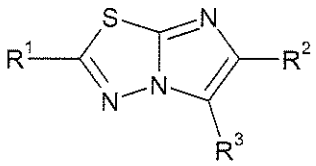
Summary

In a first aspect, there is provided a compound of formula I,



I

wherein:

R^1 represents:
(i) aryl substituted with one or more substituents selected from A^1; or
(ii) heteroaryl optionally substituted with one or more substituents selected from A^2;

R^2 represents hydrogen or C_{1-3} alkyl optionally substituted by one or more fluoro atoms;

R^3 represents aryl or heteroaryl, each of which is optionally substituted by one or more substituents selected from A^3 and A^4, respectively;

each A^1, A^2, A^3 and A^4 independently represents, on each occasion when used herein:
(i) Q^1;
(ii) C_{1-12} alkyl or heterocycloalkyl, both of which are optionally substituted by one or more substituents selected from =O, =S, =N(R^{10a}) and Q^2; or
(iii) aryl or heteroaryl, both of which are optionally substituted by one or more substituents selected from Q^3;

each Q^1, Q^2 and Q^3 independently represents, on each occasion when used herein:
halo, -CN, -NO_2, -N(R^{10a})R^{11a}, -OR^{10a}, -C(=Y)-R^{10a}, -C(=Y)-OR^{10a}, -C(=Y)N(R^{10a})R^{11a}, -OC(=Y)-R^{10a}, -OC(=Y)-OR^{10a}, -OC(=Y)N(R^{10a})R^{11a}, -$OS(O)_2OR^{10a}$, -OP(=Y)(OR^{10a})(OR^{11a}), -OP(OR^{10a})(OR^{11a}), -N(R^{12a})C(=Y)R^{11a}, -N(R^{12a})C(=Y)OR^{11a}, -N(R^{12a})C(=Y)N(R^{10a})R^{11a}, -$NR^{12a}S(O)_2R^{10a}$, -$NR^{12a}S(O)_2N(R^{10a})R^{11a}$, -$S(O)_2N(R^{10a})R^{11a}$, -SC(=Y)$R^{10a}$, -SC(=Y)$OR^{10a}$,

$-SC(=Y)N(R^{10a})R^{11a}$, $-S(O)_2R^{10a}$, $-SR^{10a}$, $-S(O)R^{10a}$, $-S(O)_2OR^{10a}$, C_{1-12} alkyl, heterocycloalkyl (which latter two groups are optionally substituted by one or more substituents selected from =O, =S, $=N(R^{20})$ and E^1), aryl or heteroaryl (which latter two groups are optionally substituted by one or more substituents selected from E^2);

each R^{10a}, R^{11a} and R^{12a} independently represents, on each occasion when used herein, hydrogen, C_{1-12} alkyl, heterocycloalkyl (which latter two groups are optionally substituted by one or more substituents selected from =O, =S, $=N(R^{20})$ and E^3), aryl or heteroaryl (which latter two groups are optionally substituted by one or more substituents selected from E^4); or

any relevant pair of R^{10a}, R^{11a} and R^{12a} may be linked together to form a 4- to 20- membered ring, optionally containing one or more heteroatoms optionally containing one or more unsaturations, and which ring is optionally substituted by one or more substituents selected from =O, =S, $=N(R^{20})$ and E^5;

each E^1, E^2, E^3, E^4 and E^5 independently represents, on each occasion when used herein:
(i) Q^4;
(ii) C_{1-12} alkyl or heterocycloalkyl, both of which are optionally substituted by one or more substituents selected from =O and Q^5; or
(iii) aryl or heteroaryl, both of which are optionally substituted by one or more substituents selected from Q^6;

