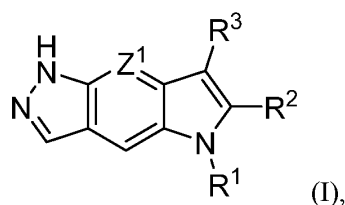


CLAIMS

1. A compound of Formula I:



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

Z¹ is chosen from **CR^Z** and N;

R^Z is chosen from hydrogen and halogen;

R¹ is chosen from 5- to 6-membered aromatic rings and 5- to 6-membered heteroaromatic rings, each of which is substituted with 0-2 **R^A** groups;

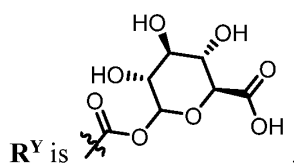
each **R^A** is independently chosen from halogen, hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, and C₁-C₆ haloalkoxy;

R² is chosen from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 **R^B** groups;

each **R^B** is independently chosen from halogen, hydroxy, C₁-C₆ alkoxy, C₁-C₆ alkyl, and cyano groups;

R³ is chosen from C₁-C₆ alkyl, C₃-C₇ cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-3 **R^C** groups;

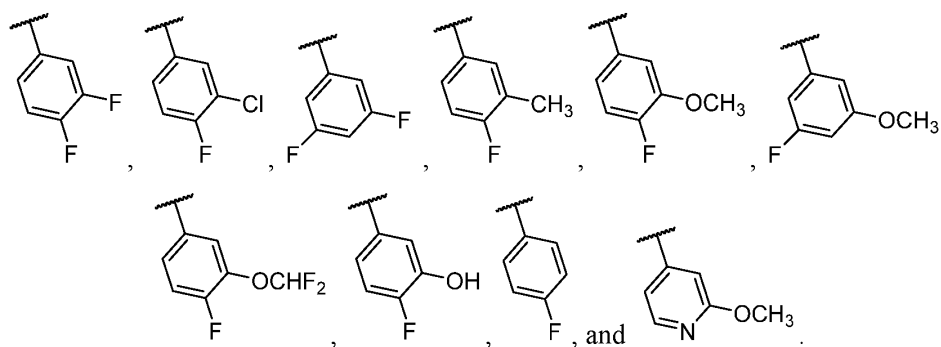
each **R^C** is independently chosen from **R^Y**, hydroxy, C₁-C₆ alkoxy, C₁-C₆ alkyl, and carboxylic acid groups, wherein the C₁-C₆ alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two **R^C** groups taken together form a 3- to 6-membered cycloalkyl group; and



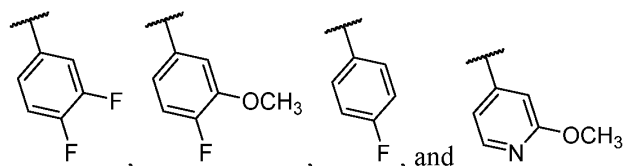
2. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein each **R^A** is independently chosen from halogen, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy.
3. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or claim 2, wherein **R²** is chosen from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, and 5- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 **R^B** groups.
4. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 3, wherein each **R^B** is independently chosen from halogen, hydroxy, C₁-C₆ 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 **R^C** is independently chosen from hydroxy, C₁-C₆ alkoxy, C₁-C₆ alkyl, and carboxylic acid groups, wherein the C₁-C₆ alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two **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:
Z¹ is chosen from **CR^Z** and N;
R^Z is chosen from hydrogen and halogen;
R¹ is chosen from 5- to 6-membered aromatic rings and 5- to 6-membered heteroaromatic rings, each of which is substituted with 0-2 **R^A** groups;
each **R^A** is independently chosen from halogen, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy;
R² is chosen from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, and 5- to 6-membered heterocyclyl groups, each of which is substituted with 0-1 **R^B** groups;
each **R^B** is independently chosen from halogen, hydroxy, C₁-C₆ alkoxy, and cyano groups;

