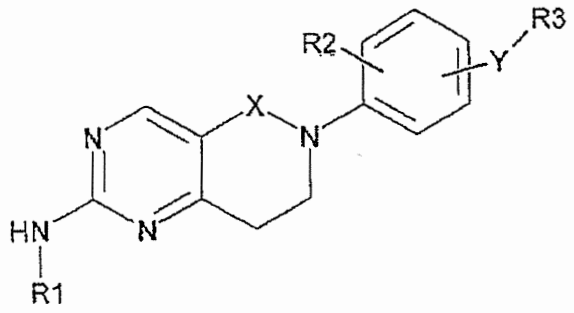
CLAIMS

1. A compound of formula (I) having the structure



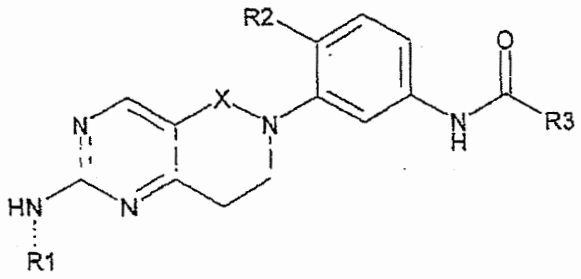
(I)

wherein

R1 is H, aryl, substituted aryl, alkyl, substituted alkyl, heteroaryl, substituted heteroaryl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl or substituted heterocyclylalkyl,
X is CH_2 or C=O
R2 is H, $(C_1$-$C_6)$alkyl, halogen, CF_3, or -O-$(C_1$-$C_6)$alkyl Y is -NHCO-, -CONH-, -$NHSO_2$-, -NH-, -NCH_3-CO-, -$NHCH_2$-, O, -NHCONH- or -$NHCOCH_2$-
R3 is alkyl, substituted alkyl, aryl, or substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl or heterocycloalkyl;
wherein the term "alkyl" refers to saturated aliphatic groups, including straight-chain alkyl groups, branched-chain alkyl groups, cycloalkyl (alicyclic) groups, alkyl substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups;
the term "cycloalkyl" refers to a saturated or partially saturated, monocyclic or fused or spiro polycyclic, carbocycle;
the term "heterocycloalkyl" or "heterocyclyl" refers to a non-aromatic partially unsaturated or fully saturated 3 to 10 membered ring system, which includes single rings of 3 to 8 atoms in size and bi-or tri-cyclic ring systems which may include aromatic six-membered aryl or heteroaryl rings fused to a non-aromatic ring;
the term "substituted" refers to substitution with any one or more or any combination of the following substituents: hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstiuted guanidine;

or a pharmaceutically acceptable salt thereof.

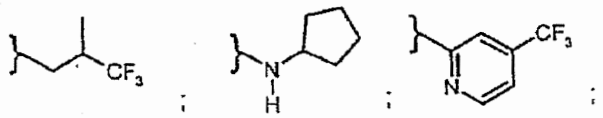
2. The compound according to claim 1, of formula (II) having the structure



(II)

wherein

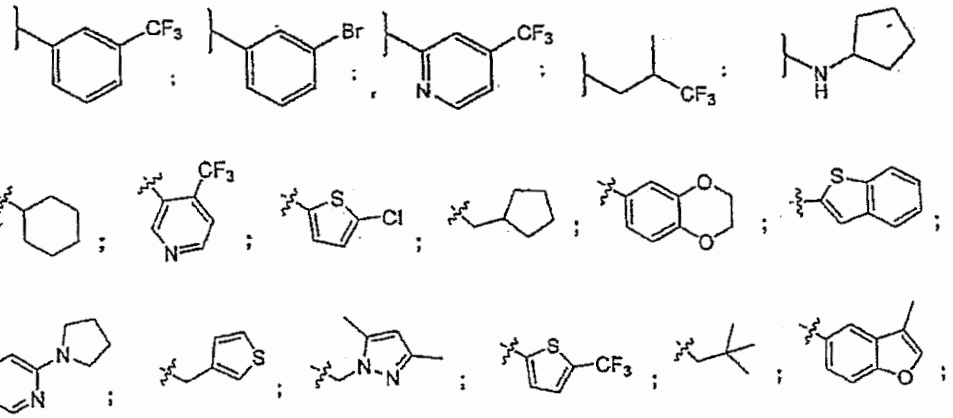
R1 is hydrogen, (C_1-C_4)alkyl, phenyl, substituted phenyl , pyridine, or substituted pyridine,
X is CH_2 or C=O
R2 is H, (C_1-C_6)alkyl, halogen, or -O(C_1-C_6)alkyl,
R3 is (C_1-C_6) alkyl, cycloalkyl, substituted cycloalkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl,

