

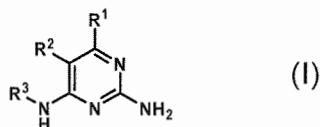
Int., Ed. (2013), Vol. 52. The compounds are organometallic and are not 2-amino-4-(*N*-alkylamino)-6-arylpyrimidines.

Summary

5 Although the finding of oncogenes and development of new anticancer treatments and diagnosis have improved the life length of cancer patients, there is still a high medical need to find more effective and less toxic treatments for e.g. breast cancer, leukemia, colon or lung cancer. Our preliminary data suggests that MTH1 inhibitors have the potential to be very effective against cancer forms with
10 dysfunctional redox status, with minimal general toxic effects. MTH1 inhibition may also be a suitable adjuvant therapy to be used in conjunction with radiotherapies or other chemotherapeutic approaches.

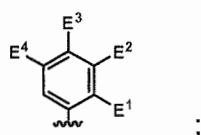
15 The present disclosure aims at providing new treatments for cancer that can be achieved by inhibition of MTH1.

In an aspect embodiment, there is provided the use of a compound of formula I,



20 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein:

25 R¹ represents heteroaryl connected to the pyrimidine of formula I via a carbon atom of the heteroaryl ring, which heteroaryl ring is optionally substituted by one or more substituents selected from Y¹, -C₁₋₆alkyl optionally substituted by one or more Y² and heterocycloalkyl optionally substituted by one or more Y³; or aryl represented by



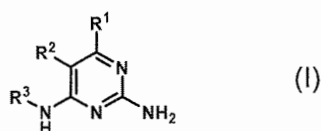
each R^{g4} , R^{k4} , R^{p4} and R^{s4} independently represent C_{1-6} alkyl optionally substituted by one or more -F;

each m independently represents 0, 1 or 2;

provided that the compound is not

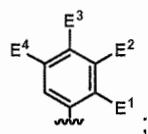
- 5 6-(3-pyridinyl)- N^4 -[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-2,4-pyrimidinediamine,
 6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyridinyl]methyl]-2,4-pyrimidinediamine,
 6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyrimidinyl]methyl]-
 10 2,4-pyrimidinediamine or
 N^4 -[2-(1-aziridinyl)ethyl]-5-fluoro-6-phenyl-2,4-pyrimidinediamine.

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



or a pharmaceutically acceptable salt thereof, wherein:

- 15 R^1 represents:
indanyl, naphthyl, tetrahydronaphthyl or heteroaryl selected from benzofuran-3-yl, benzothiophen-3-yl, dihydrobenzofuran-7-yl, indol-3-yl, indol-4-yl, indol-5-yl, isoquinolin-4-yl, pyridin-3-yl, pyridin-4-yl, pyrrol-2-yl and quinolin-5-yl, which
heteroaryl is, the latter connected to the pyrimidine of formula I via a carbon atom of
 20 the heteroaryl ring, and which indanyl, naphthyl, tetrahydronaphthyl and heteroaryl
rings are is optionally substituted by one or more substituents selected from Y^1 , $-C_{1-6}$ alkyl optionally substituted by one or more Y^2 and heterocycloalkyl optionally substituted by one or more Y^3 ; or
 aryl represented by



- 25 E^3 and E^4 represent hydrogen; and
 E^1 represents -F and E^2 represent -F, -Cl, $-CH_3$ or $-CF_3$; or
 E^1 represents -Cl and E^2 represents -F, -Cl, $-CH_3$ or $-CF_3$; or
 E^1 represents $-CH_3$ and E^2 represents -F, -Cl, $-CH_3$, $-CF_3$, -CN or $-N(H)C(O)CH=CH_2$;
 30 E^1, E^2, E^3 and E^4 represents hydrogen, Y^1 , $-C_{1-6}$ alkyl optionally substituted by one or more Y^2 or heterocycloalkyl optionally substituted by one or more Y^3 , but where at least one of E^1, E^2, E^3 and E^4 is other than hydrogen;

R^2 represents hydrogen, halogen or C_{1-12} alkyl optionally substituted by one or more Z^4 ;

5 R^3 represents C_{2-6} alkyl substituted by Z^1 C_{1-12} alkyl substituted by one or more Z^1 or heterocycloalkyl optionally substituted by one or more Z^2 ; or

R^2 and R^3 are linked together to form, along with the atoms to which they are attached, a 5- to 8-membered non-aromatic ring, wherein the link formed by R^2 and R^3 is optionally substituted by one or more substituents selected from Z^3 or C_{1-9} alkyl optionally substituted by one or more Z^4 ;

each Y^1 independently represents halogen, $-CN$, $-C(O)R^a$, $-C(O)N(R^b)R^c$, $-C(O)OR^d$, $-N(R^e)R^f$, $-N(R^g)C(O)R^h$, $-N(R^i)C(O)OR^j$, $-N(R^k)C(O)N(R^l)R^m$, $-NO_2$, $-N(R^n)S(O)_2R^o$, $-OR^p$, $-OC(O)R^q$, $-OS(O)_2R^r$, $-S(O)_mR^s$, $-S(O)_2N(R^t)R^u$, heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

20 each R^a , R^b , R^c , R^d , R^e , R^g , R^h , R^i , R^k , R^l , R^m , R^n , R^p , R^q , R^s , R^t and R^u independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ; or

any two R^b and R^c , R^e and R^f , R^i and R^m and/or R^t and R^u are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and $=O$;

35 each R^f , R^j , R^o and R^r independently represent C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted

by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

- 5 each Y^2 independently represents halogen, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 ,
10 heteroaryl optionally substituted by one or more substituents selected from W^2 ;

- ~~each Y^3 independently represents halogen, R^{a1} , CN , $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or $=O$;~~
- 15 ~~heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or $=O$;~~

- 20 each R^{a1} , R^{b1} , R^{c1} , R^{d1} , R^{e1} , R^{f1} , R^{h1} , R^{i1} , R^{j1} , R^{l1} , R^{m1} , R^{n1} , R^{o1} , R^{q1} , R^{r1} , R^{t1} , R^{u1} and R^{v1} independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ; or
25 or more substituents selected from W^3 ; or

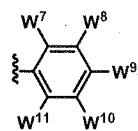
- any two R^{c1} and R^{d1} , R^{f1} and R^{g1} , R^{m1} and R^{n1} and/or R^{u1} and R^{v1} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two
30 heteroatoms and and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and $=O$;

- each R^{g1} , R^{k1} , R^{p1} and R^{s1} independently represent $-C_{1-6}$ alkyl optionally
35 substituted by one or more substituents selected from W^1 , heterocycloalkyl

optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

5 each Z^1 represents $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, or independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{e2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$;

10 heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl represented by



heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 ;

15 each Z^2 and Z^3 independently represents halogen, $-R^{a2}$, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{e2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

25 each Z^4 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{e2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , heteroaryl optionally substituted by one or more substituents selected from W^6 , or $=O$;

30 each R^{a2} , R^{b2} , R^{e2} , R^{d2} , R^{e2} , R^{f2} , R^{h2} , R^{i2} , R^{j2} , R^{l2} , R^{m2} , R^{n2} , R^{o2} , R^{r2} , R^{t2} , R^{u2} and R^{v2} independently represents hydrogen or C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or

more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; or

any two R^{c2} and R^{d2} , R^{f2} and R^{g2} , R^{m2} and R^{n2} and/or R^{u2} and R^{v2} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^5 ; C_{1-3} alkyl optionally substituted by one or more substituents selected from W^4 ; and $=O$;

each R^{g2} , R^{k2} , R^{p2} , R^{q2} and R^{s2} independently represent C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

R^{c2} , R^{f2} , R^{h2} , R^{l2} , R^{m2} , R^{o2} , and R^{u2} represents hydrogen; and R^{d2} , R^{g2} , R^{i2} , R^{n2} , R^{p2} , R^{q2} , R^{l2} and R^{v2} represents aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

each W^1 and W^4 independently represents halogen, $-CN$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl optionally substituted by one or more substituents selected from G^2 , or $=O$;

each W^2 , W^3 , W^5 and W^6 independently represents halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl (optionally substituted by one or more substituents selected from G^2 , or $=O$;

W^7 and W^{11} represents hydrogen;

each W^8 and W^{10} independently represents hydrogen, halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$,

-C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -N(R^{f3})R^{g3}, -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3},
 -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3}, -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3},
 -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally substituted by one or more
 5 substituents selected from G¹, aryl optionally substituted by one or more
 substituents selected from G², or heteroaryl optionally substituted by one or more
 substituents selected from G²;

W⁹ represents halogen, -R^{a3}, -CN, -C(O)R^{b3}, -C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -
 N(R^{f3})R^{g3},
 10 -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3}, -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3x},
 -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3}, -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally
 substituted by one or more substituents selected from G¹, aryl optionally
 substituted by one or more substituents selected from G², or heteroaryl optionally
 substituted by one or more substituents selected from G²;

15 each R^{a3}, R^{b3}, R^{c3}, R^{d3}, R^{e3}, R^{f3}, R^{h3}, Rⁱ³, R^{j3}, R^{l3}, R^{m3}, Rⁿ³, R^{o3}, R^{q3}, R^{r3}, R^{t3}, R^{u3}
 and R^{v3} independently represents hydrogen or -C₁₋₆ alkyl optionally substituted by
 one or more G³; or

20 any two R^{c3} and R^{d3}, R^{f3} and R^{g3}, R^{m3} and Rⁿ³ and/or R^{u3} and R^{v3} are linked
 together to form, along with the nitrogen atom to which they are attached, a 4- to
 6-membered ring, which ring optionally contains one heteroatom and which ring
 optionally is substituted by one or more G²;

25 each R^{g3}, R^{k3}, R^{p3}, ~~R^{q3}~~ and R^{s3} independently represent C₁₋₆ alkyl optionally
 substituted by one or more G³;

R^{q3x} represents C₂₋₆ alkyl optionally substituted by one or more G³;

30 each G¹ and G² independently represents halogen, -R^{a4}, -CN, -C(O)R^{b4},
 -C(O)N(R^{c4})R^{d4}, -C(O)OR^{e4}, -N(R^{f4})R^{g4}, -N(R^{h4})C(O)Rⁱ⁴, -N(R^{j4})C(O)OR^{k4},
 -N(R^{l4})C(O)N(R^{m4})Rⁿ⁴, -N(R^{o4})S(O)₂R^{p4}, -OR^{q4}, -OC(O)R^{r4}, -OS(O)₂R^{s4}, -S(O)_mR^{t4},
 -S(O)₂N(R^{u4})R^{v4}, or =O;

G^3 represents halogen, $-CN$, $-C(O)R^{b4}$, $-C(O)N(R^{c4})R^{d4}$, $-C(O)OR^{e4}$, $-N(R^{f4})R^{g4}$, $-N(R^{h4})C(O)R^{i4}$, $-N(R^{j4})C(O)OR^{k4}$, $-N(R^{l4})C(O)N(R^{m4})R^{n4}$, $-N(R^{o4})S(O)_2R^{p4}$, $-OR^{q4}$, $-OC(O)R^{r4}$, $-OS(O)_2R^{s4}$, $-S(O)_mR^{t4}$, $-S(O)_2N(R^{u4})R^{v4}$, or $=O$;

- 5 each R^{a4} , R^{b4} , R^{c4} , R^{d4} , R^{e4} , R^{f4} , R^{h4} , R^{i4} , R^{j4} , R^{l4} , R^{m4} , R^{n4} , R^{o4} , R^{q4} , R^{r4} , R^{t4} , R^{u4} and R^{v4} independently represents hydrogen or $-C_{1-6}$ alkyl optionally substituted by one or more $-F$; or

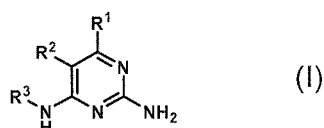
- any two R^{c4} and R^{d4} , R^{f4} and R^{g4} , R^{m4} and R^{n4} and/or R^{u4} and R^{v4} are linked
10 together to form, along with the nitrogen atom to which they are attached, a 3- to 6-membered ring, which ring optionally substituted by one or more $-F$, $-CH_3$, $-CH_2CH_3$, $-CHF_2$, $-CF_3$, $-CH_2CF_3$, or $=O$;

- each R^{g4} , R^{k4} , R^{p4} and R^{s4} independently represent C_{1-6} alkyl optionally
15 substituted by one or more $-F$;

each m independently represents 0, 1 or 2;

- provided that the compound is not
20 ~~6-(3-pyridinyl)- N^4 -[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-2,4-pyrimidinediamine,~~
~~6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyridinyl]methyl]-2,4-pyrimidinediamine,~~
~~6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyrimidinyl]-methyl]-2,4-pyrimidinediamine,~~
25 ~~N^4 -[2-(diethylamino)ethyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine,~~
 ~~N^4 -[3-(4-morpholinyl)propyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine, or~~
 ~~N^4 -[2-(4-morpholinyl)ethyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine.~~

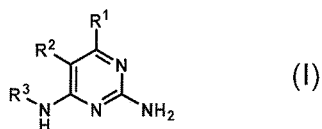
- 30 In yet another aspect embodiment, there is provided a compound of formula I,



or a pharmaceutically acceptable salt thereof,
wherein:

Claims

1. A compound of formula I,

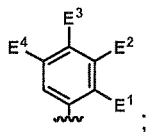


5 or a pharmaceutically acceptable salt thereof, wherein:

R¹ represents:

heteroaryl selected from benzofuran-3-yl, benzothiophen-3-yl,
 10 dihydrobenzofuran-7-yl, indol-3-yl, indol-4-yl, indol-5-yl, isoquinolin-4-yl, pyridin-3-yl, pyridin-4-yl, pyrrol-2-yl and quinolin-5-yl, which heteroaryl is connected to the pyrimidine of formula I via a carbon atom of the heteroaryl ring and which heteroaryl is optionally substituted by one or more substituents selected from Y¹, -C₁₋₆alkyl optionally substituted by one or more Y² and heterocycloalkyl optionally substituted by one or more Y³; or

15 aryl represented by



E³ and E⁴ represent hydrogen; and

E¹ represents -F and E² represent -F, -Cl, -CH₃ or -CF₃; or

20 E¹ represents -Cl and E² represents -F, -Cl, -CH₃ or -CF₃; or

E¹ represents -CH₃ and E² represents -F, -Cl, -CH₃, -CF₃, -CN or -N(H)C(O)CH=CH₂;

R² represents hydrogen;

25

R³ represents -C₂₋₆alkyl substituted by Z¹;

each Y¹ independently represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f, -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂,
 30 -N(Rⁿ)S(O)₂R^o, -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u,

heterocycloalkyl optionally substituted by one or more substituents selected from W², aryl optionally substituted by one or more substituents selected from W³, or

heteroaryl optionally substituted by one or more substituents selected from W³;

each R^a, R^b, R^c, R^d, R^e, R^g, R^h, Rⁱ, R^k, R^l, R^m, Rⁿ, R^p, R^q, R^s, R^t and R^u

independently represents hydrogen, -C₁₋₆ alkyl optionally substituted by one or
5 more substituents selected from W¹, heterocycloalkyl optionally substituted by
one or more substituents selected from W², aryl optionally substituted by one or
more substituents selected from W³, or heteroaryl optionally substituted by one or
more substituents selected from W³; or

10 any two R^b and R^c, R^e and R^f, Rⁱ and R^m and/or R^t and R^u are linked together to
form, along with the nitrogen atom to which they are attached, a 3- to 8-
membered monocyclic or bicyclic ring, which ring optionally contains one or two
heteroatoms and which ring optionally is substituted by one or more substituents
selected from W², C₁₋₃alkyl optionally substituted by one or more substituents
15 selected from W¹, and =O;

each R^f, R^j, R^o and R^r independently represent -C₁₋₆ alkyl optionally substituted by
one or more substituents selected from W¹, heterocycloalkyl optionally substituted
by one or more substituents selected from W², aryl optionally substituted by one
20 or more substituents selected from W³ or heteroaryl optionally substituted by one
or more substituents selected from W³;

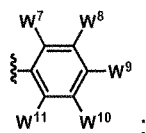
each Y² independently represents halogen, -CN, -C(O)R^{b1}, -C(O)N(R^{c1})R^{d1},
-C(O)OR^{e1}, -N(R^{f1})R^{g1}, -N(R^{h1})C(O)Rⁱ¹, -N(R^{l1})C(O)OR^{k1}, -N(R^{l1})C(O)N(R^{m1})Rⁿ¹,
25 -N(R^{o1})S(O)₂R^{p1}, -OR^{q1}, -OC(O)R^{r1}, -OS(O)₂R^{s1}, -S(O)_mR^{t1}, -S(O)₂N(R^{u1})R^{v1},
heterocycloalkyl optionally substituted by one or more substituents selected from
W¹, aryl optionally substituted by one or more substituents selected from W²,
heteroaryl optionally substituted by one or more substituents selected from W²;

30 each R^{b1}, R^{c1}, R^{d1}, R^{e1}, R^{f1}, R^{h1}, Rⁱ¹, R^{j1}, R^{l1}, R^{m1}, Rⁿ¹, R^{o1}, R^{q1}, R^{r1}, R^{t1}, R^{u1} and
R^{v1} independently represents hydrogen, C₁₋₆ alkyl optionally substituted by one or
more substituents selected from W¹, heterocycloalkyl optionally substituted by
one or more substituents selected from W², aryl optionally substituted by one or
more substituents selected from W³, or heteroaryl optionally substituted by one or
35 more substituents selected from W³; or

any two R^{c1} and R^{d1} , R^{f1} and R^{g1} , R^{m1} and R^{n1} and/or R^{u1} and R^{v1} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and $=O$;

each R^{g1} , R^{k1} , R^{p1} and R^{s1} independently represent $-C_{1-6}$ alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

Z^1 represents $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, or aryl represented by



R^{c2} , R^{f2} , R^{h2} , R^{i2} , R^{m2} , R^{o2} , and R^{u2} represents hydrogen; and R^{d2} , R^{g2} , R^{j2} , R^{n2} , R^{p2} , R^{q2} , R^{t2} and R^{v2} represents aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

each W^1 independently represents halogen, $-CN$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl optionally substituted by one or more substituents selected from G^2 , or $=O$;

each W^2 , W^3 , and W^6 independently represents halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more

substituents selected from G^2 , heteroaryl (optionally substituted by one or more substituents selected from G^2 , or =O;

W^7 and W^{11} represent hydrogen;

5

each W^8 and W^{10} independently represents hydrogen, halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$,

$-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$,
 $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$,

10 $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 ;

15 W^9 represents halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$,

$-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3x}$,
 $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally

20 substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 ;

each R^{a3} , R^{b3} , R^{c3} , R^{d3} , R^{e3} , R^{f3} , R^{h3} , R^{i3} , R^{j3} , R^{l3} , R^{m3} , R^{n3} , R^{o3} , R^{q3} , R^{r3} , R^{t3} , R^{u3}
and R^{v3} independently represents hydrogen or $-C_{1-6}$ alkyl optionally substituted by
25 one or more G^3 ; or

any two R^{c3} and R^{d3} , R^{f3} and R^{g3} , R^{m3} and R^{n3} and/or R^{u3} and R^{v3} are linked together to form, along with the nitrogen atom to which they are attached, a 4- to 6-membered ring, which ring optionally contains one heteroatom and which ring
30 optionally is substituted by one or more G^2 ;

each R^{g3} , R^{k3} , R^{p3} , and R^{s3} independently represent C_{1-6} alkyl optionally substituted by one or more G^3 ;

35 R^{q3x} represents C_{2-6} alkyl optionally substituted by one or more G^3 ;

each G^1 and G^2 independently represents halogen, $-R^{a4}$, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b4}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c4})\text{R}^{d4}$, $-\text{C}(\text{O})\text{OR}^{e4}$, $-\text{N}(\text{R}^{f4})\text{R}^{g4}$, $-\text{N}(\text{R}^{h4})\text{C}(\text{O})\text{R}^{i4}$, $-\text{N}(\text{R}^{j4})\text{C}(\text{O})\text{OR}^{k4}$, $-\text{N}(\text{R}^{l4})\text{C}(\text{O})\text{N}(\text{R}^{m4})\text{R}^{n4}$, $-\text{N}(\text{R}^{o4})\text{S}(\text{O})_2\text{R}^{p4}$, $-\text{OR}^{q4}$, $-\text{OC}(\text{O})\text{R}^{r4}$, $-\text{OS}(\text{O})_2\text{R}^{s4}$, $-\text{S}(\text{O})_m\text{R}^{t4}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u4})\text{R}^{v4}$, or $=\text{O}$;

5

G^3 represents halogen, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b4}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c4})\text{R}^{d4}$, $-\text{C}(\text{O})\text{OR}^{e4}$, $-\text{N}(\text{R}^{f4})\text{R}^{g4}$, $-\text{N}(\text{R}^{h4})\text{C}(\text{O})\text{R}^{i4}$, $-\text{N}(\text{R}^{j4})\text{C}(\text{O})\text{OR}^{k4}$, $-\text{N}(\text{R}^{l4})\text{C}(\text{O})\text{N}(\text{R}^{m4})\text{R}^{n4}$, $-\text{N}(\text{R}^{o4})\text{S}(\text{O})_2\text{R}^{p4}$, $-\text{OR}^{q4}$, $-\text{OC}(\text{O})\text{R}^{r4}$, $-\text{OS}(\text{O})_2\text{R}^{s4}$, $-\text{S}(\text{O})_m\text{R}^{t4}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u4})\text{R}^{v4}$, or $=\text{O}$;

- 10 each R^{a4} , R^{b4} , R^{c4} , R^{d4} , R^{e4} , R^{f4} , R^{h4} , R^{i4} , R^{j4} , R^{l4} , R^{m4} , R^{n4} , R^{o4} , R^{q4} , R^{r4} , R^{t4} , R^{u4} and R^{v4} independently represents hydrogen or $-\text{C}_{1-6}$ alkyl optionally substituted by one or more $-\text{F}$; or

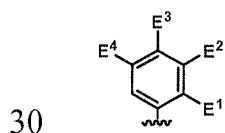
- 15 any two R^{c4} and R^{d4} , R^{f4} and R^{g4} , R^{m4} and R^{n4} and/or R^{u4} and R^{v4} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 6-membered ring, which ring optionally substituted by one or more $-\text{F}$, $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CHF}_2$, $-\text{CF}_3$, $-\text{CH}_2\text{CF}_3$, or $=\text{O}$;

- 20 each R^{g4} , R^{k4} , R^{p4} and R^{s4} independently represent C_{1-6} alkyl optionally substituted by one or more $-\text{F}$;

each m independently represents 0, 1 or 2.

- 25 2. A compound as claimed in Claim 1, wherein R^1 represents heteroaryl selected from benzofuran-3-yl, benzothiophen-3-yl, dihydrobenzofuran-7-yl, indol-3-yl, indol-4-yl, indol-5-yl, isoquinolin-4-yl, pyridin-3-yl, pyridin-4-yl, pyrrol-2-yl and quinolin-5-yl.

3. A compound as claimed in Claim 1, wherein R^1 represents



where:

E^3 and E^4 represent hydrogen; and

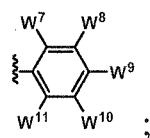
E^1 represents $-\text{F}$ and E^2 represent $-\text{F}$, $-\text{Cl}$, $-\text{CH}_3$ or $-\text{CF}_3$; or

E^1 represents $-\text{Cl}$ and E^2 represents $-\text{F}$, $-\text{Cl}$, $-\text{CH}_3$ or $-\text{CF}_3$; or

E¹ represents -CH₃ and E² represents -F, -Cl, -CH₃, -CF₃, -CN or -N(H)C(O)CH=CH₂.

4. A compound as claimed in any one of the Claims 1 to 3, wherein:

5 Z¹ represents



and

(a) W⁸ and W¹⁰ are independently selected from hydrogen, -F, -Cl, -CH₃, -CN, -CF₃; and

10 W⁹ is selected from -R^{a3}, -CN, -C(O)R^{b3}, -C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -N(R^{f3})R^{g3}, -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3}, -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3x}, -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3}, -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally substituted by one or more substituents selected from G¹, aryl optionally substituted by one or more substituents selected from G², or heteroaryl optionally substituted by one or more substituents selected from G²; or

15 (b) W⁹ and W¹⁰ are independently selected from hydrogen, -F, -Cl, -CH₃, -CN, -CF₃; and W⁸ is selected from -R^{a3}, -CN, -C(O)R^{b3}, -C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -N(R^{f3})R^{g3}, -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3}, -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3x}, -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3}, -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally substituted by one or more substituents selected from G¹, aryl optionally substituted by one or more substituents selected from G², or heteroaryl optionally substituted by one or more substituents selected from G².

5. A compound as claimed in any one of the Claims 1 to 4, wherein:

25 W⁸ and W¹⁰ represent hydrogen and W⁹ represents -F, -Cl, -CH₃, cyclopropyl, -CF₃, -CN, -NH₂, -N(CH₃)₂, -N(H)C(O)CH₃, -N(H)C(O)OC(CH₃)₃, -SO₂CH₃, -SO₂NH₂, -S(O)₂N(CH₃)₂, -S(O)₂-4-morpholinyl, 4-methylpiperazin-1-yl, 4-methylpiperidin-1-ylmethyl and 1,2,3-thiadiazol-4-yl.

