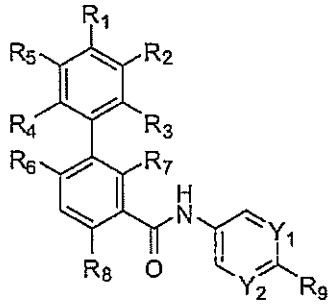
We Claim:

1. A compound of Formula I:



I

in which:

Y_1 and Y_2 are independently selected from N and CR_{10}; wherein R_{10} is selected from hydrogen, halo, dimethylamino-ethoxy, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy, halosubstituted-C_{1-6}alkoxy and -$ONR_{10a}R_{10b}$; wherein R_{10a} and R_{10b} are independently selected from hydrogen and C_{1-6}alkyl;

R_1 is selected from hydrogen, cyano, halo, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy, halosubstituted-C_{1-6}alkoxy, dimethyl-amino, C_{1-6}alkyl-sulfanyl and C_{3-8}heterocycloalkyl optionally substituted with up to 2 C_{1-6}alkyl radicals;

R_2 and R_5 are independently selected from hydrogen, cyano, halo, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy, halosubstituted-C_{1-6}alkoxy and dimethylamino;

R_3 and R_4 are independently selected from hydrogen, halo, cyano, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy and halosubstituted-C_{1-6}alkoxy;

R_6 and R_7 are independently selected from hydrogen, chloro, fluoro, bromo, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy and halosubstituted-C_{1-6}alkoxy; with the proviso that R_6 and R_7 are not both hydrogen;

R_8 is selected from hydrogen, halo, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy and halosubstituted-C_{1-6}alkoxy;

R_9 is selected from $-S(O)_2R_{11}$, $-OR_{11}$, $-C(O)R_{11}$, $-NR_{12a}R_{12b}$ and $-R_{11}$; wherein R_{11} is selected from aryl, cycloalkyl, heterocycloalkyl or any one of

thiomorpholino, sulfonomorpholino, sulfanomorpholino, morpholino, cyclohexyl, phenyl, azepan-1-yl, 2-oxopiperazin-1-yl, 1,4-oxazepan-4-yl, piperidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-3-yl, piperazinyl, pyrrolidinyl and 1,4-diazepan-1-yl; R_{12a} and R_{12b} are independently selected from C_{1-6}alkyl and hydroxy-substituted-C_{1-6}alkyl;

wherein said aryl, cycloalkyl and heterocycloalkyl of R_9 can be optionally substituted with 1 to 3 radicals independently selected from C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy, halosubstituted-C_{1-6}alkoxy, C_{6-10}aryl-C_{0-4}alkyl, C_{5-10}heteroaryl-C_{0-4}alkyl, C_{3-12}cycloalkyl and C_{3-8}heterocycloalkyl;

wherein said aryl-alkyl substituent of R_9 is optionally substituted with 1 to 3 radicals independently selected from halo, C_{1-6}alkyl, halosubstituted-C_{1-6}alkyl, C_{1-6}alkoxy, halosubstituted-C_{1-6}alkoxy and methyl-piperazinyl;

and the pharmaceutically acceptable salts, hydrates, solvates and stereoisomers thereof.

2. The compound of claim 1 in which:

Y_1 and Y_2 are selected from N and CR_{10}; wherein R_{10} is selected from hydrogen, methyl, fluoro, chloro, bromo, dimethylamino-ethoxy and trifluoromethyl;

R_6 and R_7 are independently selected from hydrogen methyl, chloro, fluoro, bromo, trifluoromethyl and methoxy; with the proviso that R_6 and R_7 are not both hydrogen; and

R_8 is selected from hydrogen, fluoro, chloro, methyl and trifluoromethyl.