each Q^4, Q^5 and Q^6 independently represents, on each occasion when used herein:
halo, -CN, $-NO_2$, $-N(R^{20})R^{21}$, $-OR^{20}$, $-C(=Y)-R^{20}$, $-C(=Y)-OR^{20}$, $-C(=Y)N(R^{20})R^{21}$, $-OC(=Y)-R^{20}$, $-OC(=Y)-OR^{20}$, $-OC(=Y)N(R^{20})R^{21}$, $-OS(O)_2OR^{20}$, $-OP(=Y)(OR^{20})(OR^{21})$, $-OP(OR^{20})(OR^{21})$, $-N(R^{22})C(=Y)R^{21}$, $-N(R^{22})C(=Y)OR^{21}$, $-N(R^{22})C(=Y)N(R^{20})R^{21}$, $-NR^{22}S(O)_2R^{20}$, $-NR^{22}S(O)_2N(R^{20})R^{21}$, $-S(O)_2N(R^{20})R^{21}$, $-SC(=Y)R^{20}$, $-SC(=Y)OR^{20}$, $-SC(=Y)N(R^{20})R^{21}$, $-S(O)_2R^{20}$, $-SR^{20}$, $-S(O)R^{20}$, $-S(O)_2OR^{20}$, C_{1-12} alkyl, heterocycloalkyl (which latter two groups are optionally substituted by one or more substituents selected from =O and J^1), aryl or heteroaryl (which latter two groups are optionally substituted by one or more substituents selected from J^2);

each Y independently represents, on each occasion when used herein, =O, =S or $=NR^{23}$;

each R^{20}, R^{21}, R^{22} and R^{23} independently represents, on each occasion when used herein, hydrogen, C_{1-6} alkyl, heterocycloalkyl (which latter two groups are optionally substituted by one or more substituents selected from J^3 and =O), aryl or heteroaryl (which latter two groups are optionally substituted by one or more substituents selected from J^4); or

any relevant pair of R^{20}, R^{21} and R^{22}, may be linked together to form a 4- to 20- membered ring, optionally containing one or more heteroatoms, optionally containing one or more unsaturations, and which ring is optionally substituted by one or more substituents selected from J^5 and =O;

each J^1, J^2, J^3, J^4 and J^5 independently represents, on each occasion when used herein:
(i) Q^7;
(ii) C_{1-6} alkyl or heterocycloalkyl, both of which are optionally substituted by one or more substituents selected from =O and Q^8; or
(iii) aryl or heteroaryl, both of which are optionally substituted by one or more substituents selected from Q^9;

each Q^7, Q^8 and Q^9 independently represents, on each occasion when used herein:
halo, -CN, $-N(R^{50})R^{51}$, $-OR^{50}$, $-C(=Y^a)-R^{50}$, $-C(=Y^a)-OR^{50}$, $-C(=Y^a)N(R^{50})R^{51}$, $-N(R^{52})C(=Y^a)R^{51}$, $-NR^{52}S(O)_2R^{50}$, $-S(O)_2R^{50}$, $-SR^{50}$, $-S(O)R^{50}$ or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

each Y^a independently represents, on each occasion when used herein, =O, =S or $=NR^{53}$;

each R^{50}, R^{51}, R^{52} and R^{53} independently represents, on each occasion when used herein, hydrogen or C_{1-6} alkyl optionally substituted by one or more substituents selected from fluoro, $-OR^{60}$ and $-N(R^{61})R^{62}$; or
any relevant pair of R^{50}, R^{51} and R^{52} may be linked together to form, a 3- to 8-membered ring, optionally containing one or more heteroatoms , optionally containing one or more unsaturations , and which ring is optionally substituted by one or more substituents selected from =O and C_{1-3} alkyl;

R^{60}, R^{61} and R^{62} independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

or a pharmaceutically acceptable ester, amide, solvate or salt thereof, wherein the pharmaceutically acceptable ester is selected from the group consisting of optionally substituted C_{1-6} alkyl, C_{5-10} aryl and C_{5-10} aryl-C_{1-6} alkyl esters; and the pharmaceutically acceptable amide portion is of the formula
$-C(O)N(R^{z1})R^{z2}$, in which R^{z1} and R^{z2} independently represent optionally substituted C_{1-6} alkyl, C_{5-10} aryl and C_{5-10} aryl-C_{1-6} alkyl;

provided that when R^2 represents H, then:
(I) when R^1 represents 4-chlorophenyl, then R^3 does not represent unsubstituted phenyl or 4-chlorophenyl;
(II) when R^1 represents 4-methoxyphenyl, then R^3 does not represent 4-chlorophenyl or unsubstituted phenyl.