30 6. A compound as claimed in Claim 1, selected from:

6-(2,3-dimethylphenyl)-4-N-(2-phenylethyl)pyrimidine-2,4-diamine;
6-(2,3-dimethylphenyl)-4-N-[2-(4-methoxyphenyl)ethyl]pyrimidine-2,4-diamine;
6-(2,3-dimethylphenyl)-4-N-[2-(4-methylphenyl)ethyl]pyrimidine-2,4-diamine;
4-N-[2-(4-chlorophenyl)ethyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;

- 6-(2,3-dimethylphenyl)-4-N-(2-phenylpropyl)pyrimidine-2,4-diamine;
 6-(2,3-dimethylphenyl)-4-N-(3-phenylpropyl)pyrimidine-2,4-diamine;
 6-(2,3-dimethylphenyl)-4-N-(2-phenoxyethyl)pyrimidine-2,4-diamine;
 6-(2,3-dimethylphenyl)-4-N-[2-(phenylamino)ethyl]pyrimidine-2,4-diamine;
 5 6-(2-chloro-3-methylphenyl)-4-N-[2-(4-chlorophenyl)ethyl]pyrimidine-2,4-diamine;
 4-N-[2-(4-chlorophenyl)ethyl]-6-(1H-indol-4-yl)pyrimidine-2,4-diamine;
 6-(3-chloro-2-methylphenyl)-4-N-[(1R)-1-phenylethyl]pyrimidine-2,4-diamine;
 6-(3-chloro-2-methylphenyl)-4-N-(2-phenylpropan-2-yl)pyrimidine-2,4-diamine;
 4-N-[2-(2-chlorophenoxy)ethyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 10 6-(2,3-dimethylphenyl)-4-N-[2-(pyridin-3-yloxy)propyl]pyrimidine-2,4-diamine;
 4-N-[2-(4-chlorophenyl)ethyl]-6-(2,3-dichlorophenyl)pyrimidine-2,4-diamine;
 4-N-[2-(4-chlorophenyl)ethyl]-6-(quinolin-5-yl)pyrimidine-2,4-diamine;
 4-N-[2-(4-chlorophenyl)cyclopropyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 15 3-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)phenol;
 4-N-[[1-(4-chlorophenyl)cyclopropyl]methyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 4-(2-[[2-amino-6-(2,3-dichlorophenyl)pyrimidin-4-yl]amino]ethyl)benzene-1-sulfonamide;
 20 4-(2-[[2-amino-6-(3-chloro-2-methylphenyl)pyrimidin-4-yl]amino]ethyl)benzene-1-sulfonamide;
 4-(2-[[2-amino-6-(2,3-dichlorophenyl)pyrimidin-4-yl]amino]ethyl)phenol;
 4-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)benzene-1-sulfonamide;
 25 6-(2,3-dimethylphenyl)-4-N-[2-(4-methanesulfonylphenyl)ethyl]pyrimidine-2,4-diamine;
 4-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)benzonitrile,
 4-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethoxy)benzonitrile,
 4-N-[2-(3-chlorophenyl)ethyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 30 4-N-[2-(4-chlorophenyl)propyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 6-(2,3-dimethylphenyl)-4-N-[2-(4-fluorophenyl)ethyl]pyrimidine-2,4-diamine;
 4-N-[2-(benzenesulfonyl)ethyl]-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 N-(3-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]propyl)-4-chlorobenzene-1-sulfonamide;
 35 3-(3-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]propyl)-1-(4-chlorophenyl)urea;

- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-3,5-dimethyl-1,2-oxazole-4-sulfonamide;
- 3-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-1-(2,6-dichloropyridin-4-yl)urea;
- 5 3-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-1-(3,4-difluorophenyl)urea;
- N-[3-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propoxy)phenyl]acetamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-3-
- 10 bromobenzamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)benzamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-3-cyanobenzene-1-sulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-4-
- 15 methanesulfonylbenzene-1-sulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)benzenesulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)-2,2-dimethylpropyl)-3-fluorobenzene-1-sulfonamide;
- 20 N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)-2,2-dimethylpropyl)-4-(morpholine-4-sulfonyl)benzene-1-sulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-3-fluorobenzene-1-sulfonamide;
- N-{4-([3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-
- 25 yl]amino)propyl)sulfamoyl]phenyl}acetamide;
- N-(2-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)ethyl)-3-fluorobenzene-1-sulfonamide;
- N-(2-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)ethyl)-4-methoxybenzene-1-sulfonamide;
- 30 N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-4,5-dichlorothiophene-2-sulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;
- N-(3-([2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino)propyl)-1,2-dimethyl-
- 35 1H-imidazole-4-sulfonamide;

- N-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;
- 4-N-{2-[(1,3-benzoxazol-2-yl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
- 5 6-(2,3-dimethylphenyl)-4-N-(4-phenylbutan-2-yl)pyrimidine-2,4-diamine;
- 6-[(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)amino]pyridine-3-carbonitrile,
- 4-N-{2-[(3-bromo-1,2,4-thiadiazol-5-yl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
- 10 N-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)-4-methanesulfonylbenzene-1-sulfonamide;
- N-(3-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]propyl)-3-methanesulfonylbenzene-1-sulfonamide;
- N-(3-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]propyl)-2-
- 15 methanesulfonylbenzene-1-sulfonamide;
- 4-(2-[[2-amino-6-(3-chloro-2-methylphenyl)pyrimidin-4-yl]amino]ethyl)-N,N-dimethylbenzene-1-sulfonamide;
- 4-(2-[[2-amino-6-(2,3-dichlorophenyl)pyrimidin-4-yl]amino]ethyl)-N,N-dimethylbenzene-1-sulfonamide;
- 20 4-(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)-N,N-dimethylbenzene-1-sulfonamide;
- 4-N-{1-[(4-chlorophenyl)methyl]cyclopropyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
- 4-N-[2-(4-chlorophenyl)ethyl]-6-(1H-pyrrol-2-yl)pyrimidine-2,4-diamine;
- 25 N-(4-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]butyl)-4-methanesulfonylbenzene-1-sulfonamide;
- 4-(2-[[2-amino-6-(3-cyano-2-methylphenyl)pyrimidin-4-yl]amino]ethyl)benzene-1-sulfonamide;
- 4-N-{2-[(6-chloropyridazin-3-yl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-
- 30 diamine;
- 2-[(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)amino]pyridine-4-carbonitrile,
- 6-[(2-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]ethyl)amino]pyridine-3-sulfonamide;
- 35 1-N-(3-[[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino]propyl)benzene-1,4-disulfonamide;

- 6-(2,3-dichlorophenyl)-4-N-[2-(4-methanesulfonylphenyl)ethyl]pyrimidine-2,4-diamine;
 6-(2,3-dimethylphenyl)-4-N-{2-[(3-methoxyphenyl)amino]ethyl}pyrimidine-2,4-diamine;
 5 6-(2,3-dimethylphenyl)-4-N-{2-[(3-fluoro-4-methylphenyl)amino]ethyl}pyrimidine-2,4-diamine;
 4-N-{2-[(3,4-dichlorophenyl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 4-N-{2-[(5-chloropyridin-2-yl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 10 4-N-{2-[(5-bromopyridin-2-yl)amino]ethyl}-6-(2,3-dimethylphenyl)pyrimidine-2,4-diamine;
 4-[(2-{[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino}ethyl)amino]benzene-1-sulfonamide; and
 15 6-(2,3-dimethylphenyl)-4-N-{2-[(pyridin-3-yl)amino]ethyl}pyrimidine-2,4-diamine;
 or a pharmaceutically acceptable salt thereof.

7. A compound as claimed in Claim 1, selected from:
 4-N-[2-(4-chlorophenyl)ethyl]-6-(2,3-dichlorophenyl)pyrimidine-2,4-diamine;
 20 4-(2-{[2-amino-6-(2,3-dichlorophenyl)pyrimidin-4-yl]amino}ethyl)benzene-1-sulfonamide;
 4-(2-{[2-amino-6-(3-chloro-2-methylphenyl)pyrimidin-4-yl]amino}ethyl)benzene-1-sulfonamide;
 4-(2-{[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino}ethyl)benzene-1-sulfonamide;
 25 6-(2,3-dimethylphenyl)-4-N-[2-(4-methanesulfonylphenyl)ethyl]pyrimidine-2,4-diamine;
 4-(2-{[2-amino-6-(3-chloro-2-methylphenyl)pyrimidin-4-yl]amino}ethyl)-N,N-dimethylbenzene-1-sulfonamide;
 30 4-(2-{[2-amino-6-(2,3-dichlorophenyl)pyrimidin-4-yl]amino}ethyl)-N,N-dimethylbenzene-1-sulfonamide;
 4-(2-{[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino}ethyl)-N,N-dimethylbenzene-1-sulfonamide;
 6-[(2-{[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino}ethyl)amino]pyridine-3-sulfonamide;
 35

6-(2,3-dichlorophenyl)-4-N-[2-(4-methanesulfonylphenyl)ethyl]pyrimidine-2,4-diamine; and
4-[(2-{[2-amino-6-(2,3-dimethylphenyl)pyrimidin-4-yl]amino}ethyl)amino]benzene-1-sulfonamide,

5 or a pharmaceutically acceptable salt thereof.

8. A pharmaceutical formulation comprising a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

10

9. Use of a pharmaceutical formulation as claimed in Claim 8, in the manufacture of a medicament for treating cancer.

15

10. Use of a compound as claimed in any one of the claims 1 to 7, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

20

11. Use of a formulation as claimed in Claim 9, or use of a compound as claimed in Claim 10, wherein the disease is selected from Soft Tissue Cancers: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung cancers/diseases: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal cancers/diseases: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract cancers/diseases: kidney (adenocarcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors,

35

- lipoma); Liver cancers/diseases: hepatoma (hepatocellular carcinoma),
 cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma,
 hemangioma; Bone cancers/diseases: osteogenic sarcoma (osteosarcoma),
 fibrosarcoma, malignant fibrous histiocyoma, chondrosarcoma, Ewing's sarcoma,
 5 malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant
 cell tumor chordoma, osteochondroma (osteochondrogenous exostoses), benign
 chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant
 cell tumors; Nervous system cancers/diseases: skull (osteoma, hemangioma,
 granuloma, xanthoma, osteitis deformans), meninges (meningioma,
 10 meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma,
 ependymoma, germinoma [pinealoma], glioblastoma multiforme,
 oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord
 neurofibroma, meningioma, glioma, sarcoma); Gynecological cancers/diseases:
 uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical
 15 dysplasia), ovaries (ovarian carcinoma [serous cystadenocarcinoma, mucinous
 cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors,
 Sertoli- Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous
 cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma,
 melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid
 20 sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma);
 Hematologic cancers/diseases: blood and bone marrow (myeloid leukemia [acute
 and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia,
 myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome),
 Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin
 25 cancers/diseases: malignant melanoma, basal cell carcinoma, squamous cell
 carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma,
 dermatofibroma, keloids; Adrenal glands cancers/diseases, neuroblastoma,
 neurofibromatosis and head and neck cancers.
- 30 12. Use of a compound or formulation as claimed in Claim 11, wherein the
 cancer is selected from the group consisting of breast cancers, prostate cancers,
 lung cancers, oesophageal cancers, colon cancers, brain cancers, skin cancers,
 ovarian cancers, testicular cancers, neurofibromatosis and leukemias.
- 35 13. A compound as claimed in any one of the Claims 1 to 7, or a
 pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

14. A combination product comprising:

(A) a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof; and

- 5 (B) one or more other therapeutic agent(s) that is/are useful in the treatment of a disease as defined in Claim 11 or 12,
wherein each one of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

- 10 15. A combination product as claimed in Claim 14, wherein component (B) is selected from the group consisting of anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors; kinase inhibitors; angiogenesis
15 inhibitors; immunotherapeutic agents; pro-apoptotic agents; and cell cycle signaling inhibitors.

16. A therapeutically effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, for use in therapy.

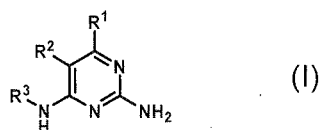
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17. Use of a compound as claimed in Claim 10, wherein the treatment further comprises radiation therapy.

25

Claims

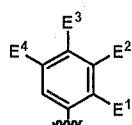
1. Use of a compound of formula I,



5

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein:

10 R¹ represents heteroaryl connected to the pyrimidine of formula I via a carbon atom of the heteroaryl ring, which heteroaryl ring is optionally substituted by one or more substituents selected from Y¹, -C₁₋₆alkyl optionally substituted by one or more Y² and heterocycloalkyl optionally substituted by one or more Y³; or aryl represented by



15

E¹ represents hydrogen, Y^{1a}, -C₁₋₆alkyl optionally substituted by one or more Y² or heterocycloalkyl optionally substituted by one or more Y³;

E² represents hydrogen, Y^{1b}, -C₁₋₆alkyl optionally substituted by one or more Y² or heterocycloalkyl optionally substituted by one or more Y³;

20 E³ and E⁴ each independently represents hydrogen, Y¹, -C₁₋₆alkyl optionally substituted by one or more Y² or heterocycloalkyl optionally substituted by one or more Y³;

25 R² represents hydrogen, halogen, -CN, -C₁₋₁₂alkyl optionally substituted by one or more Z¹, or heterocycloalkyl optionally substituted by one or more Z²;

R³ represents -C₁₋₁₂alkyl optionally substituted by one or more Z¹ or heterocycloalkyl optionally substituted by one or more Z²; or

30 R² and R³ are linked together to form, along with the atoms to which they are attached, a 5- to 8-membered non-aromatic ring, wherein the link formed by R² and R³ is optionally substituted by one or more substituents selected from Z³ and

-C₁₋₉alkyl optionally substituted by one or more Z⁴;

each Y¹ independently represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c,
-C(O)OR^d, -N(R^e)R^f, -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂,

- 5 -N(Rⁿ)S(O)₂R^o, -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u,
heterocycloalkyl optionally substituted by one or more substituents selected from
W², aryl optionally substituted by one or more substituents selected from W³ or
heteroaryl optionally substituted by one or more substituents selected from W³;

- 10 Y^{1a} represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f,
-N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂, -N(Rⁿ)S(O)₂R^o,
-OR^{px}, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u, heterocycloalkyl optionally
substituted by one or more substituents selected from W², aryl optionally
substituted by one or more substituents selected from W³ or heteroaryl optionally
15 substituted by one or more substituents selected from W³;

- Y^{1b} represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f,
-N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂, -N(Rⁿ)S(O)₂R^o,
-OR^{py}, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u, heterocycloalkyl optionally
20 substituted by one or more substituents selected from W², aryl optionally
substituted by one or more substituents selected from W³ or heteroaryl optionally
substituted by one or more substituents selected from W³;