3. The compound of claim 2 in which: R_1 is selected from cyano, chloro, fluoro, methyl, ethyl, t-butyl, propyl, isobutyl, isopropyl, isopropyloxy, butoxy, methoxy, dimethyl-amino, ethoxy, methyl-sulfanyl, trifluoromethyl, trifluoromethoxy and piperazinyl optionally substituted with up to 2 methyl radicals;

R_2 and R_5 are independently selected from hydrogen, chloro, fluoro, cyano, methyl, trifluoromethyl, isopropyloxy, methoxy, ethoxy, trifluoromethoxy and dimethylamino; and

R_3 and R_4 are independently selected from hydrogen, chloro, methyl, methoxy and cyano.

4. The compound of claim 3 in which R_9 is selected from $-S(O)_2R_{11}$, $-OR_{11}$, $-C(O)R_{11}$, $-NR_{12a}R_{12b}$ and $-R_{11}$; wherein R_{11} is selected from thiomorpholino, sulfonomorpholino, sulfanomorpholino, morpholino, cyclohexyl, phenyl, azepan-1-yl, 2-oxopiperazin-1-yl, 1,4-oxazepan-4-yl, piperidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-3-yl, piperazinyl, pyrrolidinyl and 1,4-diazepan-1-yl; R_{12a} and R_{12b} are independently selected from isobutyl, hydroxy-ethyl,

wherein said thiomorpholino, sulfonomorpholino, sulfanomorpholino, morpholino, cyclohexyl, phenyl, azepan-1-yl, 2-oxopiperazin-1-yl, 1,4-oxazepan-4-yl, piperidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-3-yl, piperazinyl, pyrrolidinyl or 1,4-diazepan-1-yl of R_9 can be optionally substituted with 1 to 3 radicals independently selected from methyl, ethyl, methoxy, benzyl, thienyl-methyl, pyridinyl-methyl, benzo[d][1,3]dioxol-6-yl and 2,3-dihydrobenzo[b][1,4]dioxin-7-yl;

wherein said phenyl or benzyl substituent of R_9 is optionally substituted with 1 to 3 radicals independently selected from methoxy, ethoxy, methyl-piperazinyl, methyl, trifluoromethoxy, chloro, fluoro and trifluoromethyl.

5. The compound of claim 4 selected from N-(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 4'-cyano-6-methyl-biphenyl-3-carboxylic acid [4-(morpholine-4-sulfonyl)-phenyl]-amide, 4'-cyano-6-methyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-2-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Methoxy-2-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Methoxy-2-methyl-biphenyl-3-carboxylic acid (4-cyclohexyl-phenyl)-amide, 4'-Methoxy-2-methyl-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Dimethylamino-2-methyl-biphenyl-3-carboxylic acid (4-cyclohexyl-phenyl)-amide, 4'-Dimethylamino-2-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 6-Chloro-4'-dimethylamino-biphenyl-

3-carboxylic acid (6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide, 6-Chloro-4'-dimethylamino-biphenyl-3-carboxylic acid (6-morpholin-4-yl-pyridin-3-yl)-amide, 6-Chloro-4'-dimethylamino-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Chloro-4'-methoxy-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 6-Chloro-4'-methoxy-biphenyl-3-carboxylic acid (6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide, 6-Chloro-4'-methoxy-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Chloro-4'-methoxy-biphenyl-3-carboxylic acid (6-morpholin-4-yl-pyridin-3-yl)-amide, 4'-Methoxy-6-methyl-biphenyl-3-carboxylic acid (6-morpholin-4-yl-pyridin-3-yl)-amide, 4'-Methoxy-6-methyl-biphenyl-3-carboxylic acid (6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide, 4'-Methoxy-6-methyl-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Dimethylamino-6-methyl-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Dimethylamino-6-methyl-biphenyl-3-carboxylic acid (6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide, 4'-Dimethylamino-6-methyl-biphenyl-3-carboxylic acid (6-morpholin-4-yl-pyridin-3-yl)-amide, 4'-Methoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Ethoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-4'-methylsulfanyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Dimethylamino-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Chloro-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 2',4'-Dichloro-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 2'-Chloro-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Chloro-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3',4'-Dichloro-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Chloro-6-methyl-4'-trifluoromethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6,4'-Dimethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Ethyl-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-tert-Butyl-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-4'-propyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Isobutyl-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Isopropyl-6-methyl-biphenyl-3-carboxylic acid (6-

