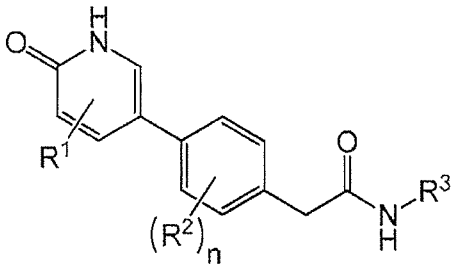
CLAIMS

1. A compound according to Formula (I):



(I)

wherein:

R^1 is hydrogen, halogen, $(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxyl, $(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, amino, $((C_1\text{-}C_6)$alkyl)amino-, or $((C_1\text{-}C_6)$alkyl$)((C_1\text{-}C_6)$alkyl)amino-;

each R^2 is independently selected from the group consisting of halogen, $(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, cyano, hydroxyl, $(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, amino, $((C_1\text{-}C_6)$alkyl)amino-, and $((C_1\text{-}C_6)$alkyl$)((C_1\text{-}C_6)$alkyl)amino-;

R^3 is phenyl or 5- or 6-membered heteroaryl, each of which is optionally substituted with one to three substituents independently selected from halogen, $(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, cyano, 5- or 6-membered heteroaryl, $-OR^4$, and $-CONR^5R^6$; wherein said $(C_1\text{-}C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1\text{-}C_4)$alkoxy, halo$(C_1\text{-}C_4)$alkoxy, or $-NR^5R^6$; and wherein said 5- or 6-membered heteroaryl substituent is optionally substituted by halogen, $(C_1\text{-}C_4)$alkyl, or halo$(C_1\text{-}C_4)$alkyl;

R^4 is hydrogen, $(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, or 4- to 6-membered heterocycloalkyl; wherein said $(C_1\text{-}C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1\text{-}C_4)$alkoxy, halo$(C_1\text{-}C_4)$alkoxy, or $-NR^5R^6$; and wherein said $(C_3\text{-}C_6)$cycloalkyl is optionally substituted with one or two substituents independently selected from $(C_1\text{-}C_4)$alkyl, halo$(C_1\text{-}C_4)$alkyl, hydroxyl, hydroxy$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, and halo$(C_1\text{-}C_4)$alkoxy; and wherein said 4- to 6-membered heterocycloalkyl is optionally substituted with one or two substituents independently selected from $(C_1\text{-}C_4)$alkyl and halo$(C_1\text{-}C_4)$alkyl;

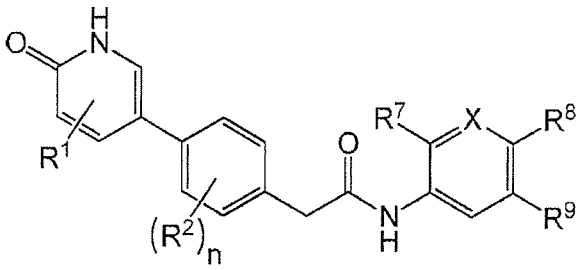
R^5 and R^6 are each independently selected from the group consisting of hydrogen, $(C_1\text{-}C_4)$alkyl, and halo$(C_1\text{-}C_4)$alkyl;

or R^5 and R^6 taken together with the nitrogen to which they are attached represent a 5- or 6-membered saturated ring, optionally containing an additional heteroatom selected from oxygen, nitrogen, and sulfur, wherein said ring is optionally substituted by halogen, $(C_1$-$C_4)$alkyl, or halo$(C_1$-$C_4)$alkyl; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

2. The compound or pharmaceutically acceptable salt according to claim 1 represented by Formula (II):



(II)

wherein:

X is N or CR^{10};

R^1 is hydrogen, halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, amino, $((C_1$-$C_6)$alkyl)amino-, or $((C_1$-$C_6)$alkyl)$((C_1$-$C_6)$alkyl)amino-;

each R^2 is independently selected from the group consisting of halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, cyano, hydroxyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, amino, $((C_1$-$C_6)$alkyl)amino-, and $((C_1$-$C_6)$alkyl)$((C_1$-$C_6)$alkyl)amino-;