- each R^a, R^b, R^c, R^d, R^e, R^g, R^h, Rⁱ, R^k, R^l, R^m, Rⁿ, R^p, R^q, R^s, R^t and R^u
25 independently represents hydrogen, -C₁₋₆ alkyl optionally substituted by one or
more substituents selected from W¹, heterocycloalkyl optionally substituted by
one or more substituents selected from W², aryl optionally substituted by one or
more substituents selected from W³, or heteroaryl optionally substituted by one or
more substituents selected from W³; or

- 30 any two R^b and R^c, R^e and R^f, Rⁱ and R^m and/or R^t and R^u are linked together to
form, along with the nitrogen atom to which they are attached, a 3- to 8-
membered monocyclic or bicyclic ring, which ring optionally contains one or two
further heteroatoms and which ring optionally is substituted by one or more

substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and =O;

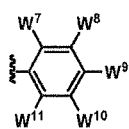
- 5 each R^f , R^j , R^o , R^r and R^{px} independently represents C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 or heteroaryl optionally substituted by one or more substituents selected from W^3 ;
- 10 R^{py} represents hydrogen, $-C_{2-6}$ alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;
- 15 each Y^2 independently represents halogen, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or =O;
- 20 each Y^3 independently represents halogen, $-R^{a1}$, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or =O;
- 25 each R^{a1} , R^{b1} , R^{c1} , R^{d1} , R^{e1} , R^{f1} , R^{h1} , R^{i1} , R^{j1} , R^{l1} , R^{m1} , R^{n1} , R^{o1} , R^{q1} , R^{r1} , R^{t1} , R^{u1} and R^{v1} independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^2 , or =O;
- 30
- 35

or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ; or

any two R^{c1} and R^{d1} , R^{f1} and R^{g1} , R^{m1} and R^{n1} and/or R^{u1} and R^{v1} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and =O;

each R^{q1} , R^{k1} , R^{p1} and R^{s1} independently represents $-C_{1-6}$ alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

each Z^1 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{i2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl represented by



heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 , or =O;

each Z^2 and Z^3 independently represents halogen, $-R^{a2}$, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{i2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

each Z^4 independently represents halogen, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b2}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c2})\text{R}^{d2}$, $-\text{C}(\text{O})\text{OR}^{e2}$, $-\text{N}(\text{R}^{f2})\text{R}^{g2}$, $-\text{N}(\text{R}^{h2})\text{C}(\text{O})\text{R}^{i2}$, $-\text{N}(\text{R}^{j2})\text{C}(\text{O})\text{OR}^{k2}$, $-\text{N}(\text{R}^{l2})\text{C}(\text{O})\text{N}(\text{R}^{m2})\text{R}^{n2}$, $-\text{N}(\text{R}^{o2})\text{S}(\text{O})_2\text{R}^{p2}$, $-\text{OR}^{q2}$, $-\text{OC}(\text{O})\text{R}^{r2}$, $-\text{OS}(\text{O})_2\text{R}^{s2}$, $-\text{S}(\text{O})_m\text{R}^{t2}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u2})\text{R}^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , heteroaryl optionally substituted by one or more substituents selected from W^6 , or $=\text{O}$;

each R^{a2} , R^{b2} , R^{c2} , R^{d2} , R^{e2} , R^{f2} , R^{h2} , R^{i2} , R^{j2} , R^{l2} , R^{m2} , R^{n2} , R^{o2} , R^{r2} , R^{t2} , R^{u2} and R^{v2} independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; or

any two R^{c2} and R^{d2} , R^{f2} and R^{g2} , R^{m2} and R^{n2} and/or R^{u2} and R^{v2} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^5 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^4 , and $=\text{O}$;

each R^{g2} , R^{k2} , R^{p2} , R^{q2} and R^{s2} independently represents C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

each W^1 and W^4 independently represents halogen, $-\text{CN}$, $-\text{N}(\text{R}^{f3})\text{R}^{g3}$, $-\text{N}(\text{R}^{h3})\text{C}(\text{O})\text{R}^{i3}$, $-\text{N}(\text{R}^{j3})\text{C}(\text{O})\text{OR}^{k3}$, $-\text{N}(\text{R}^{l3})\text{C}(\text{O})\text{N}(\text{R}^{m3})\text{R}^{n3}$, $-\text{N}(\text{R}^{o3})\text{S}(\text{O})_2\text{R}^{p3}$, $-\text{OR}^{q3}$, $-\text{OC}(\text{O})\text{R}^{r3}$, $-\text{OS}(\text{O})_2\text{R}^{s3}$, $-\text{S}(\text{O})_m\text{R}^{t3}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u3})\text{R}^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl optionally substituted by one or more substituents selected from G^2 , or $=\text{O}$;

each W^2 , W^3 , W^5 and W^6 independently represents halogen, $-R^{a3}$, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b3}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c3})\text{R}^{d3}$, $-\text{C}(\text{O})\text{OR}^{e3}$, $-\text{N}(\text{R}^{f3})\text{R}^{g3}$, $-\text{N}(\text{R}^{h3})\text{C}(\text{O})\text{R}^{i3}$, $-\text{N}(\text{R}^{j3})\text{C}(\text{O})\text{OR}^{k3}$, $-\text{N}(\text{R}^{l3})\text{C}(\text{O})\text{N}(\text{R}^{m3})\text{R}^{n3}$, $-\text{N}(\text{R}^{o3})\text{S}(\text{O})_2\text{R}^{p3}$, $-\text{OR}^{q3}$, $-\text{OC}(\text{O})\text{R}^{r3}$, $-\text{OS}(\text{O})_2\text{R}^{s3}$, $-\text{S}(\text{O})_m\text{R}^{t3}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u3})\text{R}^{v3}$, heterocycloalkyl optionally substituted by one or more
 5 substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl (optionally substituted by one or more substituents selected from G^2 , or $=\text{O}$;

each W^7 , W^8 , W^{10} and W^{11} independently represents hydrogen, halogen, $-R^{a3}$,
 10 $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b3}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c3})\text{R}^{d3}$, $-\text{C}(\text{O})\text{OR}^{e3}$, $-\text{N}(\text{R}^{f3})\text{R}^{g3}$, $-\text{N}(\text{R}^{h3})\text{C}(\text{O})\text{R}^{i3}$, $-\text{N}(\text{R}^{j3})\text{C}(\text{O})\text{OR}^{k3}$, $-\text{N}(\text{R}^{l3})\text{C}(\text{O})\text{N}(\text{R}^{m3})\text{R}^{n3}$, $-\text{N}(\text{R}^{o3})\text{S}(\text{O})_2\text{R}^{p3}$, $-\text{OR}^{q3}$, $-\text{OC}(\text{O})\text{R}^{r3}$, $-\text{OS}(\text{O})_2\text{R}^{s3}$, $-\text{S}(\text{O})_m\text{R}^{t3}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u3})\text{R}^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or
 15 more substituents selected from G^2 ;

W^9 represents hydrogen, halogen, $-R^{a3}$, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{b3}$, $-\text{C}(\text{O})\text{N}(\text{R}^{c3})\text{R}^{d3}$, $-\text{C}(\text{O})\text{OR}^{e3}$, $-\text{N}(\text{R}^{f3})\text{R}^{g3}$, $-\text{N}(\text{R}^{h3})\text{C}(\text{O})\text{R}^{i3}$, $-\text{N}(\text{R}^{j3})\text{C}(\text{O})\text{OR}^{k3}$, $-\text{N}(\text{R}^{l3})\text{C}(\text{O})\text{N}(\text{R}^{m3})\text{R}^{n3}$, $-\text{N}(\text{R}^{o3})\text{S}(\text{O})_2\text{R}^{p3}$, $-\text{OR}^{q3x}$, $-\text{OC}(\text{O})\text{R}^{r3}$, $-\text{OS}(\text{O})_2\text{R}^{s3}$, $-\text{S}(\text{O})_m\text{R}^{t3}$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{u3})\text{R}^{v3}$,
 20 heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 ;

each R^{a3} , R^{b3} , R^{c3} , R^{d3} , R^{e3} , R^{f3} , R^{h3} , R^{i3} , R^{j3} , R^{l3} , R^{m3} , R^{n3} , R^{o3} , R^{q3} , R^{r3} , R^{t3} , R^{u3}
 25 and R^{v3} independently represents hydrogen or C_{1-6} alkyl optionally substituted by one or more G^3 ; or

any two R^{c3} and R^{d3} , R^{f3} and R^{g3} , R^{m3} and R^{n3} and/or R^{u3} and R^{v3} are linked
 together to form, along with the nitrogen atom to which they are attached, a 4- to
 30 6-membered ring, which ring optionally contains one heteroatom and which ring optionally is substituted by one or more G^2 ;

each R^{g3} , R^{k3} , R^{p3} , R^{q3} and R^{s3} independently represents C_{1-6} alkyl optionally
 35 substituted by one or more G^3 ;

R^{q3x} represents C_{2-6} alkyl optionally substituted by one or more G^3 ;

each G^1 and G^2 independently represents halogen, $-R^{a4}$, $-CN$, $-C(O)R^{b4}$,
 $-C(O)N(R^{c4})R^{d4}$, $-C(O)OR^{e4}$, $-N(R^{f4})R^{g4}$, $-N(R^{h4})C(O)R^{i4}$, $-N(R^{j4})C(O)OR^{k4}$,
 5 $-N(R^{l4})C(O)N(R^{m4})R^{n4}$, $-N(R^{o4})S(O)_2R^{p4}$, $-OR^{q4}$, $-OC(O)R^{r4}$, $-OS(O)_2R^{s4}$, $-S(O)_mR^{t4}$,
 $-S(O)_2N(R^{u4})R^{v4}$, or $=O$;

G^3 represents halogen, $-CN$, $-C(O)R^{b4}$, $-C(O)N(R^{c4})R^{d4}$, $-C(O)OR^{e4}$, $-N(R^{f4})R^{g4}$,
 $-N(R^{h4})C(O)R^{i4}$, $-N(R^{j4})C(O)OR^{k4}$, $-N(R^{l4})C(O)N(R^{m4})R^{n4}$, $-N(R^{o4})S(O)_2R^{p4}$, $-OR^{q4}$,
 10 $-OC(O)R^{r4}$, $-OS(O)_2R^{s4}$, $-S(O)_mR^{t4}$, $-S(O)_2N(R^{u4})R^{v4}$, or $=O$;

each R^{a4} , R^{b4} , R^{c4} , R^{d4} , R^{e4} , R^{f4} , R^{h4} , R^{i4} , R^{j4} , R^{l4} , R^{m4} , R^{n4} , R^{o4} , R^{q4} , R^{r4} , R^{t4} , R^{u4}
 and R^{v4} independently represents hydrogen or C_{1-6} alkyl optionally substituted by
 one or more $-F$; or

15 any two R^{c4} and R^{d4} , R^{f4} and R^{g4} , R^{m4} and R^{n4} and/or R^{u4} and R^{v4} are linked
 together to form, along with the nitrogen atom to which they are attached, a 3- to
 6-membered ring, which ring optionally substituted by one or more $-F$, $-CH_3$,
 $-CH_2CH_3$, $-CHF_2$, $-CF_3$, $-CH_2CF_3$, or $=O$;

20 each R^{g4} , R^{k4} , R^{p4} and R^{s4} independently represent C_{1-6} alkyl optionally
 substituted by one or more $-F$;

each m independently represents 0, 1 or 2;

25 provided that the compound is not
 6-(3-pyridinyl)- N^4 -[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-2,4-
 pyrimidinediamine,
 6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyridinyl]methyl]-
 30 2,4-pyrimidinediamine,
 6-(3-pyridinyl)- N^4 -[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyrimidinyl]-
 methyl]-2,4-pyrimidinediamine or
 N^4 -[2-(1-aziridinyl)ethyl]-5-fluoro-6-phenyl-2,4-pyrimidinediamine.

2. The use as claimed in Claim 1, wherein:

R^2 represents hydrogen, halogen, -CN or $-C_{1-12}$ alkyl optionally substituted by one or more Z^1 ; and

R^3 represents $-C_{1-12}$ alkyl optionally substituted by one or more Z^1 or

5 heterocycloalkyl optionally substituted by one or more Z^2 .

3. The use as claimed in Claim 2, wherein:

R^2 represents hydrogen, -CN or $-C_{1-3}$ alkyl optionally substituted by one or more -F; and

10 R^3 represents $-C_{2-6}$ alkyl optionally substituted by one or more Z^1 or heterocycloalkyl optionally substituted by one or more Z^2 .

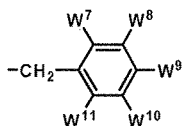
4. The use as claimed in Claim 3, wherein:

R^2 represents hydrogen; and

15 R^3 represents a $-C_{3-6}$ alkyl or a heterocycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopropylpropyl, oxetanyl, tetrahydrofuryl, tetrahydropyranyl, azetidiny, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl wherein the C_{3-6} alkyl is optionally substituted by one or more Z^1
20 and the heterocycloalkyl is optionally substituted by one or more Z^2 .

5. The use as claimed in Claim 2, wherein:

R^2 represents hydrogen and R^3 represents

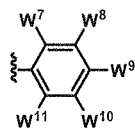


25 or heteroaryl (having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^3).