azepan-1-yl-pyridin-3-yl)-amide, 6,2',6'-Trimethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6,2',3'-Trimethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-4'-trifluoromethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-3'-trifluoromethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-3', 5'-bistrifluoromethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Isopropoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Ethoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 2',6'-Dimethoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-4'-trifluoromethoxy-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-3'-trifluoromethoxy-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 6-Methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 4'-Methoxy-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 3'-Methoxy-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 3'-Dimethylamino-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 4'-Fluoro-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 3'-Fluoro-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 2'-Fluoro-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 6-Methyl-4'-(4-methyl-piperazin-1-yl)-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 2'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 3'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (6-morpholin-4-yl-pyridin-3-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (3-chloro-4-morpholin-

4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (3-bromo-4-morpholin-4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (3-methyl-4-morpholin-4-yl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-3-trifluoromethyl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4-cyclohexyl-phenyl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid biphenyl-4-ylamide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (4'-methoxy-biphenyl-4-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [4-(4-benzyl-piperazin-1-yl)-phenyl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [4-(pyrrolidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-methoxy-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Cyano-2-methoxy-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Cyano-2-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Fluoro-4'-methoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Isopropoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Butoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 3'-Chloro-4'-methoxy-6-methyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Methoxy-6,3'-dimethyl-biphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide, 4'-Cyano-2-methyl-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-fluoro-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 6-Bromo-4'-cyano-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-benzyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-thiophen-3-ylmethyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-2-methyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Methoxy-2-methyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 2-Methyl-4'-trifluoromethyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 2-Methyl-4'-trifluoromethoxy-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-2-methyl-biphenyl-3-carboxylic acid [6-(2-methyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-2-fluoro-biphenyl-3-carboxylic acid [4-

(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-trifluoromethyl-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-4-ylmethyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-3-ylmethyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2,6-dimethoxy-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-ethoxy-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid (6-{4-[2-(4-methyl-piperazin-1-yl)-benzyl]-[1,4]diazepan-1-yl}-pyridin-3-yl)-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-methoxy-2,3-dimethyl-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2,3-dihydro-benzo[1,4]dioxin-6-ylmethyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-2-ylmethyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-benzo[1,3]dioxol-4-ylmethyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-trifluoromethoxy-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-dimethylamino-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-chloro-5-trifluoromethyl-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2,3-difluoro-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-chloro-4-fluoro-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2,6-difluoro-benzyl)-[1,4]diazepan-1-yl]-pyridin-3-yl}-amide, 2-Chloro-4'-cyano-biphenyl-3-carboxylic acid [4-(piperidine-1-sulfonyl)-phenyl]-amide, 4'-Cyano-6-trifluoromethyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 2-Chloro-4'-cyano-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-ethyl-biphenyl-3-carboxylic acid [6-(2,6-dimethyl-morpholin-4-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(3-fluoro-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(2-trifluoromethoxy-benzyl)-piperazin-1-yl]-

pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(3-chloro-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-isobutyl-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-tert-butyl-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(7-methoxy-benzo[1,3]dioxol-5-ylmethyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-benzyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-3-ylmethyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-difluoromethoxy-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-cyano-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-quinolin-5-ylmethyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-4-ylmethyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-pyridin-2-ylmethyl-piperazin-1-yl)-pyridin-3-yl]-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(4-imidazol-1-yl-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid {6-[4-(3-cyano-benzyl)-piperazin-1-yl]-pyridin-3-yl}-amide, 4'-Cyano-6-methyl-biphenyl-3-carboxylic acid [6-(4-isoquinolin-5-ylmethyl-piperazin-1-yl)-pyridin-3-yl]-amide, (R)-2-methyl-N-(6-(2-methylmorpholino)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 4'-cyano-2-methyl-N-(6-sulfonylmorpholinopyridin-3-yl)biphenyl-3-carboxamide, (S)-4'-cyano-2-methyl-N-(6-(2-methylmorpholino)pyridin-3-yl)biphenyl-3-carboxamide, (R)-6-chloro-N-(6-(2-methylmorpholino)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 4'-cyano-2-methyl-N-(6-sulfinylmorpholinopyridin-3-yl)biphenyl-3-carboxamide, 4'-cyano-N-(6-(diisobutylamino)pyridin-3-yl)-2-methylbiphenyl-3-carboxamide, 4'-cyano-N-(2-((2S,6R)-2,6-dimethylmorpholino)pyrimidin-5-yl)-2-methylbiphenyl-3-carboxamide, N-(2-((2S,6R)-2,6-dimethylmorpholino)pyrimidin-5-yl)-2-methyl-4'-(trifluoromethyl)biphenyl-3-carboxamide, N-(2-((2S,6R)-2,6-dimethylmorpholino)pyrimidin-5-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide, N-(2-(bis(2-hydroxyethyl)amino)pyrimidin-5-yl)-2-methyl-4'-

(trifluoromethoxy)biphenyl-3-carboxamide, 2-methyl-N-(6-(tetrahydro-2H-pyran-4-yloxy)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, N-(5-chloro-6-((2S,6R)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide, N-(6-((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide,

N-(6-(4-ethylpiperazine-1-carbonyl)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 2-methyl-N-(6-(2-oxopiperazin-1-yl)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 2-methyl-N-(6-(1-(pyridin-4-ylmethyl)piperidin-4-yl)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 2-methyl-N-(6-(2-oxo-4-(pyridin-4-ylmethyl)piperazin-1-yl)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide, 2-methyl-N-(6-(1-(pyridin-4-ylmethyl)piperidin-3-yl)pyridin-3-yl)-4'-(trifluoromethoxy)biphenyl-3-carboxamide and N-(6-(1-ethylpiperidin-3-yl)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide.

6. The use of a compound of claim 1 in the manufacture of a medicament for inhibiting the hedgehog pathway in a cell.

7. The use of claim 6 wherein the cell has a phenotype of Ptc loss-of-function, hedgehog gain-of-function, smoothened gain-of-function or Gli gain-of-function.

8. The use of claim 7 wherein the cell is contacted with the hedgehog antagonist in vivo or in vitro.

9. The use of claim 8 wherein the compound is administered to an animal as part of a therapeutic application.

10. The use of claim 9 wherein the therapeutic application is selected from pancreatic cancer, prostrate cancer, medulloblastoma, basal cell carcinoma and small-cell lung cancer.

11. The use of a compound of claim 1 in the manufacture of a medicament for inhibiting unwanted proliferation of a cell.

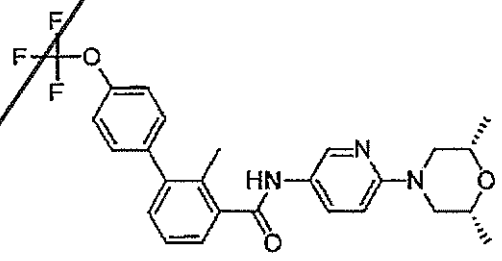
12. The use of claim 11 wherein the cell is selected from pancreatic cancer, prostrate cancer, medulloblastoma, basal cell carcinoma and small-cell lung cancer.

13. A compound with the formula of 4-Methyl-N-(4-morpholin-4-yl-phenyl)-3-quinoxalin-6-yl-benzamide.

14. A compound with the formula of 6-Methyl-[1,1';4',1"]terphenyl-3-carboxylic acid (6-azepan-1-yl-pyridin-3-yl)-amide.

15. A compound with the formula of 4'-(2-Dimethylamino-ethoxy)-6-methyl-biphenyl-3-carboxylic acid (4-morpholin-4-yl-phenyl)-amide.