R^4 is hydrogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, or 4- to 6-membered heterocycloalkyl; wherein said $(C_1$-$C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1$-$C_4)$alkoxy, halo$(C_1$-$C_4)$alkoxy, or $-NR^5R^6$; and wherein said $(C_3$-$C_6)$cycloalkyl is optionally substituted with one or two substituents independently selected from $(C_1$-$C_4)$alkyl, halo$(C_1$-$C_4)$alkyl, hydroxyl, hydroxy$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy, and halo$(C_1$-$C_4)$alkoxy; and wherein said 4- to 6-membered heterocycloalkyl is optionally substituted with one or two substituents independently selected from $(C_1$-$C_4)$alkyl and halo$(C_1$-$C_4)$alkyl;

R^5 and R^6 are each independently selected from the group consisting of hydrogen, $(C_1$-$C_4)$alkyl, and halo$(C_1$-$C_4)$alkyl;

or R^5 and R^6 taken together with the nitrogen to which they are attached represent a 5- or 6-membered saturated ring, optionally containing an additional heteroatom selected from oxygen, nitrogen, and sulfur, wherein said ring is optionally substituted by halogen, $(C_1$-$C_4)$alkyl, or halo$(C_1$-$C_4)$alkyl;

R^7 is hydrogen, halogen, or $(C_1$-$C_4)$alkoxy;

R^8 is hydrogen, halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, cyano, 5- or 6-membered heteroaryl, -OR^4, or -$CONR^5R^6$; wherein said $(C_1$-$C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1$-$C_4)$alkoxy, halo$(C_1$-$C_4)$alkoxy, or -NR^5R^6; and wherein said 5- or 6-membered heteroaryl is optionally substituted by halogen, $(C_1$-$C_4)$alkyl, or halo$(C_1$-$C_4)$alkyl;

R^9 is hydrogen, halogen, or halo$(C_1$-$C_4)$alkyl;

R^{10} is hydrogen, halogen, halo$(C_1$-$C_4)$alkyl, or 5- or 6-membered heteroaryl, wherein said 5- or 6-membered heteroaryl is optionally substituted by halogen, $(C_1$-$C_4)$alkyl, or halo$(C_1$-$C_4)$alkyl; and

n is 0, 1, or 2;

provided that when X is CR^{10} at least one of R^7, R^8, R^9, and R^{10} is hydrogen.

3. The compound or pharmaceutically acceptable salt according to claim 2, wherein R^7 is hydrogen or fluorine.

4. The compound or pharmaceutically acceptable salt according to claim 2 or claim 3, wherein R^8 is hydrogen, fluorine, chlorine, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_4)$alkyl, cyano, $(C_1$-$C_4)$alkoxy, hydroxy$(C_2$-$C_4)$alkoxy-, $(C_1$-$C_4)$alkoxy$(C_2$-$C_4)$alkoxy-, amino$(C_2$-$C_4)$alkoxy-, $((C_1$-$C_4)$alkyl)amino$(C_2$-$C_4)$alkoxy-, $((C_1$-$C_4)$alkyl$)((C_1$-$C_4)$alkyl)amino$(C_2$-$C_4)$alkoxy-, or -$CONH_2$; wherein said $(C_1$-$C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1$-$C_4)$alkoxy, amino, $((C_1$-$C_4)$alkyl)amino-, or $((C_1$-$C_4)$alkyl$)((C_1$-$C_4)$alkyl)amino-.

5. The compound or pharmaceutically acceptable salt according to claim 4, wherein R^8 is hydrogen or $(C_1$-$C_6)$alkyl; wherein said $(C_1$-$C_6)$alkyl is optionally substituted by cyano, hydroxyl, $(C_1$-$C_4)$alkoxy, amino, $((C_1$-$C_4)$alkyl)amino-, or $((C_1$-$C_4)$alkyl$)((C_1$-$C_4)$alkyl)amino-.

6. The compound or pharmaceutically acceptable salt according to any one of claims 2-5, wherein R^9 is halo(C_1-C_4)alkyl.

7. The compound or pharmaceutically acceptable salt according to claim 6, wherein R^9 is trifluoromethyl.

8. The compound or pharmaceutically acceptable salt according to any one of claims 2-7, wherein X is CH.

9. The compound or pharmaceutically acceptable salt according to any one of claims 2-7, wherein X is N.

10. The compound or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^1 is (C_1-C_4)alkoxy.

11. The compound or pharmaceutically acceptable salt according to claim 10, wherein R^1 is ethoxy.

12. The compound or pharmaceutically acceptable salt according to any one of claims 1-11, wherein n is 1 or 2 and each R^2 is independently halogen.

