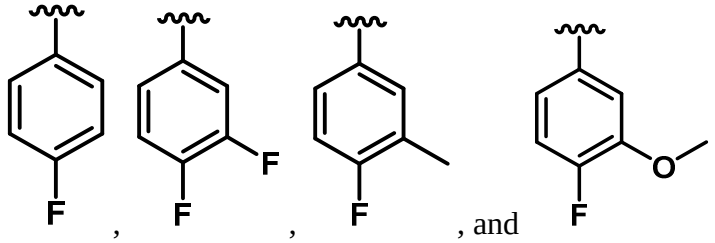
13. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or any one of claims 3 to 5, wherein **R^1** is chosen from:



14. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or any one of claims 3 to 5, wherein **R^1** is chosen from:



15. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein $\mathbf{R^1}$ is chosen from:



, , , and .

16. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 15, wherein $\mathbf{R^2}$ is a C_2-C_6 branched alkyl optionally substituted with cyano or C_1-C_6 alkoxy.

17. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 16, wherein $\mathbf{R^2}$ is a C_2-C_6 branched alkyl substituted with OMe.

18. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 15, wherein $\mathbf{R^2}$ is a C_6 heterocyclyl.

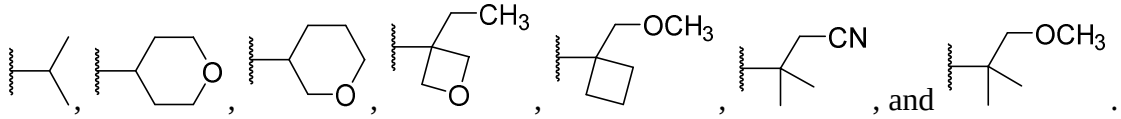
19. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 18, wherein the heteroatom in the C_6 heterocyclyl is oxygen.

20. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein $\mathbf{R^2}$ is a C_4 heterocyclyl optionally substituted with C_1-C_6 alkoxy or C_1-C_6 alkyl.

21. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 20, wherein the heteroatom in the C_4 heterocyclyl is oxygen.

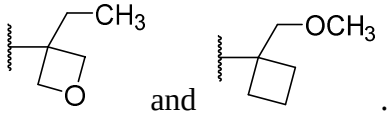
22. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein $\mathbf{R^2}$ is a C_4 cycloalkyl optionally substituted with C_1-C_6 alkoxy or C_1-C_6 alkyl.

23. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein $\mathbf{R^2}$ is chosen from:



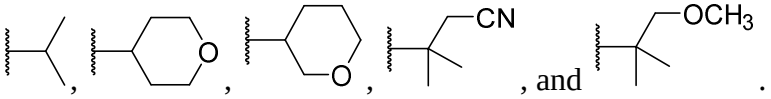
, and .

24. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein $\mathbf{R^2}$ is chosen from:



and .

25. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 15, wherein $\mathbf{R^2}$ is chosen from:



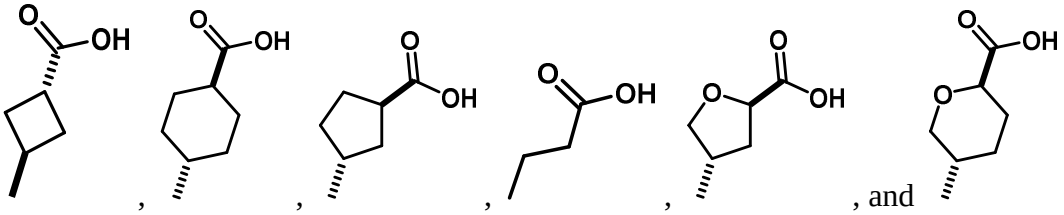
, and .

26. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein $\mathbf{R^3}$ is a linear or branched C_2-C_6 alkyl, and each $\mathbf{R^C}$ is independently chosen from hydroxy, methoxy and carboxylic acid.

27. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein $\mathbf{R^3}$ is a C_3-C_7 cycloalkyl, and $\mathbf{R^C}$ is chosen from C_1-C_6 alkyl, hydroxy, methoxy, and carboxylic acid.