6. The use as claimed in any one of Claims 1 to 5 wherein:

Z^1 represents -F, -CN, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$,
30 $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$,
 $-S(O)_mR^{i2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl selected from dihydropyridinyl, morpholinyl, piperazinyl, piperidinyl and pyrrolidinyl which heterocycloalkyl is

optionally substituted by one or more substituents selected from W^5 , aryl represented by



heteroaryl selected from benzimidazolyl, benzodioxinyl, benzoxazolyl, furanyl,

- 5 imidazolyl, imidazopyridinyl, indolyl, isoquinolinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridyl, pyrrolopyridinyl, quinolinyl, thiazolyl, thiophenyl and triazolyl, which heteroaryl is optionally substituted by one or more substituents selected from W^6 ;

- 10 Z^2 represents $-F$, $-R^{a2}$, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

- 15 each W^7 , W^{10} and W^{11} independently represents hydrogen, halogen, $-R^{a3}$ or $-CN$; and

- one of W^8 and W^9 represents hydrogen, halogen, $-R^{a3}$ or $-CN$ and the other represents halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3x}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{l3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 .

25

7. The use as claimed in Claim 2, wherein:

R^2 represents hydrogen; and

R^3 represents $-C_{1-2}$ alkyl optionally substituted with one or more $-F$.

30

8. The use as claimed in Claim 1, wherein:

R^2 and R^3 are linked together to form, along with the atoms to which they are attached, a 5- to 6-membered non-aromatic ring, wherein the link formed by R^2

and R^3 is optionally substituted by one or more substituents selected from Z^3 and/or $-C_{1-9}$ alkyl optionally substituted by one or more Z^4 .

9. The use as claimed in Claim 8, wherein:

- 5 Z^3 is not present or is selected from $-F$, $-R^{a2}$, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; and/or
- 10 Z^4 is not present or is selected from $-F$, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 .
- 15 substituents selected from W^6 .

10. The use as claimed in any one of Claims 1 to 9 wherein:

- E^1 is Y^{1a} or $-C_{1-6}$ alkyl optionally substituted by one or more Y^2 and at least one of
- 20 E^2 , E^3 and E^4 represents Y^{1b} , $-C_{1-6}$ alkyl optionally substituted by one or more Y^2 .

11. The use as claimed in any one of Claims 1 to 10 wherein:

- Y^1 independently represents halogen, $-CN$, $-C(O)R^a$, $-C(O)N(R^b)R^c$, $-C(O)OR^d$, $-N(R^e)R^f$, $-N(R^g)C(O)R^h$, $-N(R^i)C(O)OR^j$, $-N(R^k)C(O)N(R^l)R^m$, $-NO_2$, $-N(R^n)S(O)_2R^o$,
- 25 $-OC(O)R^q$, $-OS(O)_2R^r$, $-S(O)_mR^s$ or $-S(O)_2N(R^t)R^u$;
- Y^{1a} represents halogen, $-CN$, $-C(O)R^a$, $-C(O)N(R^b)R^c$, $-C(O)OR^d$, $-N(R^e)R^f$, $-N(R^g)C(O)R^h$, $-N(R^i)C(O)OR^j$, $-N(R^k)C(O)N(R^l)R^m$, $-NO_2$, $-N(R^n)S(O)_2R^o$, $-OC(O)R^q$, $-OS(O)_2R^r$, $-S(O)_mR^s$ or $-S(O)_2N(R^t)R^u$; and
- Y^{1b} represents halogen, $-CN$, $-C(O)R^a$, $-C(O)N(R^b)R^c$, $-C(O)OR^d$, $-N(R^e)R^f$,
- 30 $-N(R^g)C(O)R^h$, $-N(R^i)C(O)OR^j$, $-N(R^k)C(O)N(R^l)R^m$, $-NO_2$, $-N(R^n)S(O)_2R^o$, $-OC(O)R^q$, $-OS(O)_2R^r$, $-S(O)_mR^s$ or $-S(O)_2N(R^t)R^u$.

12. The use as claimed in Claim 11 wherein:

- 35 E^1 , E^3 and E^4 represent hydrogen and

E^2 represents $-\text{CH}=\text{CHC}(\text{O})\text{OCH}_3$, $-\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}_2$, $-\text{CH}_2\text{OH}$,
 $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}_2$, $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CHCH}_2\text{NMe}_2$, $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CHPh}$,
 $-\text{N}(\text{H})\text{C}(\text{O})\text{C}\equiv\text{CH}$, $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}_2(\text{OH})$, $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}(\text{OH})\text{Ph}$, $-\text{N}(\text{H})\text{C}(\text{O})\text{C}(\text{O})\text{CH}_3$,
 $-\text{N}(\text{H})\text{C}(\text{O})\text{C}(\text{O})\text{Ph}$ or $-\text{N}(\text{H})\text{S}(\text{O})_2\text{CH}=\text{CH}_2$; or

5 E^1 , E^2 and E^4 represent hydrogen and

E^3 represents $-\text{CH}=\text{CH}_2$, $-\text{CH}=\text{CHC}(\text{O})\text{OH}$, $-\text{CH}=\text{CHC}(\text{O})\text{OCH}_3$, $-\text{CH}_2\text{NH}_2$,
 $-\text{CH}_2\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}_2$, $-\text{CH}_2\text{OH}$, $-\text{C}(\text{O})\text{H}$, $-\text{C}(\text{O})\text{CH}_3$, $-\text{C}(\text{O})\text{CF}_3$,
 $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}_2$; or

E^3 and E^4 represent hydrogen; and

10 E^1 represents $-\text{F}$ and E^2 represents $-\text{F}$, $-\text{Cl}$, or $-\text{CF}_3$; or

E^1 represents $-\text{Cl}$ and E^2 represents $-\text{Cl}$, $-\text{CH}_3$ or $-\text{CF}_3$; or

E^1 represents $-\text{CH}_3$ and E^2 represents $-\text{Cl}$, $-\text{CH}_3$, $-\text{CN}$ or $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}_2$; or

E^2 and E^4 represent hydrogen; and

E^1 and E^3 represent $-\text{F}$; or

15 E^1 represents $-\text{Cl}$ and E^3 represents $-\text{F}$ or $-\text{Cl}$; or

E^1 represents $-\text{CH}_3$ and E^3 represents $-\text{Cl}$; or

E^2 and E^3 represent hydrogen; and

E^1 represents $-\text{F}$ and E^4 represents $-\text{Cl}$, $-\text{CH}_3$ or $-\text{CN}$; or

E^1 represents $-\text{Cl}$ and E^4 represents $-\text{F}$, $-\text{Cl}$, $-\text{CH}_3$ or $-\text{CF}_3$; or

20 E^1 represents $-\text{CH}_3$ and E^4 represent, $-\text{Cl}$, $-\text{CH}_3$, $-\text{CF}_3$, $-\text{CN}$ or
 $-\text{N}(\text{H})\text{C}(\text{O})\text{CH}=\text{CH}$; or

E^1 represents $-\text{CF}_3$ and E^4 represents $-\text{F}$ or $-\text{CF}_3$; or

E^1 represents $-\text{CN}$ and E^4 represents $-\text{Cl}$; or

E^4 represents hydrogen; and

25 E^1 , E^2 and E^3 represent $-\text{F}$; or

E^1 and E^2 represent $-\text{CH}_3$ and E^3 represents $-\text{F}_3$; or

E^2 and E^3 represent $-\text{Cl}$ and E^1 represents $-\text{CH}_3$; or

E^2 represents hydrogen; and

E^1 , E^3 and E^4 represent $-\text{F}$; or

30 E^3 and E^4 represent $-\text{Cl}$ and E^1 represents $-\text{CH}_3$; or

E^1 and E^4 represent $-\text{CH}_3$ and E^3 represents $-\text{F}$ or $-\text{CH}_3$; or

E^1 represents $-\text{F}$, E^3 represents $-\text{CH}_3$ and E^4 represents $-\text{Cl}$; or

E^1 represents $-\text{Cl}$, E^3 represents $-\text{F}$ and E^4 represents $-\text{CH}_3$; or

E^1 represents $-\text{Cl}$, E^3 represents $-\text{CH}_3$ and E^4 represents $-\text{F}$; or

35 E^1 and E^4 represent $-\text{CH}_3$ and E^3 represents $-\text{F}$; or

E^1 represents $-CH_3$, E^3 represents $-CF_3$ and E^4 represents $-Cl$; or

E^1 represents hydrogen; and

E^2 and E^4 represent $-CH_3$ and E^3 represents $-OH$; or

E^3 represents hydrogen; and

5 E^1 and E^2 represent $-Cl$ and E^4 represents $-CH_3$.

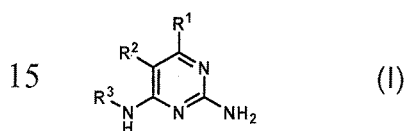
13. The use as claimed in any one of Claims 1 to 9 wherein:

R^1 represents heteroaryl.

10 14. The use as claimed in Claim 13 wherein:

R^1 represents benzofuranyl, benzothiophenyl, dihydrobenzofuranyl, indolyl, isoquinoliny, pyridinyl or quinoliny.

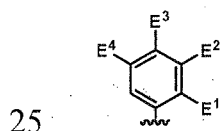
15. A compound of formula I,



or a pharmaceutically acceptable salt thereof, wherein:

R^1 represents:

indanyl, naphthyl, tetrahydronaphthyl or heteroaryl, the latter connected to the
20 pyrimidine of formula I via a carbon atom of the heteroaryl ring, which indanyl,
naphthyl, tetrahydronaphthyl and heteroaryl rings are optionally substituted by
one or more substituents selected from Y^1 , $-C_{1-6}$ alkyl optionally substituted by one
or more Y^2 and heterocycloalkyl optionally substituted by one or more Y^3 ; or
aryl represented by



E^1 , E^2 , E^3 and E^4 represents hydrogen, Y^1 , $-C_{1-6}$ alkyl optionally substituted by one
or more Y^2 or heterocycloalkyl optionally substituted by one or more Y^3 , but where
at least one of E^1 , E^2 , E^3 and E^4 is other than hydrogen;

R² represents hydrogen, halogen or -C₁₋₁₂alkyl optionally substituted by one or more Z¹;

5 R³ represents -C₁₋₁₂alkyl substituted by one or more Z¹ or heterocycloalkyl optionally substituted by one or more Z²; or

10 R² and R³ are linked together to form, along with the atoms to which they are attached, a 5- to 8-membered non-aromatic ring, wherein the link formed by R² and R³ is optionally substituted by one or more substituents selected from Z³ or -C₁₋₉alkyl optionally substituted by one or more Z⁴;

15 each Y¹ independently represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f, -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂, -N(Rⁿ)S(O)₂R^o, -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u, heterocycloalkyl optionally substituted by one or more substituents selected from W², aryl optionally substituted by one or more substituents selected from W³, or heteroaryl optionally substituted by one or more substituents selected from W³;

20 each R^a, R^b, R^c, R^d, R^e, R^g, R^h, Rⁱ, R^k, R^l, R^m, Rⁿ, R^p, R^q, R^s, R^t and R^u independently represents hydrogen, -C₁₋₆ alkyl optionally substituted by one or more substituents selected from W¹, heterocycloalkyl optionally substituted by one or more substituents selected from W², aryl optionally substituted by one or more substituents selected from W³, or heteroaryl optionally substituted by one or more substituents selected from W³; or

25

30 any two R^b and R^c, R^e and R^f, Rⁱ and R^m and/or R^t and R^u are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W², C₁₋₃alkyl optionally substituted by one or more substituents selected from W¹, and =O;

35 each R^f, R^j, R^o and R^r independently represent -C₁₋₆ alkyl optionally substituted by one or more substituents selected from W¹, heterocycloalkyl optionally substituted

by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

- 5 each Y^2 independently represents halogen, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 ,
 10 heteroaryl optionally substituted by one or more substituents selected from W^2 ;

- each Y^3 independently represents halogen, $-R^{a1}$, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$,
 15 heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or $=O$;

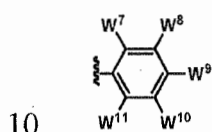
- 20 each R^{a1} , R^{b1} , R^{c1} , R^{d1} , R^{e1} , R^{f1} , R^{h1} , R^{i1} , R^{j1} , R^{l1} , R^{m1} , R^{n1} , R^{o1} , R^{q1} , R^{r1} , R^{t1} , R^{u1} and R^{v1} independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ; or
 25

- any two R^{c1} and R^{d1} , R^{f1} and R^{g1} , R^{m1} and R^{n1} and/or R^{u1} and R^{v1} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two
 30 heteroatoms and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^1 , and $=O$;

- each R^{g1} , R^{k1} , R^{p1} and R^{s1} independently represent $-C_{1-6}$ alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl
 35

optionally substituted by one or more substituents selected from W^2 , aryl
optionally substituted by one or more substituents selected from W^3 , or heteroaryl
optionally substituted by one or more substituents selected from W^3 ;

- 5 each Z^1 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$,
 $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$,
 $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$,
heterocycloalkyl optionally substituted by one or more substituents selected from
 W^5 , aryl represented by



heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom
and optionally substituted by one or more substituents selected from W^6 ;

- each Z^2 and Z^3 independently represents halogen, $-R^{a2}$, $-CN$, $-C(O)R^{b2}$,
15 $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$,
 $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$,
 $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more
substituents selected from W^5 , aryl optionally substituted by one or more
substituents selected from W^6 , or heteroaryl optionally substituted by one or more
20 substituents selected from W^6 ;

- each Z^4 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$,
 $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$,
 $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$,
25 heterocycloalkyl optionally substituted by one or more substituents selected from
 W^5 , aryl optionally substituted by one or more substituents selected from W^6 ,
heteroaryl optionally substituted by one or more substituents selected from W^6 , or
 $=O$;