13. The compound or pharmaceutically acceptable salt according to claim 12, wherein each R^2 is fluorine.

14. The compound according to claim 1 which is:

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(6-(2-hydroxypropan-2-yl)-5-(trifluoromethyl)pyridin-3-yl)acetamide;

N-(6-ethoxy-5-(trifluoromethyl)pyridin-3-yl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(4-(3-hydroxy-2,2-dimethylpropyl)-3-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2,3-difluorophenyl)-*N*-(4-(2-hydroxyethoxy)-3-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(4-(3-hydroxy-2,2-dimethylpropyl)-3-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-3-fluorophenyl)-*N*-(4-(3-hydroxy-2,2-dimethylpropyl)-3-(trifluoromethyl)phenyl)acetamide;

N-(4-cyano-3-(trifluoromethyl)phenyl)-2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-3-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2,6-difluorophenyl)-*N*-(4-(2-hydroxyethoxy)-3-(trifluoromethyl)phenyl)acetamide;

N-(4-cyano-3-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(6-(2-(dimethylamino)ethoxy)-5-(trifluoromethyl)pyridin-3-yl)-2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(4-methyl-1*H*-imidazol-1-yl)-5-(trifluoromethyl)phenyl)acetamide;

N-(6-(2-cyanopropan-2-yl)-5-(trifluoromethyl)pyridin-3-yl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(4-(2-hydroxyethoxy)-3-(trifluoromethyl)phenyl)acetamide;

N-(6-(cyanomethyl)-5-(trifluoromethyl)pyridin-3-yl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(6-(1-cyanoethyl)-5-(trifluoromethyl)pyridin-3-yl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(4-chloro-3-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(4-((dimethylamino)methyl)-3-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(3,4-dichlorophenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(5-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(4-(2-hydroxyethoxy)-3-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(4-((4-ethylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)acetamide;

N-(2,5-difluorophenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

4-(2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamido)-2-(trifluoromethyl)benzamide;

N-(2,4-difluoro-5-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

N-(3,5-*bis*(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(2-fluoro-5-(trifluoromethyl)phenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(5-methyl-1,3,4-oxadiazol-2-yl)-5-(trifluoromethyl)phenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(5-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(6-(1-hydroxy-2-methylpropan-2-yl)-5-(trifluoromethyl)pyridin-3-yl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-3-fluorophenyl)-*N*-(4-(3-hydroxy-2,2-dimethylpropyl)-3-(trifluoromethyl)phenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(4-methyl-1*H*-pyrazol-1-yl)-5-(trifluoromethyl)phenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(3-methyl-1*H*-pyrazol-1-yl)-5-(trifluoromethyl)phenyl)acetamide;

N-(3-(1*H*-pyrazol-4-yl)-5-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(6-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-3-yl)acetamide;

N-(4-cyano-3-(trifluoromethyl)phenyl)-2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(2-morpholinoethoxy)-5-(trifluoromethyl)phenyl)acetamide;

2-(4-(4-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(1-methyl-3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1*H*-pyrazol-5-yl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1*H*-pyrazol-5-yl)acetamide;

N-(4-(2,2-difluoro-3-hydroxypropyl)-3-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

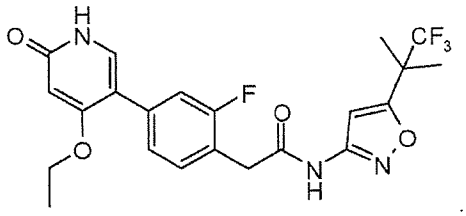
N-(3-(2*H*-tetrazol-5-yl)-5-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)-*N*-(3-(1-methyl-1*H*-pyrazol-4-yl)-5-(trifluoromethyl)phenyl)acetamide; or

N-(3-(2-(dimethylamino)ethoxy)-5-(trifluoromethyl)phenyl)-2-(4-(5-ethoxy-6-oxo-1,6-dihydropyridin-3-yl)-2-fluorophenyl)acetamide;

or pharmaceutically acceptable salts thereof.

15. The compound according to claim 1 which is:



or a pharmaceutically acceptable salt thereof.

16. The compound according to claim 15 wherein the compound is a free base.

17. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt according to any one of claims 1-16 and a pharmaceutically acceptable excipient.

18. Use of the compound or pharmaceutically acceptable salt according to any one of claims 1-16, in the manufacture of a medicament for the treatment of irritable bowel syndrome.

19. Use of the compound or pharmaceutically acceptable salt according to any one of claims 1-16, in the manufacture of a medicament for the treatment of cancer.