R³ is chosen from C₁-C₆ alkyl, C₃-C₇ cycloalkyl, and 4- to 6-membered heterocyclyl groups, each of which is substituted with 0-3 **R^C** groups; and each **R^C** is independently chosen from hydroxy, C₁-C₆ alkoxy, C₁-C₆ alkyl, and carboxylic acid groups, wherein the C₁-C₆ alkyl groups are substituted with 0-2 groups independently chosen from oxo, hydroxy, and carboxylic acid, or two **R^C** groups taken together form a 3- to 6-membered cycloalkyl group.

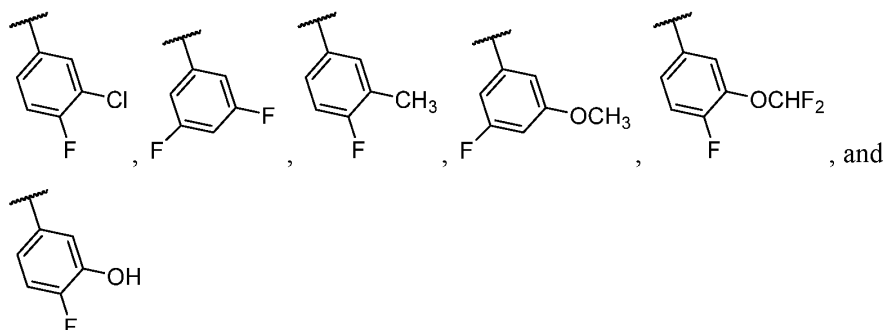
7. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein **R¹** is a C₆ aryl optionally substituted with halogen and/or C₁-C₆ alkoxy.
8. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein **R¹** is a C₆ heteroaryl optionally substituted with halogen and C₁-C₆ alkoxy.
9. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6 or 8, wherein **R¹** is a C₆ 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 **R¹** is a C₆ 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 **R¹** is chosen from:



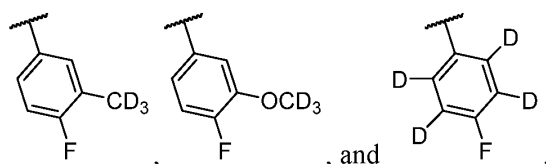
12. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein R^1 is chosen from:



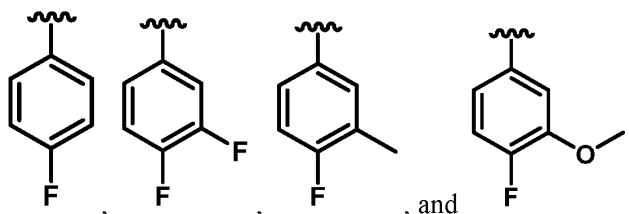
13. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1 or any one of claims 3 to 5, wherein R^1 is chosen from:



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:



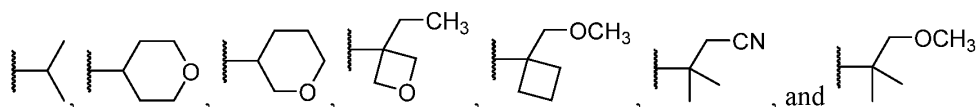
15. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein **R**¹ is chosen from:



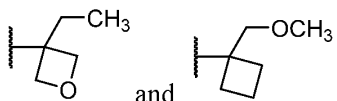
16. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 15, wherein **R**² is a C₂-C₆ branched alkyl optionally substituted with cyano or C₁-C₆ alkoxy.
17. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 16, wherein **R**² is a C₂-C₆ 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 **R**² is a C₆ heterocyclyl.
19. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 18, wherein the heteroatom in the C₆ heterocyclyl is oxygen.
20. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein **R**² is a C₄ heterocyclyl optionally substituted with C₁-C₆ alkoxy or C₁-C₆ alkyl.
21. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 20, wherein the heteroatom in the C₄ heterocyclyl is oxygen.

22. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein **R**² is a C₄ cycloalkyl optionally substituted with C₁-C₆ alkoxy or C₁-C₆ alkyl.

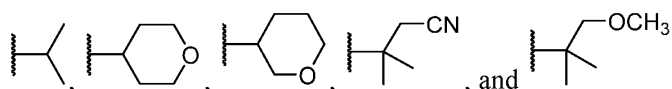
23. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein **R**² is chosen from:



24. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, 2, or 5, wherein **R**² is chosen from:



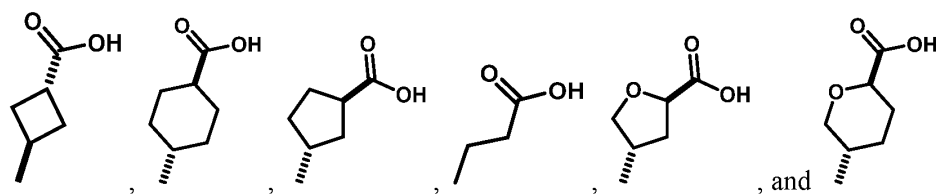
25. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 15, wherein **R**² is chosen from:



26. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein **R**³ is a linear or branched C₂-C₆ alkyl, and each **R**^C is independently chosen from hydroxy, methoxy and carboxylic acid.

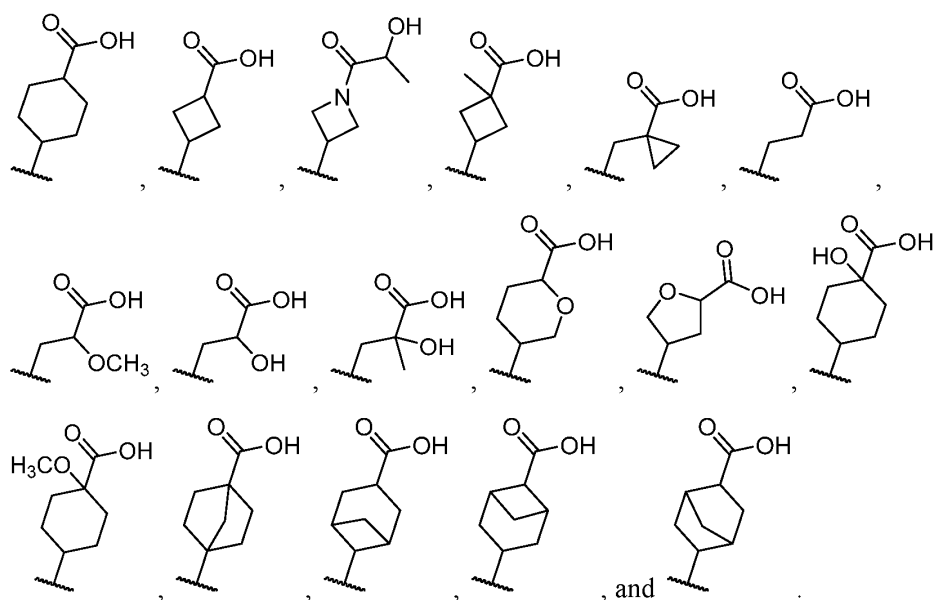
27. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein **R**³ is a C₃-C₇ cycloalkyl, and **R**^C is chosen from C₁-C₆ alkyl, hydroxy, methoxy, and carboxylic acid.

28. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein **R³** is a 4- to 6-membered heterocycl, and **R^C** is chosen from hydroxy, methoxy, carboxylic acid, and C₁-C₆ 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 **R³** is chosen from:

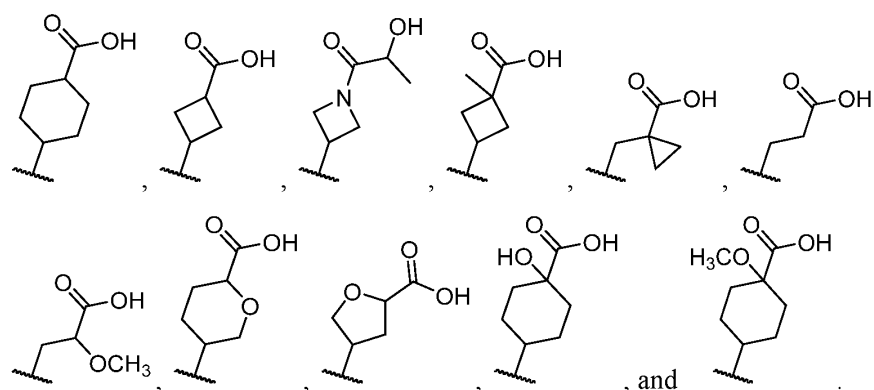


and wherein **R**³ is with 0-2 **R**^C groups selected from methyl, OMe, fluorine, and hydroxy.

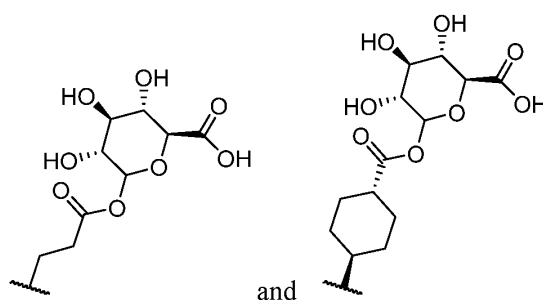
30. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 25, wherein **R**³ is chosen from:



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

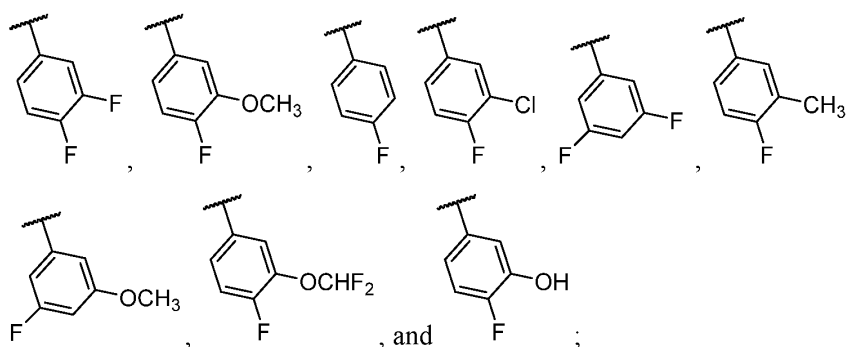


32. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to any one of claims 1 to 4 or 7 to 25, wherein **R**³ is chosen from:

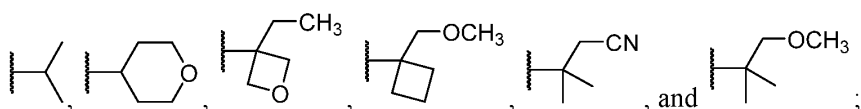


33. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein

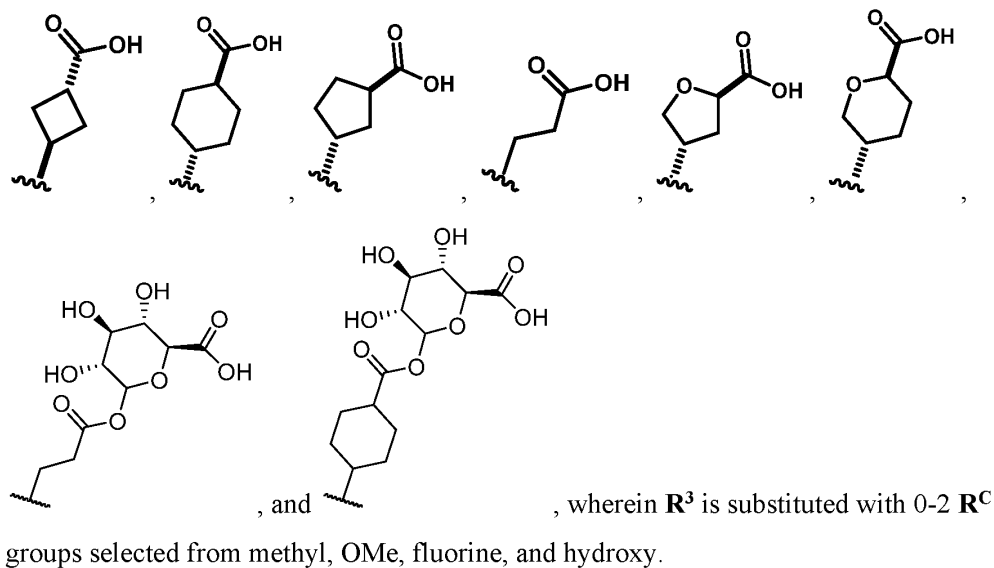
R¹ is selected from:



R² is selected from:

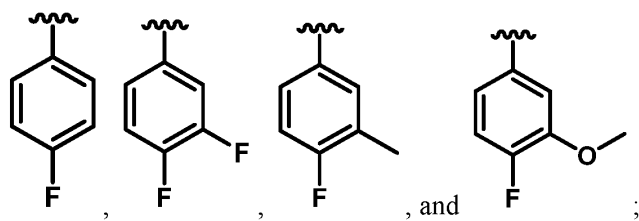


and $\mathbf{R}^3$ is selected from:

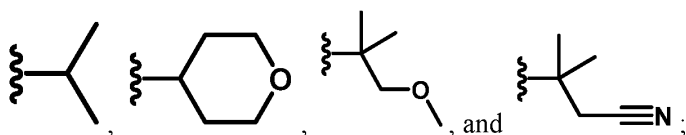


34. The compound, tautomer, deuterated derivative, or pharmaceutically acceptable salt according to claim 1, wherein

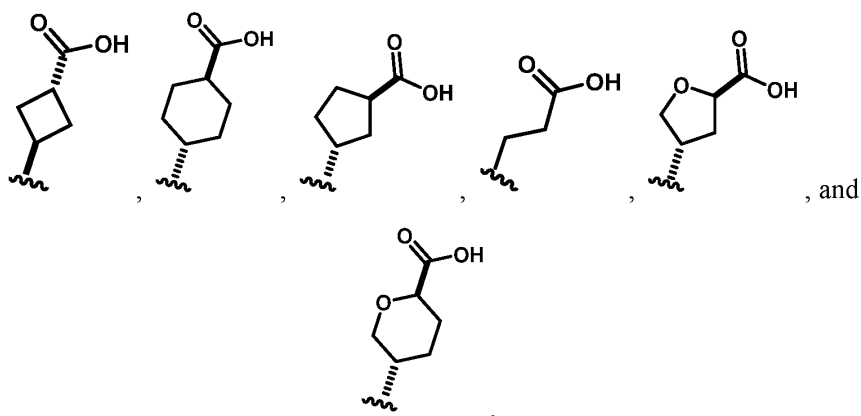
$\mathbf{R}^1$ is selected from:



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

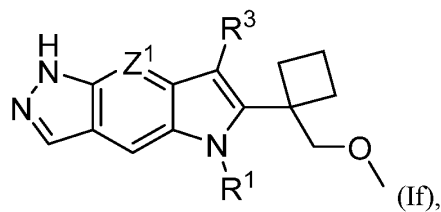
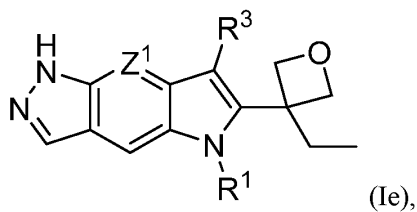
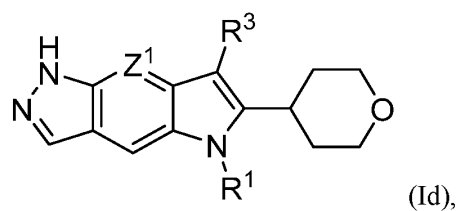
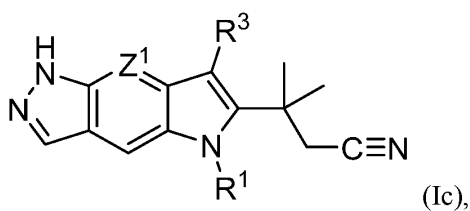
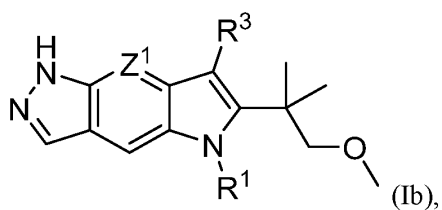
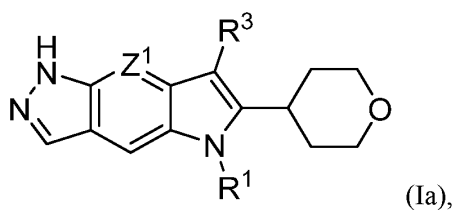


and R^3 is selected from:



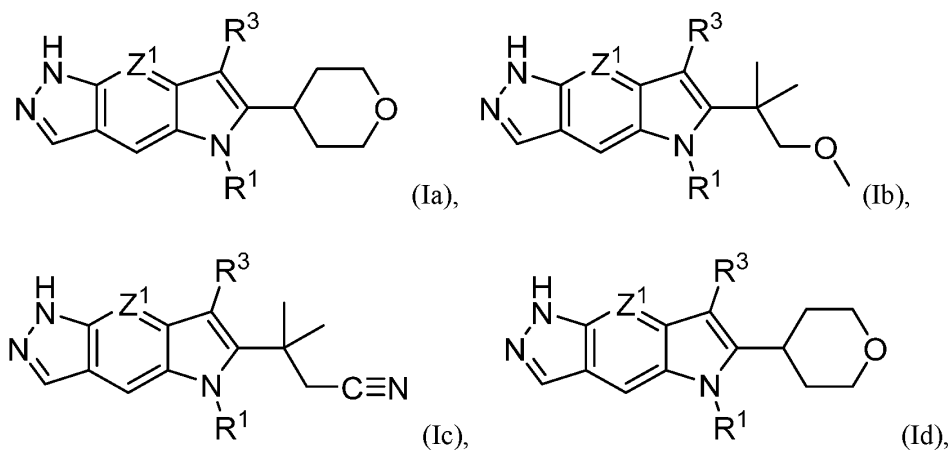
wherein R^3 is substituted with 0-2 R^C groups selected from methyl, OMe, fluorine, and hydroxy.

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:



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:



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. A method of treating alpha-1 antitrypsin deficiency comprising administering to a patient in need thereof a compound, derivative, or salt according to any one of claims 1-38, or a pharmaceutical composition according to claim 39.
41. The method according to claim 40, wherein the patient has a Z mutation in alpha-1 antitrypsin.
42. The method according to claim 40, wherein the patient has an SZ mutation in alpha-1 antitrypsin.
43. The method according to claim 40, wherein the patient is homozygous for Z-mutations in alpha-1 antitrypsin.
44. A method of modulating alpha-1 antitrypsin activity comprising contacting said alpha-1-antitrypsin with a compound, derivative, or salt according to any one of claims 1-38, or a pharmaceutical composition according to claim 39.