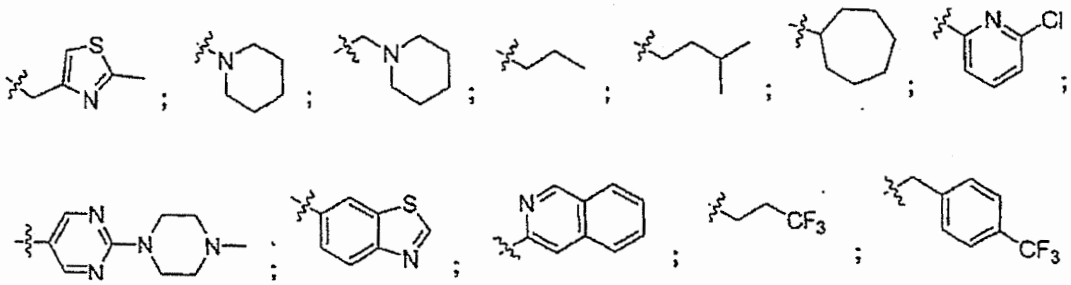


and wherein the substituents are selected from the group comprising C_1-C_4 linear or branched alkyl, halo or nitrile substituted C_1-C_4 alkyl, -O-alkyl (C_1-C_4), halogen;

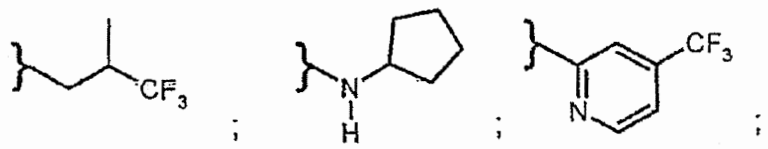
or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1 or 2, wherein R3 is selected from the group consisting of:



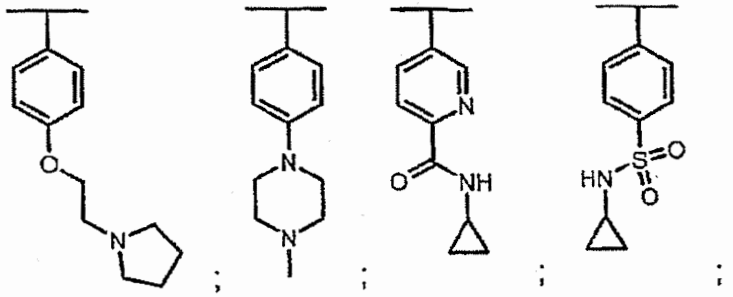


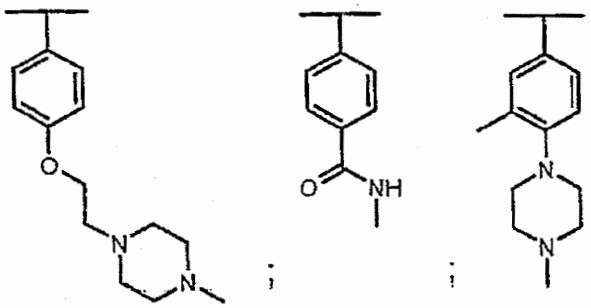
4. The compound according to any of claims 1 to 3, wherein
R1 is substituted phenyl or substituted pyridine,
X is CH_2 or C=O
R2 is H, CH_3, Cl or F
R3 is selected from the group consisting of:



and
substituted phenyl, wherein the substituents are selected from the group comprising Cl, F, Br, CF_3 and CH_3.

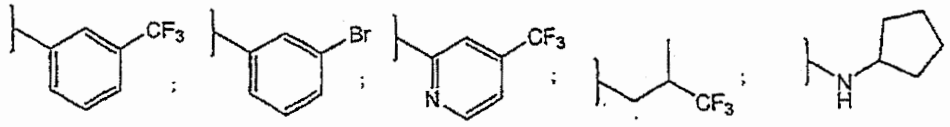
5. The compound according to any of claims 1 to 4, wherein
R1 is selected from the group consisting of:





and

R3 is selected from the group consisting of:



6. The compound of any of claims 1 to 5, selected from the group consisting of:

N-(4-Methyl-3-{2-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
N-(4-Methyl-3-{2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
5-{6-[2-Methyl-5-(3-trifluoromethyl-benzoylamino)-phenyl]-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-2-ylamino}-pyridine-2-carboxylic acid cyclopropylamide
N-{3-[2-(4-Cyclopropylsulfamoyl-phenylamino)-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-4-methyl-phenyl}-3-trifluoromethyl-benzamide
N-(4-Chloro-3-{2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
4-Trifluoromethyl-pyridine-2-carboxylic acid {4-chloro-3-[2-(4-methylcarbamoyl-phenylamino)-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-phenyl}-amide
4,4,4-Trifluoro-3-methyl-N-[4-methyl-3-(2-{4-[2-(4-methyl-piperazin-1-yl)-ethoxy]-phenylamino}-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl)-phenyl]-butyramide
1-Cyclopentyl-3-(4-methyl-3-{2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-urea
N-(4-Methyl-3-{5-oxo-2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide N-{4-Chloro-3-[2-(4-cyclopropylcarbamoylmethoxy-phenylamino}-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-phenyl}-3-trifluoromethyl-benzamide N-(4-Chloro-3-{2-[3-methyl-4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
3-Bromo-N-(4-methyl-3-{2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-benzamide
N-(4-Chloro-3-{2-[4-(4-methyl-piperazin-1-ylmethyl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide

or a pharmaceutically acceptable salt thereof.

7. The compound of any of claims 1 to 6, selected from the group consisting of:

N-(4-Methyl-3-{2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
5-{6-[2-Methyl-5-(3-trifluoromethyl-benzoylamino)-phenyl]-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-2-ylamino}-pyridine-2-carboxylic acid cyclopropylamide
4-Trifluoromethyl-pyridine-2-carboxylic acid {4-chloro-3-[2-(4-methylcarbamoyl-phenylamino)-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-phenyl}-amide

or a pharmaceutically acceptable salt thereof.

8. The compound of any of claims 1 to 7, selected from the group consisting of:

N-(4-Chloro-3-{2-[3-methyl-4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-phenyl)-3-trifluoromethyl-benzamide
N-{4-Chloro-3-[2-(4-cyclopropylcarbamoylmethoxy-phenylamino)-5-oxo-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-phenyl}-3-trifluoromethyl-benzamide

or a pharmaceutically acceptable salt thereof.

9. The compound according to any of claims 1 to 8, for use in therapy.

10. A pharmaceutical composition comprising the compound of any of claims 1 to 8, and at least one pharmaceutically acceptable excipient, carrier or diluent.

11. The compound according to any of claims 1 to 8, for use in a method for treating diseases associated with activation of STAT3 pathway, through multi-target inhibition of c-SRC and JAK2.

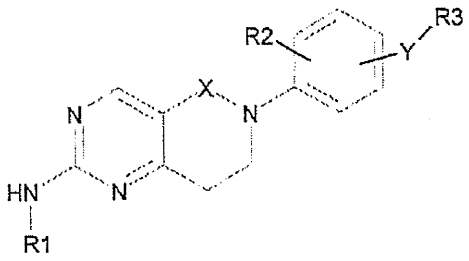
12. The compound of claim 11, wherein said disease is cancer, auto-immune, bone related and heamatological diseases.

13. The compound of claim 12, wherein said cancer is breast cancer, head and neck cancer, melanoma, ovarian cancer, lung cancer, pancreatic cancer, colon cancer, uterine cancer, gastric cancer, renal cancer, bladder cancer, liver cancer and prostate cancer, and wherein said compound is any of the compounds of claim 7.

14. The compound of claim 12, wherein said cancer is multiple myeloma, leukaemias, myeloproliferative neoplasms and lymphomas and wherein said compound is any of the compounds of claim 8.

Claims

1. A compound of formula (I) having the structure



(I)

wherein

R1 is H, aryl, substituted aryl, alkyl, substituted alkyl, heteroaryl, substituted heteroaryl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl or substituted heterocyclylalkyl,

X is CH_2 or C=0

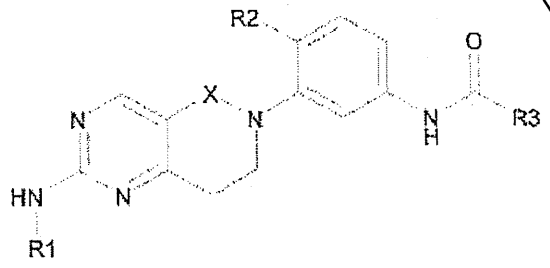
R2 is H, (Ci-C_6)alkyl, halogen, CF_3, or -0-(Ci-C_6)alkyl

Y is -NHCO-, -CONH-, -$NHSO_2$-, -NH-, -NCH_3-CO-, -$NHCH_2$-, O, -NHCONH- or -$NHCOCH_2$-

R3 is alkyl, substituted alkyl, aryl, or substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl or heterocycloalkyl;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, of formula (II) having the structure