In a second aspect, there is provided a pharmaceutical formulation including a compound of formula I, as defined above, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

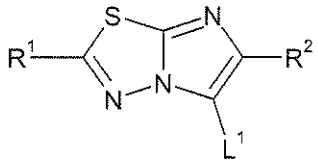
In a third aspect, there is provided a compound, as defined above but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above, for use in the treatment of a disease in which inhibition of a PI3-K id desired and/or required.

In a fourth aspect, there is provided the use of a compound of formula I, as defined above but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above, for the manufacture of a medicament for the treatment of a disease in which inhibition of a PI3-K is desired and/or required.

In a fifth aspect, there is provided a combination product comprising: (A) a compound of formula I as defined above but without the provisos, or a pharmaceutically-acceptable ester, amide, solvate or salt thereof as defined above; and (B) another therapeutic agent that is useful in the treatment of cancer and/or a proliferative disease, wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

In a sixth aspect, there is provided a process for the preparation of a compound of formula I as defined above or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above, which process comprises:

(i) reaction of a corresponding compound of formula II,



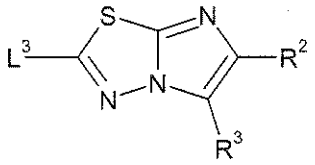
II

wherein L^1 represents a suitable leaving group, and R^1 and R^2 are as defined above, with a compound of formula III,

L^2-R^3 III

wherein L^2 represents a suitable group, and R^3 is as defined above;

(ii) reaction of a compound of formula IV,



IV

wherein L^3 represents a suitable leaving group, and R^2 and R^3 are as defined above, with a compound of formula V,

R^1-L^4 V

wherein L^4 represents a suitable leaving group;

(iii) for compounds of formula I in which there is a Q^1 to Q^6 substituent present, in which such groups represent -OR^{10a} or -OR^{20}, as appropriate, in which R^{10a} and R^{20} do not represent hydrogen, reaction of a corresponding compound of formula I in which there is a Q^1 to Q^6 present, which represents -OR^{10a} and -OR^{20} (as appropriate), in which R^{10a} and R^{20} do represent hydrogen, with a compound of formula VI,

R^x-L^5 VI

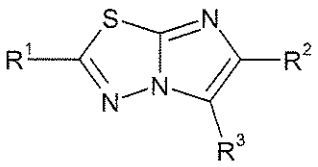
wherein L^5 represents a suitable leaving group and R^x represents R^{10a} or R^{20} (as appropriate), provided that it does not represent hydrogen.

In a seventh aspect, there is provided a process for the preparation of a pharmaceutical formulation as defined above, which process comprises bringing into association a compound of formula I, as defined above, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above with a pharmaceutically-acceptable adjuvant, diluent or carrier.

In an eighth aspect, there is provided a process for the preparation of a combination product as defined above, which process comprises bringing into association of a compound of formula I, as defined above but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined above with the other therapeutic agent that is useful in the treatment of cancer and/or a proliferative disease, and at least one pharmaceutically-acceptable adjuvant, diluent or carrier.

Description~~isclosure of the Invention~~

According to the invention, there is provided a compound of formula I,



I

wherein:

R^1 represents:
(i) aryl substituted with one or more substituents selected from A^1;
(ii) heteroaryl optionally substituted with one or more substituents selected from A^2;

R^2 represents hydrogen or C_{1-3} alkyl optionally substituted by one or more fluoro atoms;

R^3 represents aryl or heteroaryl, each of which is optionally substituted by one or more substituents selected from A^3 and A^4, respectively;

each A^1, A^2, A^3 and A^4 independently represents, on each occasion when used herein:

(i) Q^1;