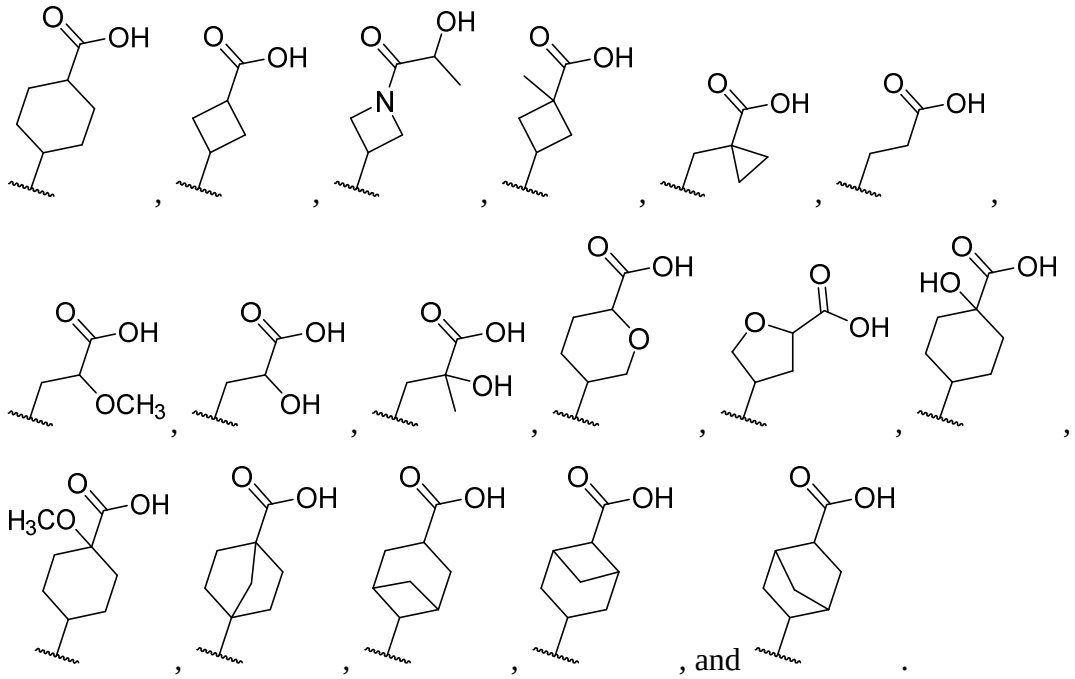
28. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein $\mathbf{R^3}$ is a 4- to 6-membered heterocyclyl, and $\mathbf{R^C}$ is chosen from hydroxy, methoxy, carboxylic acid, and C_1-C_6 alkyl optionally substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid.

29. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein $\mathbf{R^3}$ is chosen from:

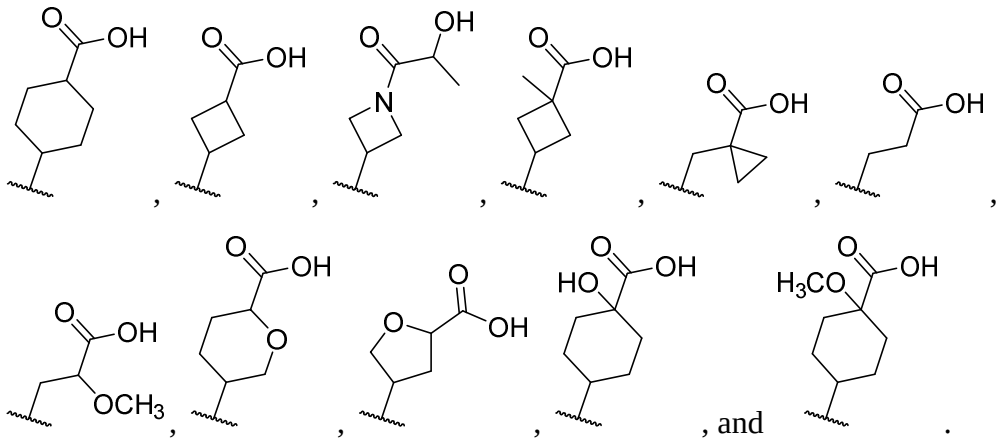

, and ,

and wherein $\mathbf{R^3}$ is with 0-2 $\mathbf{R^C}$ groups selected from methyl, OMe, fluorine, and hydroxy.

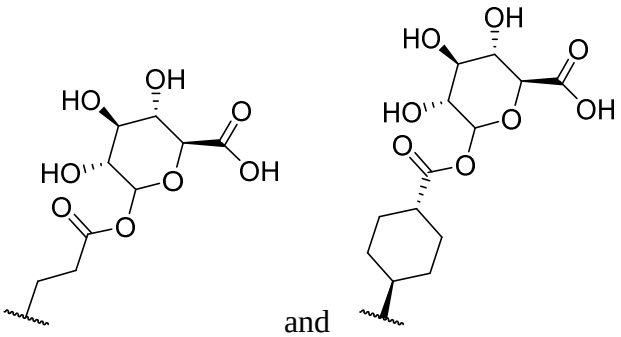
30. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein $\mathbf{R^3}$ is chosen from:


, and .

31. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to according to any one of claims 1 to 25, wherein **R^3** is chosen from:

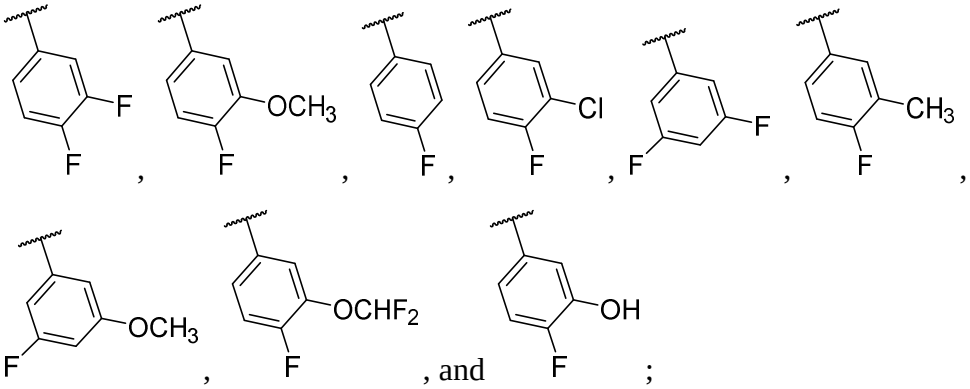


32. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to according to any one of claims 1 to 4 or 7 to 25, wherein **R^3** is chosen from:

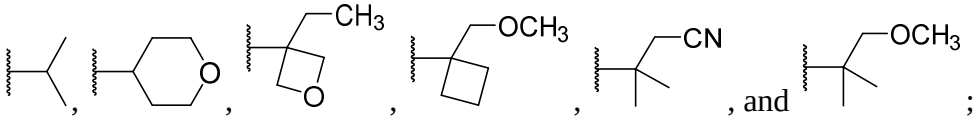


33. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein

R^1 is selected from:

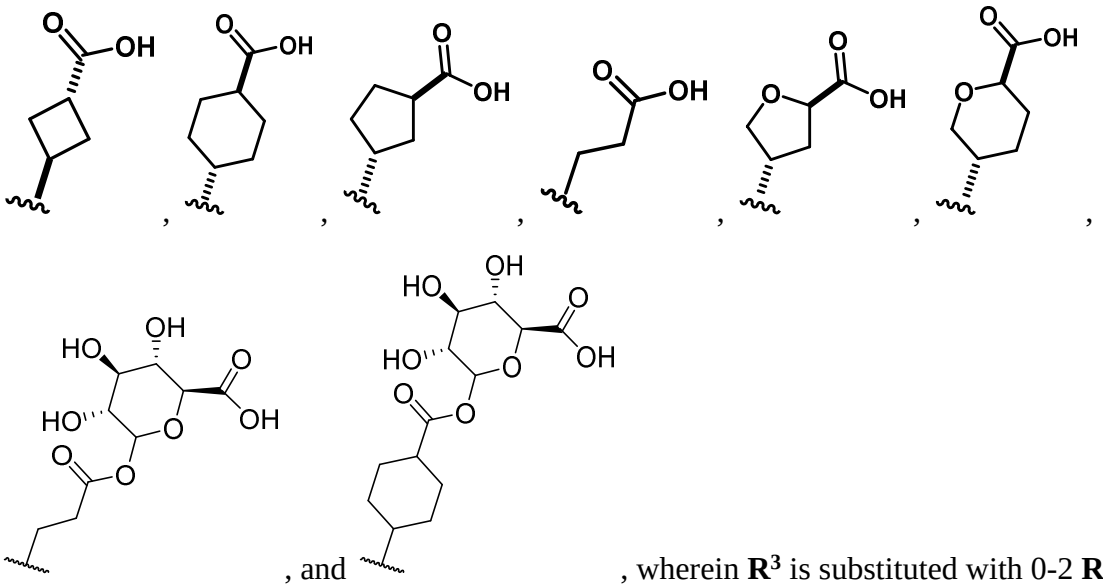


R^2 is selected from:



, and ;

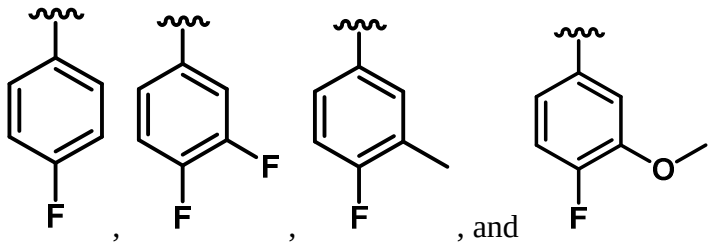
and $\mathbf{R^3}$ is selected from:



, and , wherein $\mathbf{R^3}$ is substituted with 0-2 $\mathbf{R^C}$ groups selected from methyl, OMe, fluorine, and hydroxy.