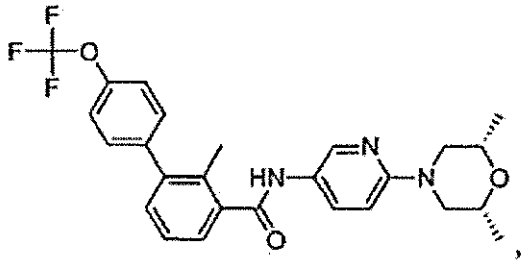
16. The compound, N-(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-carboxamide, having the formula:



and a pharmaceutically acceptable salt thereof.

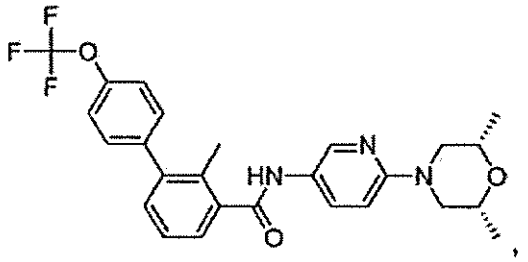
Claims

1. The compound, N-(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide of formula:



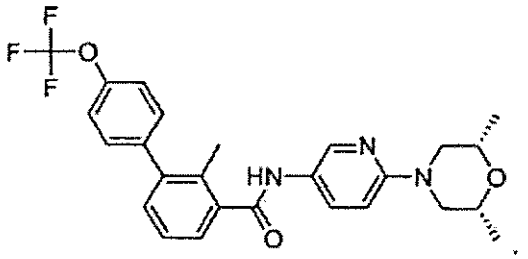
or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

2. The compound, N-(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide of formula:

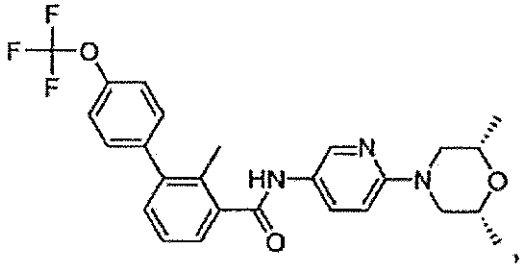


or a pharmaceutically acceptable salt thereof.

3. The compound, N-(6-((2R,6S)-2,6-dimethylmorphalino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide of formula:

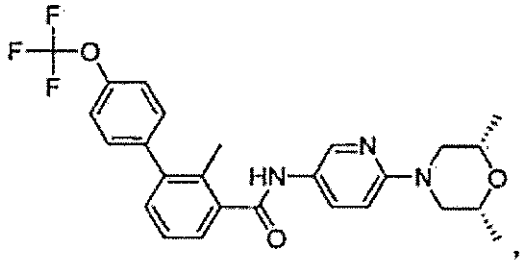


4. A pharmaceutical composition comprising
the compound, N-(6-((2R,6S)2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide of formula:



in free form or in a pharmaceutically acceptable salt form in association with at least one pharmaceutically acceptable carrier or diluent.

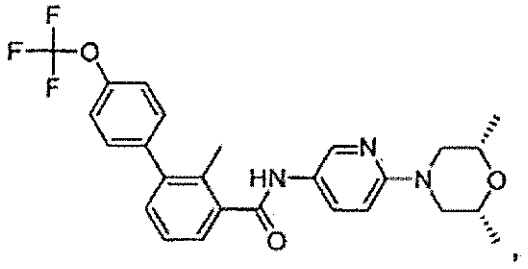
5. A pharmaceutical composition comprising a therapeutically effective amount of the compound, N=(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide-of formula:



or a pharmaceutically acceptable salt thereof, in combination with one or more therapeutic agents.

6. A pharmaceutical combination according to claim 5 wherein the additional therapeutic agent is selected from immunomodulatory, anti-inflammatory substances or other anti-tumor therapeutic agents.

7. The compound, N-(6-((2R,6S)-2,6-dimethylmorpholino)pyridin-3-yl)-2-methyl-4'-(trifluoromethoxy)biphenyl-3-carboxamide of formula:



or a pharmaceutically acceptable salt, thereof, for use in the treatment of pancreatic cancer, prostrate cancer, medulloblastoma, basal cell carcinoma and small-cell lung cancer.