(II)

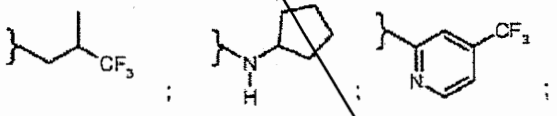
wherein

Rl is hydrogen, (Ci-C_4)alkyl, phenyl, substituted phenyl , pyridine, or substituted pyridine,

X is CH_2 or C=0

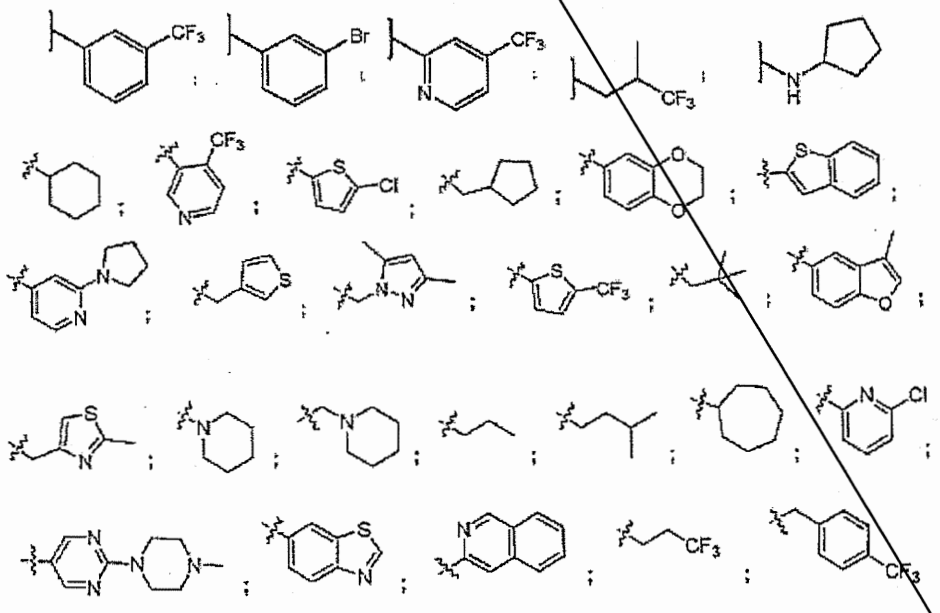
R2 is H, (Ci-C_6)alkyl, halogen, or -0(Ci-C_6)alkyl,

R3 is (Ci-C_6) alkyl, cycloalkyl, substituted cycloalkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl,



and wherein the substituents are selected from the group comprising C_1-C_4 linear or branched alkyl, halo or nitrile substituted C_1-C_4 alkyl, -O-alkyl (C_1-C_4), halogen; or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1 or 2, wherein R3 is selected from the group consisting of:



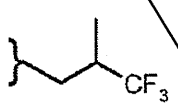
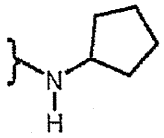
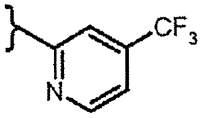
4. The compound according to any of claims 1 to 3, wherein

Rl is substituted phenyl or substituted pyridine,

X is CH_2 or C=0

R2 is H, CH_3, Cl or F

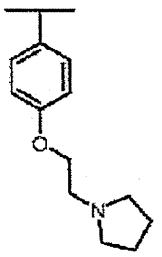
R3 is selected from the group consisting of:

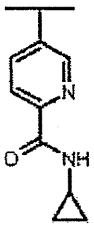
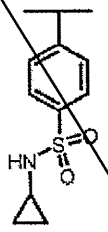

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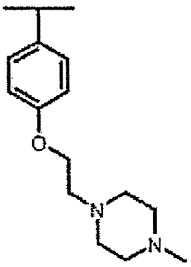
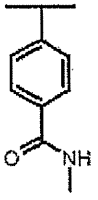
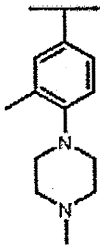
substituted phenyl, wherein the substituents are selected from the group comprising Cl, F, Br, CF_3 and CH_3.

5. The compound according to any of claims 1 to 4, wherein

RI is selected from the group consisting of:

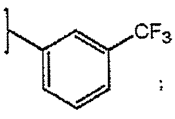
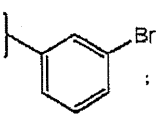
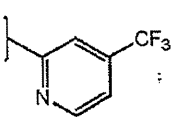
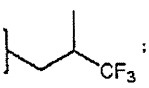

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and

R3 is selected from the group consisting of:


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