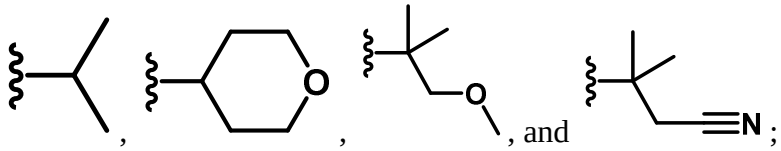
34. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein

$\mathbf{R^1}$ is selected from:



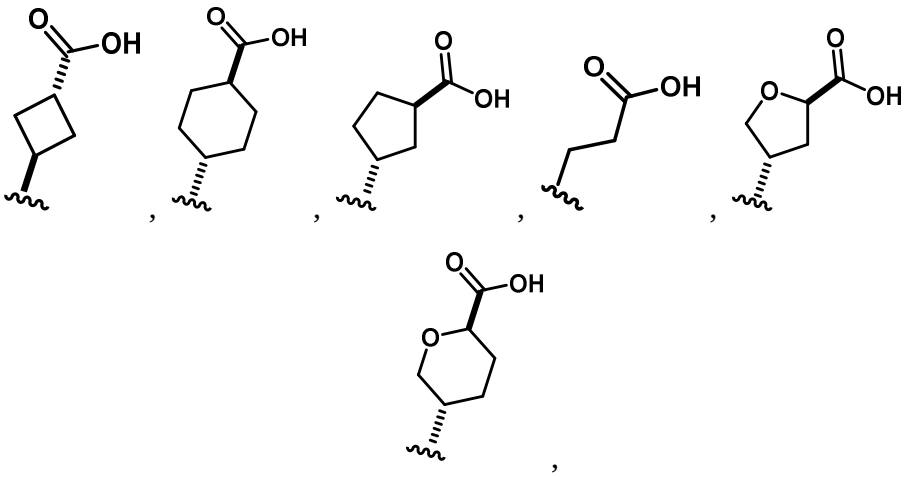
, and ;

$\mathbf{R^2}$ is selected from:



, and ;

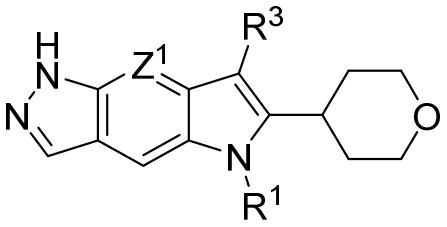
and **R^3** is selected from:



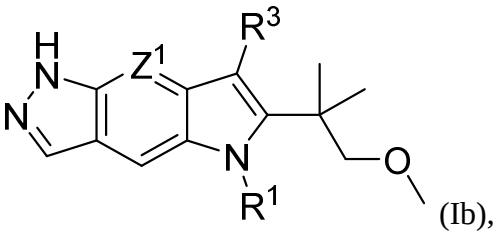
, and

wherein **R^3** is substituted with 0-2 **R^C** groups selected from methyl, OMe, fluorine, and hydroxy.

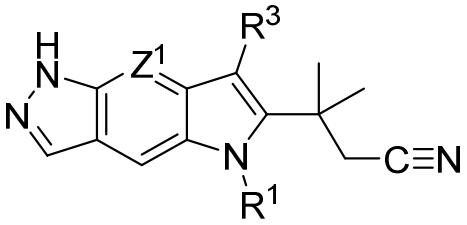
35. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein the compound is selected from compounds of Formulae Ia, Ib, Ic, Id, Ie, or If:



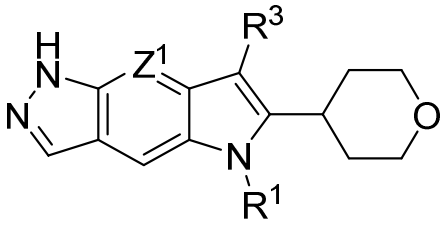
(Ia),



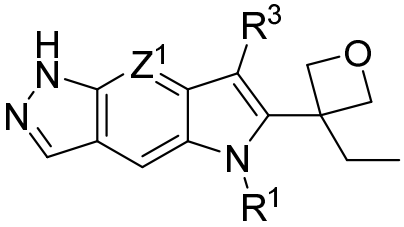
(Ib),



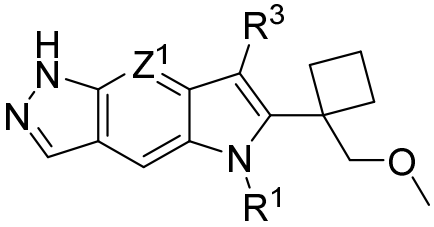
(Ic),



(Id),



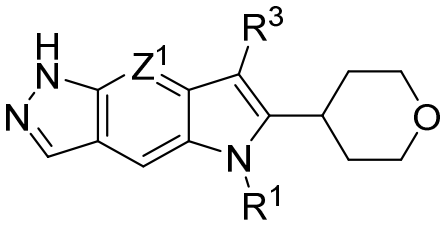
(Ie),

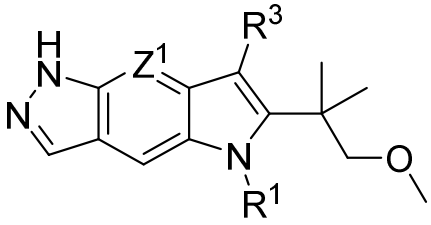


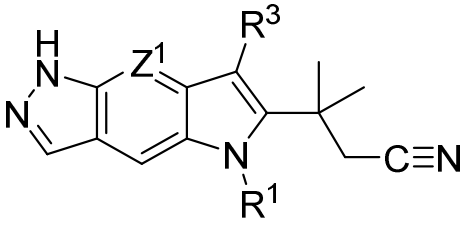
(If),

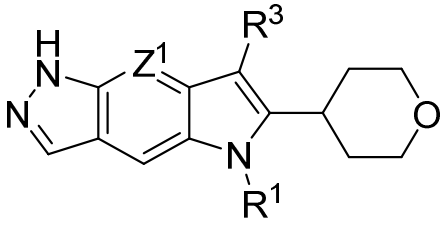
and tautomers thereof, deuterated derivatives of those compounds and tautomers, and pharmaceutically acceptable salts of any of the foregoing.

36. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein the compound is selected from compounds of Formulae Ia, Ib, Ic, or Id:


(Ia),


(Ib),


(Ic),


(Id),

and tautomers thereof, deuterated derivatives of those compounds and tautomers, and pharmaceutically acceptable salts of any of the foregoing.

37. A compound chosen from Compounds 1-46, Compounds 47-73, Compounds 74-96, Compounds Ia-1-348, Compounds Ib-1-348, Compounds Ic-1-348, and Compounds Id-1-348, and deuterated derivatives thereof, and pharmaceutically acceptable salts of any of the foregoing.

38. A compound chosen from Compounds 1-46, Compounds 47-73, Compounds Ia-1-348, Compounds Ib-1-348, Compounds Ic-1-348, and Compounds Id-1-348, and deuterated derivatives thereof, and pharmaceutically acceptable salts of any of the foregoing.

39. A pharmaceutical composition comprising the compound, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1-38 and a pharmaceutically acceptable carrier.

40. Use of a compound, tautomer, deuterated derivative of the compound or tautomer, or pharmaceutically acceptable salt of any of the foregoing according to any one of claims 1-38, or a pharmaceutical composition according to claim 39, in the manufacture of a medicament for treating alpha-1 antitrypsin deficiency in a patient.

41. The use according to claim 40, wherein the patient has a Z mutation in alpha-1 antitrypsin.

42. The use according to claim 40, wherein the patient has an SZ mutation in alpha-1 antitrypsin.

43. The use according to claim 40, wherein the patient is homozygous for Z-mutations in alpha-1 antitrypsin.

44. Use of a compound, tautomer, deuterated derivative of the compound or tautomer, or pharmaceutically acceptable salt of any of the foregoing according to any one of claims 1-38, or a pharmaceutical composition according to claim 39, in the manufacture of a medicament for modulating alpha-1 antitrypsin activity.

45. A compound, tautomer, deuterated derivative of the compound or tautomer, or pharmaceutically acceptable salt of any of the foregoing according to any one of claims 1-38, or a pharmaceutical composition according to claim 39, for use in treating alpha-1 antitrypsin deficiency in a patient.