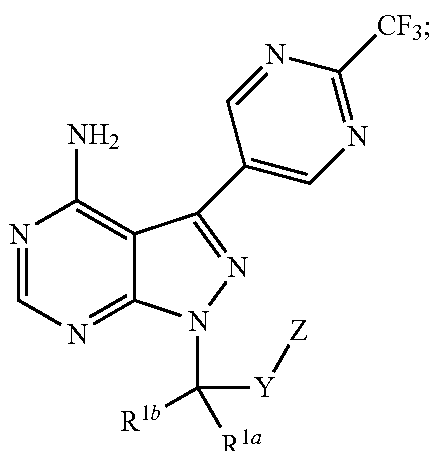


The invention claimed is:

1. A compound of Formula I



or a pharmaceutically acceptable salt thereof; wherein

Y is a five membered heteroaryl comprising one to four heteroatoms each of which is independently selected from the group consisting of N, O and S(O)<sub>n</sub>; wherein the heteroaryl is optionally substituted with one to three substituents each of which is independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> haloalkyl;

Z is phenyl, optionally substituted with one to three halo;

R<sup>1a</sup> and R<sup>1b</sup> are each independently selected from the group consisting of -H, -OH, halo,

C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three substituents each of which is independently selected from the group consisting of halo, -OH, C<sub>1</sub>-C<sub>3</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl and a four to seven membered heterocycloalkyl comprising one to three heteroatoms each of which is independently selected from the group consisting of N, O and S(O)<sub>n</sub>,

C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted with one to three substituents each of which is independently selected from the group consisting of -OH, halo and C<sub>1</sub>-C<sub>6</sub> alkyl, and

four to seven membered heterocycloalkyl comprising one to three heteroatoms each of which is independently selected from the group consisting of N, O and S(O)<sub>n</sub>; and wherein the four to seven membered heterocycloalkyl is optionally substituted with one to three substituents each of which is independently selected from the group consisting of -OH, halo and C<sub>1</sub>-C<sub>6</sub> alkyl;

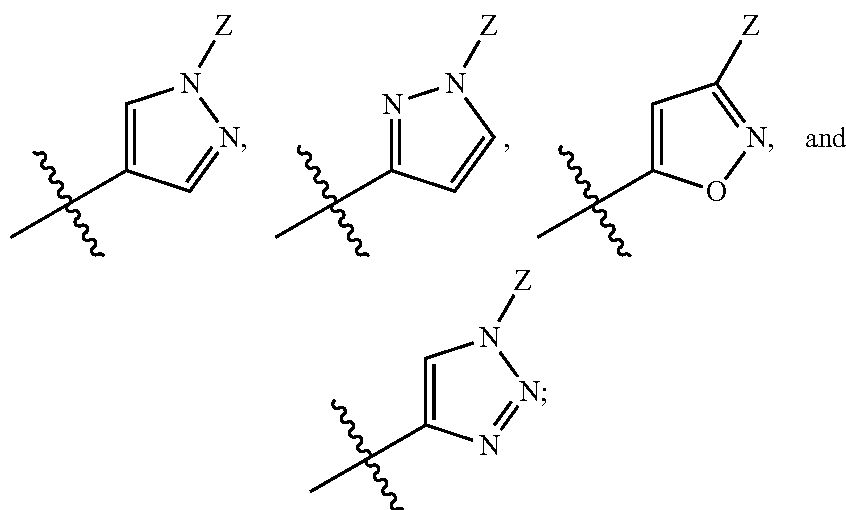
or R<sup>1a</sup> and R<sup>1b</sup> taken together with the carbon to which they are attached form a C<sub>3</sub>-C<sub>7</sub> cycloalkyl or a four to seven membered heterocycloalkyl comprising one to three heteroatoms each of which is independently selected from the group consisting of N, O and S(O)<sub>n</sub>; and wherein the C<sub>3</sub>-C<sub>7</sub> cycloalkyl or four to seven membered

heterocycloalkyl are optionally substituted with one to three substituents each of which is independently selected from the group consisting of -OH, halo and C<sub>1</sub>-C<sub>6</sub> alkyl; and

n at each occurrence is independently 0, 1 or 2.