(ii) $C_{1\text{-}12}$ alkyl or heterocycloalkyl, both of which are optionally substituted by one or more substituents selected from =O, =S, =N(R^{10a}) and Q^2;

(iii) aryl or heteroaryl, both of which are optionally substituted by one or more substituents selected from Q^3;

each Q^1, Q^2 and Q^3 independently represents, on each occasion when used herein:

halo, -CN, -NO_2, -N(R^{10a})R^{11a}, -OR^{10a}, -C(=Y)-R^{10a}, -C(=Y)-OR^{10a}, -C(=Y)N(R^{10a})R^{11a}, -OC(=Y)-R^{10a}, -OC(=Y)-OR^{10a}, -OC(=Y)N(R^{10a})R^{11a}, -$OS(O)_2OR^{10a}$, -OP(=Y)(OR^{10a})(OR^{11a}), -OP(OR^{10a})(OR^{11a}), -N(R^{12a})C(=Y)R^{11a}, -N(R^{12a})C(=Y)OR^{11a}, -N(R^{12a})C(=Y)N(R^{10a})R^{11a}, -NR^{12a}S(O)$_2R^{10a}$,

6. A compound as claimed in claim 1, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1; selected from the group consisting of:

(I) 2-(3,4-Dimethoxy-phenyl)-5-(3-fluoro-4-methanesulfonyl-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazole;

(II) 5-[2-(3,4-Dimethoxy-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyridine-2-carbonitrile;

(III) 5-[2-(3,4-Dimethoxy-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(IV) 2-(3,4-Dimethoxy-phenyl)-6-methyl-5-pyridin-3-yl-imidazo[2,1-b][1,3,4]thiadiazole;

(V) 2-(3,4-Dimethoxy-phenyl)-5-(6-methoxy-pyridin-3-yl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazole;

(VI) 2,5-Bis-(3,4-dimethoxy-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazole;

(VII) 5-[2-(3,4-Dimethoxy-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyrimidin-2-ylamine;

(VIII) 5-[2-(3,4-Dimethoxy-phenyl)-6-methyl-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyridin-2-ol;

(IX) tert-Butyl 2-(4-(5-(6-amino-5-(trifluoromethyl)pyridin-3-yl)-6-methylimidazo-[2,1-b][1,3,4]thiadiazol-2-yl)-2-methoxyphenoxy)ethylcarbamate;

(X) 2-(4-(5-(6-amino-5-(trifluoromethyl)pyridin-3-yl)-6-methylimidazo[2,1-b][1,3,4]thiadiazol-2-yl)-2-methoxyphenoxy)-N,N-dimethylacetamide;

(XI) 5-(2-(4-(2-morpholinoethoxy)-3-methoxyphenyl)-6-methylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)-3-(trifluoromethyl)pyridin-2-amine;

(XII) 5-{2-[3-Methoxy-4-(piperidin-4-yloxy)-phenyl]-imidazo[2,1-b][1,3,4]thiadiazol-5-yl}-3-trifluoromethyl-pyridin-2-ylamine;

(XIII) 2-[3-Methoxy-4-(piperidin-4-yloxy)-phenyl]-5-(6-methoxy-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XIV) 4-{4-[5-(2-Amino-pyrimidin-5-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-2-methoxy-phenoxy}-piperidine-1-carboxylic acid tert-butyl ester;

(XV) 5-{2-[3-Methoxy-4-(piperidin-4-yloxy)-phenyl]-imidazo[2,1-b][1,3,4]thiadiazol-5-yl}-pyrimidin-2-ylamine;

(XVI) 2,5-Bis-(3,4-dimethoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XVII) 5-[2-(3,4-Dimethoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyridine-2-carbonitrile;

(XVIII) 2-Amino-5-[2-(3,4-dimethoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-nicotinonitrile;

(XIX) 4-{5-[2-(3,4-Dimethoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyrimidin-2-yl}-piperazine-1-carboxylic acid tert-butyl ester;