- 30 each R^{a2} , R^{b2} , R^{c2} , R^{d2} , R^{e2} , R^{f2} , R^{h2} , R^{i2} , R^{j2} , R^{l2} , R^{m2} , R^{n2} , R^{o2} , R^{r2} , R^{t2} , R^{u2} and
 R^{v2} independently represents hydrogen or C_{1-6} alkyl optionally substituted by one
or more substituents selected from W^4 , heterocycloalkyl optionally substituted by
one or more substituents selected from W^5 , aryl optionally substituted by one or

more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; or

any two R^{c2} and R^{d2} , R^{f2} and R^{g2} , R^{m2} and R^{n2} and/or R^{u2} and R^{v2} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^5 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^4 , and =O;

each R^{q2} , R^{k2} , R^{p2} , R^{q2} and R^{s2} independently represent $-C_{1-6}$ alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ;

each W^1 and W^4 independently represents halogen, $-CN$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl optionally substituted by one or more substituents selected from G^2 , or =O;

each W^2 , W^3 , W^5 and W^6 independently represents halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl (optionally substituted by one or more substituents selected from G^2 , or =O;

W^7 and W^{11} represents hydrogen;

each W^8 and W^{10} independently represents hydrogen, halogen, $-R^{a3}$, $-CN$, $-C(O)R^{b3}$,

- C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -N(R^{f3})R^{g3}, -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3},
 -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3}, -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3},
 -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally substituted by one or more
 substituents selected from G¹, aryl optionally substituted by one or more
 5 substituents selected from G², or heteroaryl optionally substituted by one or more
 substituents selected from G²;

- W^a represents halogen, -R^{a3}, -CN, -C(O)R^{b3}, -C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -
 N(R^{f3})R^{g3},
 10 -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3}, -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3x},
 -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3}, -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally
 substituted by one or more substituents selected from G¹, aryl optionally
 substituted by one or more substituents selected from G², or heteroaryl optionally
 substituted by one or more substituents selected from G²;

- 15 each R^{a3}, R^{b3}, R^{c3}, R^{d3}, R^{e3}, R^{f3}, R^{h3}, Rⁱ³, R^{j3}, R^{l3}, R^{m3}, Rⁿ³, R^{o3}, R^{q3}, R^{r3}, R^{t3}, R^{u3}
 and R^{v3} independently represents hydrogen or -C₁₋₆ alkyl optionally substituted by
 one or more G³; or
 20 any two R^{c3} and R^{d3}, R^{f3} and R^{g3}, R^{m3} and Rⁿ³ and/or R^{u3} and R^{v3} are linked
 together to form, along with the nitrogen atom to which they are attached, a 4-
 to 6-membered ring, which ring optionally contains one heteroatom and which ring
 optionally is substituted by one or more G²;

- 25 each R^{g3}, R^{k3}, R^{p3}, R^{q3} and R^{s3} independently represent C₁₋₆ alkyl optionally
 substituted by one or more G³;

R^{q3x} represents C₂₋₆ alkyl optionally substituted by one or more G³;

- 30 each G¹ and G² independently represents halogen, -R^{a4}, -CN, -C(O)R^{b4},
 -C(O)N(R^{c4})R^{d4}, -C(O)OR^{e4}, -N(R^{f4})R^{g4}, -N(R^{h4})C(O)Rⁱ⁴, -N(R^{j4})C(O)OR^{k4},
 -N(R^{l4})C(O)N(R^{m4})Rⁿ⁴, -N(R^{o4})S(O)₂R^{p4}, -OR^{q4}, -OC(O)R^{r4}, -OS(O)₂R^{s4}, -S(O)_mR^{t4},
 -S(O)₂N(R^{u4})R^{v4}, or =O;

G³ represents halogen, -CN, -C(O)R^{b4}, -C(O)N(R^{c4})R^{d4}, -C(O)OR^{e4}, -N(R^{f4})R^{g4}, -N(R^{h4})C(O)Rⁱ⁴, -N(R^{j4})C(O)OR^{k4}, -N(R^{l4})C(O)N(R^{m4})Rⁿ⁴, -N(R^{o4})S(O)₂R^{p4}, -OR^{q4}, -OC(O)R^{r4}, -OS(O)₂R^{s4}, -S(O)_mRⁱ⁴, -S(O)₂N(R^{u4})R^{v4}, or =O;

- 5 each R^{a4}, R^{b4}, R^{c4}, R^{d4}, R^{e4}, R^{f4}, R^{h4}, Rⁱ⁴, R^{j4}, R^{l4}, R^{m4}, Rⁿ⁴, R^{o4}, R^{q4}, R^{r4}, R^{t4}, R^{u4} and R^{v4} independently represents hydrogen or -C₁₋₆ alkyl optionally substituted by one or more -F; or

- 10 any two R^{c4} and R^{d4}, R^{f4} and R^{g4}, R^{m4} and Rⁿ⁴ and/or R^{u4} and R^{v4} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 6-membered ring, which ring optionally substituted by one or more -F, -CH₃, -CH₂CH₃, -CHF₂, -CF₃, -CH₂CF₃, or =O;

- 15 each R^{g4}, R^{k4}, R^{p4} and R^{s4} independently represent C₁₋₆ alkyl optionally substituted by one or more -F;

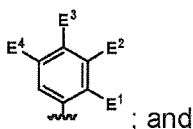
each m independently represents 0, 1 or 2;

- 20 provided that the compound is not
 6-(3-pyridinyl)-N⁴-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-2,4-pyrimidinediamine,
 6-(3-pyridinyl)-N⁴-[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyridinyl]methyl]-2,4-pyrimidinediamine,
 6-(3-pyridinyl)-N⁴-[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-pyrimidinyl]-methyl]-2,4-pyrimidinediamine,
 25 N⁴-[2-(diethylamino)ethyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine,
 N⁴-[3-(4-morpholinyl)propyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine, or
 N⁴-[2-(4-morpholinyl)ethyl]-6-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine.

- 30 16. A compound as claimed in Claim 15 wherein:

R¹ represents heteroaryl connected to the pyrimidine of formula I via a carbon atom of the heteroaryl ring, which heteroaryl is optionally substituted by one or more substituents selected from Y¹, or -C₁₋₆alkyl optionally substituted by one or more Y²; or

- 35 aryl represented by



; and

R² represents hydrogen or methyl; and

R³ represents -C₁₋₆alkyl substituted by Z¹ or heterocycloalkyl optionally substituted by one or more Z².

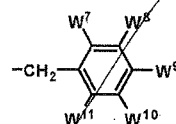
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17. A compound as claimed in Claim 16 wherein:

R² represents hydrogen and R³ represents -C₂₋₆alkyl substituted by Z¹.

18. A compound as claimed in Claim 16 wherein:

10 R² represents hydrogen and R³ represents



19. A compound as claimed in Claim 16 wherein:

R² represents hydrogen and Z¹ represents heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and which heteroaryl is optionally substituted by one or more substituents selected from W³.

15

20. A compound as claimed in Claim 16 wherein:

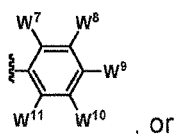
R² represents hydrogen and R³ represents -C₃₋₆alkyl or a heterocycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopropylpropyl, oxetanyl, tetrahydrofuryl, tetrahydropyranyl, azetidiny, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl wherein the C₃₋₆alkyl is substituted by one or two Z¹ and the heterocycloalkyl is optionally substituted by one or two Z².

25

21. A compound as claimed in any one of Claims 16, 17, 18 and 20 wherein:

Z¹ represents halogen, -CN, -C(O)R^{b2}, -C(O)N(R^{c2})R^{d2}, -C(O)OR^{e2}, -N(R^{f2})R^{g2}, -N(R^{h2})C(O)Rⁱ², -N(R^{l2})C(O)N(R^{m2})Rⁿ², -N(R^{o2})S(O)₂R^{p2}, -OR^{q2}, -S(O)_mRⁱ², -S(O)₂N(R^{u2})R^{v2}, heterocycloalkyl optionally substituted by one or more substituents selected from W⁵, aryl represented by

30

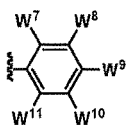


, or

heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 .

- 5 22. A compound as claimed in Claim 21 wherein:

Z^1 represents -F, -CN, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl represented by



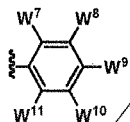
, or

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heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 .

23. A compound as claimed in Claim 22 wherein:

- 15 Z^1 represents $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$ or aryl represented by



; and

R^{c2} , R^{f2} , R^{h2} , R^{l2} , R^{m2} , R^{o2} , and R^{u2} represents hydrogen; and

- 20 R^{d2} , R^{g2} , R^{i2} , R^{n2} , R^{p2} , R^{q2} , R^{l2} and R^{v2} represents aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 .

24. A compound as claimed in Claim 15, wherein:

- 25 R^2 and R^3 are linked together to form, along with the atoms to which they are attached, a 5- to 6-membered non-aromatic ring, wherein the link formed by R^2 and R^3 is optionally substituted by one or more substituents selected from Z^3 and/or $-C_{1-9}$ alkyl optionally substituted by one or more Z^4 .

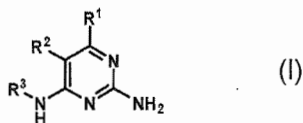
25. A compound as claimed in Claim 24, wherein:

- Z^3 is not present or is selected from -F, $-R^{a2}$, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; and/or
- Z^4 is not present or is selected from -F, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 .

26. A compound as claimed in any one of Claims 15 to 25 wherein:
- E^2 , E^3 and E^4 represent hydrogen and E^1 represents -F, -Cl, $-CH_3$, $-CF_3$, CN or $-OCH_3$; or
- E^1 , E^3 and E^4 represent hydrogen and E^2 represents -F, -Cl, $-CH_3$, $-CF_3$, -CN; or
- E^1 , E^2 and E^4 represent hydrogen and E^3 represents -F, -Cl, $-CH_3$, $-CF_3$, $-C(CH_3)_3$, $-CH=CH_2$, $-OCF_3$, $-S(O)_2CH_3$, or $-S(O)_2(4\text{-morpholinyl})$; or
- E^3 and E^4 represent hydrogen; and
- E^1 represents -F and E^2 represent -F, -Cl, $-CH_3$ or $-CF_3$; or
- E^1 represents -Cl and E^2 represents -F, -Cl, $-CH_3$ or $-CF_3$; or
- E^1 represents $-CH_3$ and E^2 represents -F, -Cl, $-CH_3$, $-CF_3$ or -CN; or
- E^2 and E^4 represent hydrogen; and
- E^1 represents -Cl and E^3 represents -F or -Cl; or
- E^1 represents $-CH_3$ and E^3 represents -Cl; or
- E^1 represents $-OCH_3$ and E^3 represents -F; or
- E^2 and E^3 represent hydrogen; and
- E^1 represents -F and E^4 represents -Cl, $-CH_3$ or -CN; or
- E^1 represents -Cl and E^4 represent -F, -Cl, $-CH_3$, $-CF_3$ or $-OCH_3$; or
- E^1 represents $-CH_3$ and E^4 represent -F, -Cl, $-CH_3$, $-CF_3$ or -CN; or
- E^1 represents $-CF_3$ and E^4 represents -F or $-CF_3$; or
- E^1 represents -CN and E^4 represents -Cl; or
- E^1 represents $-OCH_3$ and E^4 represents -F, -Cl, Br, $-CH_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, -CN or $-OCH_3$; or

- E¹ and E⁴ represent hydrogen; and
E² represents -F and E³ represents -F, -Cl, -OH or -OCH₃; or
E² represents -Cl and E³ represents -F; or
E² represents -CH₃ and E³ represents -F or -OCH₃; or
5 E¹ represents -OCH₃ and E³ represents -OH; or
E¹ and E³ represent hydrogen; and
E² and E⁴ represent -F; or
E² and E⁴ represent -CF₃; or
E⁴ represents hydrogen; and
10 E¹, E² and E³ represent -F; or
E¹ and E² represent -Cl and E³ represents -Cl, -OH or -OCH₃; or
E¹ and E² represent -CH₃ and E³ represents -F or -OCH₃; or
E² and E³ represent -Cl and E¹ represents -CH₃; or
E² represents hydrogen; and
15 E¹, E³ and E⁴ represent -F; or
E³ and E⁴ represent -Cl and E¹ represents -CH₃; or
E¹ and E⁴ represent -Cl and E¹ represents -OCH₃; or
E¹ and E⁴ represent -CH₃ and E³ represents -F, -CH₃ or -OCH₃; or
E¹ represents -F, E³ represents -CH₃ and E⁴ represents -Cl; or
20 E¹ represents -Cl, E³ represents -F and E⁴ represents -CH₃; or
E¹ represents -Cl, E³ represents -CH₃ and E⁴ represents -F; or
E¹ and E⁴ represent -CH₃ and E³ represents -F; or
E¹ represents -CH₃, E⁴ represents -Cl and E³ represents -CF₃ or -OCH₃; or
E¹ represents hydrogen; and
25 E² and E⁴ represent -CH₃ and E³ represents -OH; or
E³ represents hydrogen; and
E¹ and E² represent -Cl and E⁴ represents -CH₃.
27. A compound as claimed in any one of Claims 16 to 25 wherein:
30 R¹ represents heteroaryl.
28. A compound as claimed in Claim 27 wherein:
R¹ represents benzofuranyl, benzothiophenyl, dihydrobenzofuranyl, indolyl,
isoquinolinyl, pyridinyl and quinolinyl.