2. The compound of claim 1 wherein one of R<sup>1a</sup> and R<sup>1b</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl and the other is -H; or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2 wherein the moiety Y-Z is selected from the group consisting of



or a pharmaceutically acceptable salt thereof.

4. The compound of claim 3 wherein Z is phenyl optionally substituted with one or two fluoro or chloro; or a pharmaceutically acceptable salt thereof.

5. The compound of claim 1, wherein the compound is selected from the group consisting of

1-{(1S)-1-[1-(2-fluorophenyl)-1H-pyrazol-4-yl]propyl}-3-[2-(trifluoromethyl)pyrimidin-5-yl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine;

1-{(1R)-1-[1-(2-fluorophenyl)-1H-pyrazol-4-yl]propyl}-3-[2-(trifluoromethyl)pyrimidin-5-yl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine;

1-{(1S)-1-[1-(2-fluorophenyl)-1H-1,2,3-triazol-4-yl]propyl}-3-[2-(trifluoromethyl)pyrimidin-5-yl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine; and

1-{(1R)-1-[1-(2-fluorophenyl)-1H-1,2,3-triazol-4-yl]propyl}-3-[2-(trifluoromethyl)pyrimidin-5-yl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine;

or a pharmaceutically acceptable salt thereof.

6. The compound of claim 1, wherein the compound is 1-{(1S)-1-[1-(2-

fluorophenyl)-1H-pyrazol-4-yl]propyl}-3-[2-(trifluoromethyl)pyrimidin-5-yl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine or a pharmaceutically acceptable salt thereof.

7. Use of a therapeutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt of said compound, in the preparation of a medicament for the treatment of cystic fibrosis, asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), constipation, Diabetes mellitus, dry eye disease, pancreatitis, rhinosinusitis, or Sjogren's Syndrome in a patient in need of treatment thereof, wherein the medicament is to be administered to the patient in need of treatment thereof.

8. The use of claim 7, wherein the medicament is for the treatment of cystic fibrosis.

9. A pharmaceutical composition comprising a therapeutically effective amount of one or more of a compound according to claim 1, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier.

10. The pharmaceutical composition of claim 9, further comprising one or more additional therapeutic agents.

11. The pharmaceutical composition of claim 10, wherein the one or more additional therapeutic agents are independently selected from the group consisting of a CFTR potentiator, a CFTR corrector, an epithelial sodium channel (ENaC) inhibitor, a CFTR amplifier, a CFTR stabilizer, a read-through agent, an oligonucleotide patch, an autophagy inducer, and a proteostasis modulator.

12. The pharmaceutical composition of claim 11, wherein the CFTR potentiator at each occurrence is selected from the group consisting of VX-770 (Ivacaftor), GLPG-1837, GLPG-2451, QBW-251, FDL-176, FDL-129, CTP-656, and PTI-P271.

13. The pharmaceutical composition of claim 11, wherein the CFTR corrector at each occurrence is selected from the group consisting of VX-809 (lumacaftor), VX-661 (tezacaftor), VX-983, VX-152, VX-440, VX-659, GLPG-2737, P247-A, GLPG-2222, GLPG-2665, GLPG-2851, FDL-169, and PTI-C1811.

14. The pharmaceutical composition of claim 11, wherein the epithelial sodium channel (ENaC) inhibitor at each occurrence is selected from the group consisting of SPX-101, QBW-276 and VX-371.

15. The pharmaceutical composition of claim 11, wherein the CFTR amplifier at each occurrence is selected from the group consisting of PTI-428 and PTI-130.

16. The pharmaceutical composition of claim 11, wherein the CFTR stabilizer is N-91115 (Cavosonstat).

17. The pharmaceutical composition of claim 11, wherein the read-through agent

is ataluren.

18. The pharmaceutical composition of claim 11, wherein the oligonucleotide patch is QR-010.

19. The pharmaceutical composition of claim 11, wherein the autophagy inducer at each occurrence is selected from the group consisting of CX-4945 and the combination of cysteamine and epigallocatechin gallate (EGCG).