(XX) 2-(3,4-Dimethoxy-phenyl)-5-(2-piperazin-1-yl-pyrimidin-5-yl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XXI) 2-(3,4-Dimethoxy-phenyl)-5-[2-(4-methyl-piperazin-1-yl)-pyrimidin-5-yl]-imidazo[2,1-b][1,3,4]thiadiazole;

(XXII) 2-(3,4-Dimethoxy-phenyl)-5-(6-piperazin-1-yl-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XXIII) 2-(3,4-Dimethoxy-phenyl)-5-[6-(4-methyl-piperazin-1-yl)-5-trifluoromethyl-pyridin-3-yl]-imidazo[2,1-b][1,3,4]thiadiazole;

(XXIV) 2-(3,4-Dimethoxy-phenyl)-5-(2-methylsulfanyl-pyrimidin-5-yl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XXV) 2-(3,4-Dimethoxy-phenyl)-5-(2-methanesulfinyl-pyrimidin-5-yl)-imidazo[2,1-b][1,3,4]thiadiazole;

(XXVI) N'-{5-[2-(3,4-Dimethoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-pyrimidin-2-yl}-N,N-dimethyl-ethane-1,2-diamine;

(XXVII) 2-(3,4-dimethoxyphenyl)-5-(5-methoxypyridin-3-yl)imidazo[2,1-b][1,3,4]thiadiazole;

(XXVIII) 5-[2-(3-Methoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XXIX) 3-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-benzonitrile;

(XXX) 5-[2-(4-Methoxy-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XXXI) N-{3-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-phenyl}-methanesulfonamide;

(XXXII) 5-(2-Pyridin-3-yl-imidazo[2,1-b][1,3,4]thiadiazol-5-yl)-3-trifluoromethyl-pyridin-2-ylamine;

(XXXIII) 4-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-benzonitrile;

(XXXIV) N-{3-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-benzyl}-methanesulfonamide;

(XXXV) 3-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-benzamide;

(XXXVI) 5-[2-(1-Ethyl-1H-pyrazol-4-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XXXVII) 5-[2-(4-Methyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XXXVIII) 5-[2-(1'-(tert-butoxycarbonyl)-2-oxo-1,2-dihydrospiro[indole-3,4'-piperidine]-5-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XXXIX) 5-[2-(2-oxo-1,2-dihydrospiro[indole-3,4'-piperidine]-5-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XL) 5-[2-(1H-Indol-5-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XLI) 5-[2-(3-Methanesulfonyl-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XLII) 5-[2-(3-Dimethylamino-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XLIII) 5-[2-(6-Methyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XLIV) 5-{2-[4-(Morpholine-4-sulfonyl)-phenyl]-imidazo[2,1-b][1,3,4]thiadiazol-5-yl}-3-trifluoromethyl-pyridin-2-ylamine;

(XLV) 5-{2-[3-(Morpholine-4-sulfonyl)-phenyl]-imidazo[2,1-b][1,3,4]thiadiazol-5-yl}-3-trifluoromethyl-pyridin-2-ylamine;

(XLVI) N-{3-[5-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-phenyl}-acetamide;

(XLVII) 5-[2-(5-Methoxy-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(XLVIII) 2,4-Difluoro-N-[2-methoxy-5-(5-pyridazin-4-yl-imidazo[2,1-b][1,3,4]thiadiazol-2-yl)-pyridin-3-yl]-benzenesulfonamide;

(XLIX) 5-[5-(4-Methanesulfonyl-phenyl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-3-trifluoromethyl-pyridin-2-ylamine;

(L) 5-[5-(6-Fluoro-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-2-yl]-3-trifluoromethyl-pyridin-2-ylamine; and

(LI) 4-[2-(6-Amino-5-trifluoromethyl-pyridin-3-yl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]-2-methoxy-benzoic acid methyl ester.

76. A compound of formula I as defined in any one of Claims 1 to 65, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1, for use as a pharmaceutical.

87. A pharmaceutical formulation including a compound of formula I, as defined in any one of Claims 1 to 65, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

98. A compound, as defined in any one of Claims 1 to 65 but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1, for use in the treatment of a disease in which inhibition of a PI3-K is desired and/or required.