29. A compound of formula I,



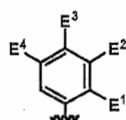
or a pharmaceutically acceptable salt thereof,
wherein:

5

R¹ represents heteroaryl connected to the pyrimidine of formula I via a carbon atom of the heteroaryl ring, which heteroaryl ring is substituted by one or more substituents selected from Y¹, -C₁₋₆alkyl optionally substituted by one or more Y² and heterocycloalkyl optionally substituted by one or more Y³; or aryl represented

10

by



E¹ represents Y^{1a} or -C₁₋₆alkyl optionally substituted by one or more Y²; and
at least one of E², E³ and E⁴ represents Y^{1b} or -C₁₋₆alkyl optionally substituted by
one or more Y²;

15

R² represents hydrogen, halogen, -CN, -C₁₋₁₂alkyl optionally substituted by one or more Z¹, or heterocycloalkyl optionally substituted by one or more Z²;

20

R³ represents -C₁₋₁₂alkyl optionally substituted by one or more Z¹ or
heterocycloalkyl optionally substituted by one or more Z²; or

25

R² and R³ are linked together to form, along with the atoms to which they are
attached, a 5- to 8-membered non-aromatic ring, wherein the link formed by R²
and R³ is optionally substituted by one or more substituents selected from Z³ and
-C₁₋₉alkyl optionally substituted by one or more Z⁴;

30

each Y¹ independently represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c,
-C(O)OR^d, -N(R^e)R^f, -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂,
-N(Rⁿ)S(O)₂R^o, -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u,
heterocycloalkyl optionally substituted by one or more substituents selected from
W², aryl optionally substituted by one or more substituents selected from W³ or

heteroaryl optionally substituted by one or more substituents selected from W^3 ;

Y^{1a} represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f,
 -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂, -N(Rⁿ)S(O)₂R^o,
 5 -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u, heterocycloalkyl optionally
 substituted by one or more substituents selected from W^2 , aryl optionally
 substituted by one or more substituents selected from W^3 or heteroaryl optionally
 substituted by one or more substituents selected from W^3 ;

10 Y^{1b} represents halogen, -CN, -C(O)R^a, -C(O)N(R^b)R^c, -C(O)OR^d, -N(R^e)R^f,
 -N(R^g)C(O)R^h, -N(Rⁱ)C(O)OR^j, -N(R^k)C(O)N(R^l)R^m, -NO₂, -N(Rⁿ)S(O)₂R^o,
 -OR^p, -OC(O)R^q, -OS(O)₂R^r, -S(O)_mR^s, -S(O)₂N(R^t)R^u, heterocycloalkyl optionally
 substituted by one or more substituents selected from W^2 , aryl optionally
 substituted by one or more substituents selected from W^3 or heteroaryl optionally
 15 substituted by one or more substituents selected from W^3 ;

each R^a, R^b, R^c, R^d, R^e, R^g, R^h, Rⁱ, R^k, R^l, R^m, Rⁿ, R^p, R^q, R^s, R^t and R^u
 independently represents hydrogen, -C₁₋₆ alkyl optionally substituted by one or
 more substituents selected from W^1 , heterocycloalkyl optionally substituted by
 20 one or more substituents selected from W^2 , aryl optionally substituted by one or
 more substituents selected from W^3 , or heteroaryl optionally substituted by one or
 more substituents selected from W^3 ; or

any two R^b and R^c, R^g and R^f, R^l and R^m and/or R^t and R^u are linked together to
 25 form, along with the nitrogen atom to which they are attached, a 3- to 8-
 membered monocyclic or bicyclic ring, which ring optionally contains one or two
 further heteroatoms and which ring optionally is substituted by one or more
 substituents selected from W^2 , C₁₋₃alkyl optionally substituted by one or more
 substituents selected from W^1 , and =O;

30 each R^f, R^j, R^o, R^r and R^{px} independently represents C₁₋₆ alkyl optionally
 substituted by one or more substituents selected from W^1 , heterocycloalkyl
 optionally substituted by one or more substituents selected from W^2 , aryl
 optionally substituted by one or more substituents selected from W^3 or heteroaryl
 35 optionally substituted by one or more substituents selected from W^3 ;

each Y^2 independently represents halogen, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$,

- 5 heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 , heteroaryl optionally substituted by one or more substituents selected from W^2 , or $=O$;

- 10 each Y^3 independently represents halogen, $-R^{a1}$, $-CN$, $-C(O)R^{b1}$, $-C(O)N(R^{c1})R^{d1}$, $-C(O)OR^{e1}$, $-N(R^{f1})R^{g1}$, $-N(R^{h1})C(O)R^{i1}$, $-N(R^{j1})C(O)OR^{k1}$, $-N(R^{l1})C(O)N(R^{m1})R^{n1}$, $-N(R^{o1})S(O)_2R^{p1}$, $-OR^{q1}$, $-OC(O)R^{r1}$, $-OS(O)_2R^{s1}$, $-S(O)_mR^{t1}$, $-S(O)_2N(R^{u1})R^{v1}$,

- heterocycloalkyl optionally substituted by one or more substituents selected from W^1 , aryl optionally substituted by one or more substituents selected from W^2 ,
15 heteroaryl optionally substituted by one or more substituents selected from W^2 , or $=O$;

each R^{a1} , R^{b1} , R^{c1} , R^{d1} , R^{e1} , R^{f1} , R^{h1} , R^{i1} , R^{j1} , R^{l1} , R^{m1} , R^{n1} , R^{o1} , R^{q1} , R^{r1} , R^{t1} , R^{u1} and R^{v1} independently represents hydrogen, C_{1-6} alkyl optionally substituted by

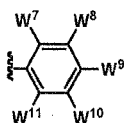
- 20 one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ; or

- 25 any two R^{c1} and R^{d1} , R^{f1} and R^{g1} , R^{m1} and R^{n1} and/or R^{u1} and R^{v1} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^2 , C_{1-3} alkyl optionally substituted by one or more substituents
30 selected from W^1 , and $=O$;

each R^{g1} , R^{k1} , R^{p1} and R^{s1} independently represents $-C_{1-6}$ alkyl optionally substituted by one or more substituents selected from W^1 , heterocycloalkyl optionally substituted by one or more substituents selected from W^2 , aryl

optionally substituted by one or more substituents selected from W^3 , or heteroaryl optionally substituted by one or more substituents selected from W^3 ;

- 5 each Z^1 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl represented by



- 10 heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 , or $=O$;

- each Z^2 and Z^3 independently represents halogen, $-R^{a2}$, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ,

- 20 each Z^4 independently represents halogen, $-CN$, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-OC(O)R^{r2}$, $-OS(O)_2R^{s2}$, $-S(O)_mR^{t2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , heteroaryl optionally substituted by one or more substituents selected from W^6 , or $=O$;

- each R^{a2} , R^{b2} , R^{c2} , R^{d2} , R^{e2} , R^{f2} , R^{h2} , R^{i2} , R^{j2} , R^{l2} , R^{m2} , R^{n2} , R^{o2} , R^{q2} , R^{r2} , R^{t2} , R^{u2} and R^{v2} independently represents hydrogen, C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one

or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 ; or

5 any two R^{c2} and R^{d2} , R^{f2} and R^{g2} , R^{m2} and R^{n2} and/or R^{u2} and R^{v2} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 8-membered monocyclic or bicyclic ring, which ring optionally contains one or two heteroatoms and which ring optionally is substituted by one or more substituents selected from W^5 , C_{1-3} alkyl optionally substituted by one or more substituents selected from W^4 , and =O;

10 each R^{g2} , R^{k2} , R^{p2} and R^{s2} independently represents C_{1-6} alkyl optionally substituted by one or more substituents selected from W^4 , heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl
15 optionally substituted by one or more substituents selected from W^6 ;

each W^1 and W^4 independently represents halogen, -CN, $-N(R^{f3})R^{g3}$,
- $N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$,
- $OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally
20 substituted by one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , heteroaryl optionally substituted by one or more substituents selected from G^2 , or =O;

each W^2 , W^3 , W^5 and W^6 independently represents halogen, $-R^{a3}$, -CN, $-C(O)R^{b3}$,
25 $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$, $-N(R^{j3})C(O)OR^{k3}$,
- $N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$, $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$,
- $S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by one or more
substituents selected from G^1 , aryl optionally substituted by one or more
substituents selected from G^2 , heteroaryl (optionally substituted by one or more
30 substituents selected from G^2 , or =O;

each W^7 , W^8 , W^9 , W^{10} and W^{11} independently represents hydrogen, halogen,
- R^{a3} , -CN, $-C(O)R^{b3}$, $-C(O)N(R^{c3})R^{d3}$, $-C(O)OR^{e3}$, $-N(R^{f3})R^{g3}$, $-N(R^{h3})C(O)R^{i3}$,
- $N(R^{j3})C(O)OR^{k3}$, $-N(R^{l3})C(O)N(R^{m3})R^{n3}$, $-N(R^{o3})S(O)_2R^{p3}$, $-OR^{q3}$, $-OC(O)R^{r3}$,
35 $-OS(O)_2R^{s3}$, $-S(O)_mR^{t3}$, $-S(O)_2N(R^{u3})R^{v3}$, heterocycloalkyl optionally substituted by

one or more substituents selected from G^1 , aryl optionally substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 ;

- 5 each R^{a3} , R^{b3} , R^{c3} , R^{d3} , R^{e3} , R^{f3} , R^{h3} , R^{i3} , R^{j3} , R^{l3} , R^{m3} , R^{n3} , R^{o3} , R^{q3} , R^{r3} , R^{t3} , R^{u3} and R^{v3} independently represents hydrogen or C_{1-6} alkyl optionally substituted by one or more G^3 ; or

- 10 any two R^{c3} and R^{d3} , R^{f3} and R^{g3} , R^{m3} and R^{n3} and/or R^{u3} and R^{v3} are linked together to form, along with the nitrogen atom to which they are attached, a 4- to 6-membered ring, which ring optionally contains one heteroatom and which ring optionally is substituted by one or more G^2 ;

- 15 each R^{g3} , R^{k3} , R^{p3} , R^{q3} and R^{s3} independently represents C_{1-6} alkyl optionally substituted by one or more G^3 ;

- 20 each G^1 and G^2 independently represents halogen, $-R^{a4}$, $-CN$, $-C(O)R^{b4}$, $-C(O)N(R^{c4})R^{d4}$, $-C(O)OR^{e4}$, $-N(R^{f4})R^{g4}$, $-N(R^{h4})C(O)R^{i4}$, $-N(R^{j4})C(O)OR^{k4}$, $-N(R^{l4})C(O)N(R^{m4})R^{n4}$, $-N(R^{o4})S(O)_2R^{p4}$, $-OR^{q4}$, $-OC(O)R^{r4}$, $-OS(O)_2R^{s4}$, $-S(O)_mR^{t4}$, $-S(O)_2N(R^{u4})R^{v4}$, or $=O$;

- 25 G^3 represents halogen, $-CN$, $-C(O)R^{b4}$, $-C(O)N(R^{c4})R^{d4}$, $-C(O)OR^{e4}$, $-N(R^{f4})R^{g4}$, $-N(R^{h4})C(O)R^{i4}$, $-N(R^{j4})C(O)OR^{k4}$, $-N(R^{l4})C(O)N(R^{m4})R^{n4}$, $-N(R^{o4})S(O)_2R^{p4}$, $-OR^{q4}$, $-OC(O)R^{r4}$, $-OS(O)_2R^{s4}$, $-S(O)_mR^{t4}$, $-S(O)_2N(R^{u4})R^{v4}$, or $=O$;

- each R^{a4} , R^{b4} , R^{c4} , R^{d4} , R^{e4} , R^{f4} , R^{h4} , R^{i4} , R^{j4} , R^{l4} , R^{m4} , R^{n4} , R^{o4} , R^{q4} , R^{r4} , R^{t4} , R^{u4} and R^{v4} independently represents hydrogen or C_{1-6} alkyl optionally substituted by one or more $-F$; or

- 30 any two R^{c4} and R^{d4} , R^{f4} and R^{g4} , R^{m4} and R^{n4} and/or R^{u4} and R^{v4} are linked together to form, along with the nitrogen atom to which they are attached, a 3- to 6-membered ring, which ring optionally substituted by one or more $-F$, $-CH_3$, $-CH_2CH_3$, $-CHF_2$, $-CF_3$, $-CH_2CF_3$, or $=O$;

each R^{g4} , R^{k4} , R^{p4} and R^{s4} independently represent C_{1-6} alkyl optionally substituted by one or more -F;

each m independently represents 0, 1 or 2;

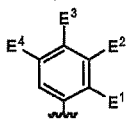
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provided that the compound is not

N^4 -cyclopropyl-6-(4-methoxy-2-methylphenyl)-2,4-pyrimidinediamine.