109. Use of a compound of formula I, as defined in any one of Claims 1 to 65 but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1, for the manufacture of a medicament for the treatment of a disease in which inhibition of a PI3-K is desired and/or required.

1110. A compound as claimed in Claim 98 or a use as claimed in Claim 109, wherein the disease is cancer, an immune disorder, a cardiovascular disease, a viral infection, inflammation, a metabolism/endocrine function disorder, a neurological disorder, an obstructive airways disease, an allergic disease, an inflammatory disease, immunosuppression, a disorder commonly connected with organ transplantation, an AIDS-related disease, benign prostate hyperplasia, familial adenomatosis, polyposis, neuro-fibromatosis, psoriasis, a bone disorder, atherosclerosis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis glomerulonephritis and post-surgical stenosis, restenosis, stroke, diabetes, hepatomegaly, Alzheimer's disease, cystic fibrosis, a hormone-related disease, an immunodeficiency disorder, a destructive bone disorder, an infectious disease, a condition associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukaemia, liver disease, a pathologic immune condition involving T cell activation, CNS disorders, and other associated diseases.

1211. A combination product comprising:

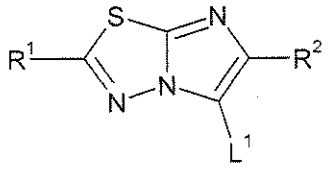
(A) a compound of formula I as defined in any one of Claims 1 to 65 but without the provisos, or a pharmaceutically-acceptable ester, amide, solvate or salt thereof as defined in claim 1; and

(B) another therapeutic agent that is useful in the treatment of cancer and/or a proliferative disease,

wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

1312.A process for the preparation of a compound of formula I as defined in Claim 1 or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1, which process comprises:

(i) reaction of a corresponding compound of formula II,



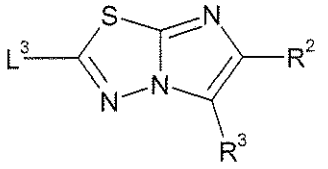
II

wherein L^1 represents a suitable leaving group, and R^1 and R^2 are as defined in Claim 1, with a compound of formula III,

$$L^2\text{-}R^3 \qquad \text{III}$$

wherein L^2 represents a suitable group, and R^3 is as defined in Claim 1;

(ii) reaction of a compound of formula IV,



IV

wherein L^3 represents a suitable leaving group, and R^2 and R^3 are as defined in Claim 1, with a compound of formula V,

$$R^1\text{-}L^4 \qquad \text{V}$$

wherein L^4 represents a suitable leaving group;

(iii) for compounds of formula I in which there is a Q^1 to Q^6 substituent present, in which such groups represent $-OR^{10a}$ or $-OR^{20}$, as appropriate, in which R^{10a} and R^{20} do not represent hydrogen, reaction of a corresponding compound of formula I in which there is a Q^1 to Q^6 present, which represents $-OR^{10a}$ and $-OR^{20}$ (as appropriate), in which R^{10a} and R^{20} do represent hydrogen, with a compound of formula VI,

$$R^x\text{-}L^5 \qquad \text{VI}$$

wherein L^5 represents a suitable leaving group and R^x represents R^{10a} or R^{20} (as appropriate), provided that it does not represent hydrogen.

1413. A process for the preparation of a pharmaceutical formulation as defined in Claim 87, which process comprises bringing into association a compound of formula I, as defined in any one of one of Claims 1 to 65, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1 with a pharmaceutically-acceptable adjuvant, diluent or carrier.

1514. A process for the preparation of a combination product as defined in Claim 1211, which process comprises bringing into association a compound of formula I, as defined in any one of Claims 1 to 65 but without the provisos, or a pharmaceutically acceptable ester, amide, solvate or salt thereof as defined in claim 1 with the other therapeutic agent that is useful in the treatment of cancer and/or a proliferative disease, and at least one pharmaceutically-acceptable adjuvant, diluent or carrier.