30. A compound as claimed in Claim 29, wherein:

10 R^1 is represented by



and;

E^3 and E^4 represent hydrogen; and

E^1 represents -F and E^2 represent -F, -Cl, -CH₃ or -CF₃; or

E^1 represents -Cl and E^2 represents -F, -Cl, -CH₃ or -CF₃; or

15 E^1 represents -CH₃ and E^2 represents -F, -Cl, -CH₃, -CF₃, -CN or -N(H)C(O)CH=CH₂; or

E^2 and E^4 represent hydrogen; and

E^1 represents -F and E^3 represents -F or phenyl; or

E^1 represents -Cl and E^3 represents -F or -Cl; or

20 E^1 represents -CH₃ and E^3 represents -Cl or -OCH₂phenyl; or

E^1 represents -OCH₃ and E^3 represents -F; or

E^2 and E^3 represent hydrogen; and

E^1 represents -F and E^4 represents -Cl, -CH₃ or -CN; or

E^1 represents -Cl and E^4 represent -F, -Cl, -CH₃, -CF₃ or -OCH₃; or

25 E^1 represents -CH₃ and E^4 represent -F, -Cl, -CH₃, -CF₃, -CN, -N(H)C(O)CH=CH₂ or -S(O)₂(4-morpholinyl); or

E^1 represents -CF₃ and E^4 represents -F or -CF₃; or

E^1 represents -CN and E^4 represents -Cl; or

E^1 represents -OCH₃ and E^4 represents -F, -Cl, Br, -CH₃, -CH(CH₃)₂, -C(CH₃)₃,

30 -CN or -OCH₃; or

E^1 and E^4 represent hydrogen; and

E^2 represents -F and E^3 represents -F, -Cl, -OH or -OCH₃; or

E^2 represents -Cl and E^3 represents -F or -C(O)(4-morpholinyl); or

- E² represents -CH₃ and E³ represents -F or -OCH₃; or
E¹ represents -OCH₃ and E³ represents -OH; or
E¹ represents -CH₂OCH₃ and E³ represents (piperidin-4-yl)methoxy or
((1-*tert*butoxycarbonyl)piperidin-4-yl)methoxy; or
- 5 E¹ and E³ represent hydrogen; and
E² and E⁴ represent -F; or
E² and E⁴ represent -CF₃; or
E⁴ represents hydrogen; and
E¹, E² and E³ represent -F; or
- 10 E¹ and E² represent -Cl and E³ represents -Cl, -OH or -OCH₃; or
E¹ and E² represent -CH₃ and E³ represents -F or -OCH₃; or
E² and E³ represent -Cl and E¹ represents -CH₃; or
E² represents hydrogen; and
E¹, E³ and E⁴ represent -F; or
- 15 E³ and E⁴ represent -Cl and E¹ represents -CH₃; or
E¹ and E⁴ represent -Cl and E¹ represents -OCH₃; or
E¹ and E⁴ represent -CH₃ and E³ represents -F, -CH₃ or -OCH₃; or
E¹ represents -F, E³ represents -CH₃ and E⁴ represents -Cl; or
E¹ represents -Cl, E³ represents -F and E⁴ represents -CH₃; or
- 20 E¹ represents -Cl, E³ represents -CH₃ and E⁴ represents -F; or
E¹ and E⁴ represent -CH₃ and E³ represents -F; or
E¹ represents -CH₃, E⁴ represents -Cl and E³ represents -CF₃ or -OCH₃; or
E¹ represents hydrogen; and
E² and E⁴ represent -CH₃ and E³ represents -OH; or
- 25 E³ represents hydrogen; and
E¹ and E² represent -Cl and E⁴ represents -CH₃.
31. A compound as claimed in Claim 30, wherein:
E³ and E⁴ represent hydrogen; and
- 30 E¹ represents -F and E² represents -F, -Cl, or -CF₃; or
E¹ represents -Cl and E² represents -Cl, -CH₃ or -CF₃; or
E¹ represents -CH₃ and E² represents -Cl, -CH₃, -CN or -N(H)C(O)CH=CH₂; or
E² and E⁴ represent hydrogen; and
E¹ and E³ represent -F; or
- 35 E¹ represents -Cl and E³ represents -F or -Cl; or

- E¹ represents -CH₃ and E³ represents -Cl; or
E² and E³ represent hydrogen; and
E¹ represents -F and E⁴ represents -Cl, -CH₃ or -CN; or
E¹ represents -Cl and E⁴ represents -F, -Cl, -CH₃ or -CF₃; or
5 E¹ represents -CH₃ and E⁴ represent, -Cl, -CH₃, -CF₃, -CN or
-N(H)C(O)CH=CH; or
E¹ represents -CF₃ and E⁴ represents -F or -CF₃; or
E¹ represents -CN and E⁴ represents -Cl; or
E⁴ represents hydrogen; and
10 E¹, E² and E³ represent -F; or
E¹ and E² represent -CH₃ and E³ represents -F₃; or
E² and E³ represent -Cl and E¹ represents -CH₃; or
E² represents hydrogen; and
E¹, E³ and E⁴ represent -F; or
15 E³ and E⁴ represent -Cl and E¹ represents -CH₃; or
E¹ and E⁴ represent -CH₃ and E³ represents -F or -CH₃; or
E¹ represents -F, E³ represents -CH₃ and E⁴ represents -Cl; or
E¹ represents -Cl, E³ represents -F and E⁴ represents -CH₃; or
E¹ represents -Cl, E³ represents -CH₃ and E⁴ represents -F; or
20 E¹ and E⁴ represent -CH₃ and E³ represents -F; or
E¹ represents -CH₃, E³ represents -CF₃ and E⁴ represents -Cl; or
E¹ represents hydrogen; and
E² and E⁴ represent -CH₃ and E³ represents -OH; or
E³ represents hydrogen; and
25 E¹ and E² represent -Cl and E⁴ represents -CH₃.
32. A compound as claimed in any one of Claims 29 to 31, wherein:
R² represents hydrogen, halogen, -CN or -C₁₋₆alkyl optionally substituted by one
or more Z¹.
- 30 33. A compound as claimed in Claim 32, wherein:
R² represents hydrogen or methyl.
34. A compound as claimed in any one of Claims 29 to 33, wherein:
35 R³ represents -C₁₋₆alkyl optionally substituted by Z¹.

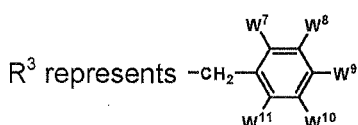
35. A compound as claimed in any one of Claims 29 to 33, wherein:
 R^3 represents $-C_{2-6}$ alkyl optionally substituted by Z^1 or heterocycloalkyl optionally substituted by Z^2 .

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36. A compound as claimed in any one of Claims 29 to 33, wherein:
 R^3 represents $-C_{1-2}$ alkyl optionally substituted with one or more -F.

37. A compound as claimed in any one of Claims 29 to 33, wherein:

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38. A compound as claimed in any one of Claims 29 to 33, wherein:
 R^3 represents $-C_{1-6}$ alkyl substituted by heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and which heteroaryl is optionally substituted by one or more substituents selected from W^3

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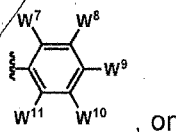
39. A compound as claimed in any one of Claims 29 to 33, wherein:
 R^3 represents $-C_{3-6}$ alkyl or a heterocycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopropylpropyl, oxetanyl, tetrahydrofuryl, tetrahydropyranyl, azetidiny, pyrrolidiny, piperidiny, piperaziny or morpholiny wherein the C_{3-6} alkyl is optionally substituted by Z^1 and the heterocycloalkyl is optionally substituted by Z^2 .

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40. A compound as claimed in any one of Claims 34, 35, 38 and 39 wherein:
 Z^1 represents -F, -CN, $-C(O)R^{b2}$, $-C(O)N(R^{c2})R^{d2}$, $-C(O)OR^{e2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{i2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl represented by

30



heteroaryl having 1 to 3 nitrogen atoms, one oxygen atom and/or one sulfur atom and optionally substituted by one or more substituents selected from W^6 .

41. A compound as claimed in Claim 40 wherein:

- 5 Z^1 represents -F, -CN, -C(O)NH₂, -C(O)N(R^{c2})R^{d2}, -C(O)-(4-morpholinyl), -C(O)OEt, -N(H)C(O)Me, -N(H)C(O)Rⁱ², -N(H)C(O)CH₂NMe₂, -N(H)C(O)OCMe₃, -N(H)C(O)OCH₂Ph, -N(Me)C(O)OCMe₃, -N(H)C(O)N(H)Me, -N(H)C(O)N(H)CHMe₂, -N(H)S(O)₂Me, -OMe, -OCF₃, -OEt, or heterocycloalkyl selected from dihydropyridinyl, imidazolinyl, morpholinyl, oxanyl, piperazinyl, 10 piperidinyl, pyrrolidinyl and quinuclidinyl, wherein the heterocycloalkyl is optionally substituted by one or more substituents selected from W^5 .

42. A compound as claimed in Claim 40 wherein:

- each W^7 , W^{10} and W^{11} independently represents hydrogen, halogen, -R^{a3} or -CN; 15 and one of W^8 and W^9 represents hydrogen, halogen, -R^{a3} or -CN and the other represents halogen, -R^{a3}, -CN, -C(O)R^{b3}, -C(O)N(R^{c3})R^{d3}, -C(O)OR^{e3}, -N(Rⁱ³)R^{g3}, -N(R^{h3})C(O)Rⁱ³, -N(R^{j3})C(O)OR^{k3}, -N(R^{l3})C(O)N(R^{m3})Rⁿ³, -N(R^{o3})S(O)₂R^{p3}, -OR^{q3x}, -OC(O)R^{r3}, -OS(O)₂R^{s3}, -S(O)_mR^{t3}, -S(O)₂N(R^{u3})R^{v3}, heterocycloalkyl optionally substituted by one or more substituents selected from G^1 , aryl optionally 20 substituted by one or more substituents selected from G^2 , or heteroaryl optionally substituted by one or more substituents selected from G^2 .

43. A compound as claimed in any one of Claims 29 to 31, wherein:

- R^2 and R^3 are linked together to form, along with the atoms to which they are 25 attached, a 5- to 6-membered non-aromatic ring, wherein the link formed by R^2 and R^3 is optionally substituted by one or more substituents selected from Z^3 or -C₁₋₉alkyl optionally substituted by one or more Z^4 .

44. A compound as claimed in Claim 43, wherein:

- 30 Z^3 is not present or is selected from -F, -R^{a2}, -C(O)N(R^{c2})R^{d2}, -N(R^{f2})R^{g2}, -N(R^{h2})C(O)Rⁱ², -N(R^{j2})C(O)OR^{k2}, -N(R^{l2})C(O)N(R^{m2})Rⁿ², -N(R^{o2})S(O)₂R^{p2}, -OR^{q2}, -S(O)_mRⁱ², -S(O)₂N(R^{u2})R^{v2}, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more 35 substituents selected from W^6 ; and/or

(b) Z^4 is not present or is selected from $-F$, $-C(O)N(R^{c2})R^{d2}$, $-N(R^{f2})R^{g2}$, $-N(R^{h2})C(O)R^{i2}$, $-N(R^{j2})C(O)OR^{k2}$, $-N(R^{l2})C(O)N(R^{m2})R^{n2}$, $-N(R^{o2})S(O)_2R^{p2}$, $-OR^{q2}$, $-S(O)_mR^{l2}$, $-S(O)_2N(R^{u2})R^{v2}$, heterocycloalkyl optionally substituted by one or more substituents selected from W^5 , aryl optionally substituted by one or more substituents selected from W^6 , or heteroaryl optionally substituted by one or more substituents selected from W^6 .

45. A pharmaceutical formulation comprising a compound as claimed in any one of Claims 15 to 44, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

46. Use of a pharmaceutical formulation as claimed in Claim 45, in the manufacture of a medicament for treating cancer.

47. Use of a compound as claimed in any one of the claims 15 to 44, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

48. Use of a compound as claimed in any one of Claims 1 to 14, or use of a formulation as claimed in Claim 46, or use of a compound as claimed in Claim 47, wherein the disease is selected from Soft Tissue Cancers: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung cancers/diseases: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal cancers/diseases: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract cancers/diseases: kidney (adenocarcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis

(seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver cancers/diseases: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Bone cancers/diseases: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochondroma (osteochondrogenous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system cancers/diseases: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma [pinealoma], glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological cancers/diseases: uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma [serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors, Sertoli- Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic cancers/diseases: blood and bone marrow (myeloid leukemia [acute and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin cancers/diseases: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids; Adrenal glands cancers/diseases, neuroblastoma, neurofibromatosis and head and neck cancers.

49. Use of a compound or formulation as claimed in Claim 48, wherein the cancer is selected from the group consisting of breast cancers, prostate cancers, lung cancers, oesophageal cancers, colon cancers, brain cancers, skin cancers, ovarian cancers, testicular cancers, neurofibromatosis and leukemias.

50. A compound as claimed in any one of the Claims 15 to 44, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

51. A combination product comprising:

- 5 (A) a compound as claimed in any one of Claims 15 to 44, or a pharmaceutically acceptable salt thereof; and
(B) one or more other therapeutic agent(s) that is/are useful in the treatment of a disease as defined in Claim 48 or 49,
wherein each one of components (A) and (B) is formulated in admixture with a
10 pharmaceutically-acceptable adjuvant, diluent or carrier.

52. A combination product as claimed in Claim 51, wherein component (B) is selected from the group consisting of anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II
15 inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors; kinase inhibitors; angiogenesis inhibitors; immunotherapeutic agents; pro-apoptotic agents; and cell cycle signaling inhibitors.

20 53. A therapeutically effective amount of a compound as claimed in any one of Claims 15 to 44, or a pharmaceutically acceptable salt thereof, for use in therapy.

25 54. Use of a compound as claimed in any one of Claims 1 to 14 or Claim 47, wherein the treatment further comprises radiation therapy.