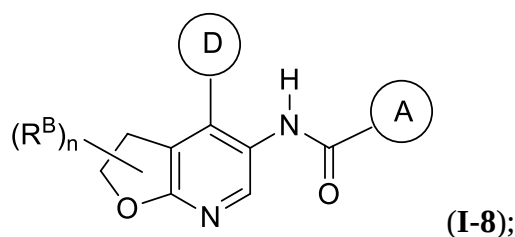


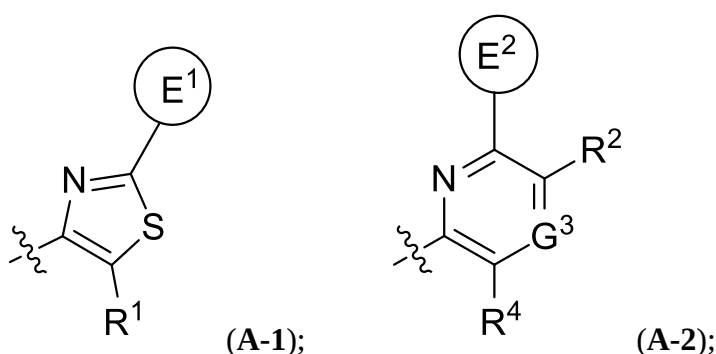
What is claimed is:

1. A compound of Formula (I-8):



or a pharmaceutically acceptable salt thereof, wherein:

- 5 A and D are rings;
 ring A is of the formula (A-1) or (A-2):



wherein E¹ and E² are rings;

wherein n is selected from 0, 1, 2 and 3;

- 10 ring D is a piperidine ring, which is substituted by k substituents
 independently selected from R^D, wherein k is 0, 1, 2 or 3;

 ring E¹ is phenyl optionally substituted by 1, 2 or 3, substituents independently
 selected from R^E;

- ring E² is phenyl optionally substituted by 1, 2 or 3, substituents independently
 15 selected from R^E;

 G³ is N or CR³;

 R¹ is selected from H, F and NH₂;

 R² is selected from H, halo and CN;

 R³ is selected from H, halo and CN;

- 20 R⁴ is selected from H, F and NH₂;

 each R^B is independently selected from Cy^B, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆
 alkynyl, C₁₋₆ haloalkyl, CN, NO₂, OR^{a1}, SR^{a1}, C(O)R^{b1}, C(O)NR^{c1}R^{d1}, C(O)OR^{a1},
 OC(O)R^{b1}, OC(O)NR^{c1}R^{d1}, C(=NR^{e1})NR^{c1}R^{d1}, NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}, NR^{c1}R^{d1},
 NR^{c1}C(O)R^{b1}, NR^{c1}C(O)OR^{a1}, NR^{c1}C(O)NR^{c1}R^{d1}, NR^{c1}S(O)R^{b1}, NR^{c1}S(O)₂R^{b1},

$C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$, $NR^{c4}R^{d4}$,
 $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$, $NR^{c4}C(O)NR^{c4}R^{d4}$, $C(=NR^{e4})R^{b4}$, $C(=NR^{e4})NR^{c4}R^{d4}$,
 $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)R^{b4}$,
 $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$, and $S(O)_2NR^{c4}R^{d4}$, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6}
 5 alkynyl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered
 heterocycloalkyl substituents of Cy^B or Cy^E are each optionally substituted with 1, 2
 or 3 substituents independently selected from halo, C_{1-4} haloalkyl, CN, NO_2 , OR^{a4} ,
 SR^{a4} , $C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$,
 $C(=NR^{e4})NR^{c4}R^{d4}$, $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$, $NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$,
 10 $NR^{c4}C(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)R^{b4}$,
 $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$ and $S(O)_2NR^{c4}R^{d4}$;

each R^{a1} , R^{b1} , R^{c1} , R^{d1} , R^{a2} , R^{c2} , R^{d2} , R^{a3} , R^{b3} , R^{c3} , R^{d3} , R^{a4} , R^{b4} , R^{c4} and R^{d4} is
 independently selected from H, C_{1-6} alkyl, C_{1-4} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl,
 C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered
 15 heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, (5-10 membered
 heteroaryl)- C_{1-4} alkyl or (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, wherein said
 C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered
 heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4}
 alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl and (4-10 membered heterocycloalkyl)-
 20 C_{1-4} alkyl is optionally substituted with 1, 2, 3, 4, or 5 substituents independently
 selected from C_{1-4} alkyl, C_{1-4} haloalkyl, halo, CN, OR^{a5} , SR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$,
 $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$,
 $NR^{c5}C(O)OR^{a5}$, $C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$,
 $S(O)_2R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$ and $S(O)_2NR^{c5}R^{d5}$;

25 or any R^{c1} and R^{d1} attached to the same N atom, together with the N atom to
 which they are attached, form a 4-, 5-, 6- or 7-membered heterocycloalkyl group
 optionally substituted with 1, 2 or 3 substituents independently selected from C_{1-6}
 alkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, C_{6-10} aryl, 5-6 membered
 heteroaryl, C_{1-6} haloalkyl, halo, CN, OR^{a5} , SR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)OR^{a5}$,
 30 $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$,
 $NR^{c5}C(O)OR^{a5}$, $C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$,
 $S(O)_2R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$ and $S(O)_2NR^{c5}R^{d5}$, wherein said C_{1-6}
 alkyl, C_{3-7} cycloalkyl, 4-7 membered heterocycloalkyl, C_{6-10} aryl and 5-6 membered
 heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected

from halo, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ cyanoalkyl, CN, OR^{a5}, SR^{a5}, C(O)R^{b5}, C(O)NR^{c5}R^{d5}, C(O)OR^{a5}, OC(O)R^{b5}, OC(O)NR^{c5}R^{d5}, NR^{c5}R^{d5}, NR^{c5}C(O)R^{b5}, NR^{c5}C(O)NR^{c5}R^{d5}, NR^{c5}C(O)OR^{a5}, C(=NR^{e5})NR^{c5}R^{d5}, NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}, S(O)R^{b5}, S(O)NR^{c5}R^{d5}, S(O)₂R^{b5}, NR^{c5}S(O)₂R^{b5}, NR^{c5}S(O)₂NR^{c5}R^{d5} and S(O)₂NR^{c5}R^{d5};

or any R^{c2} and R^{d2} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6- or 7-membered heterocycloalkyl group optionally substituted with 1, 2 or 3 substituents independently selected from C₁₋₆ alkyl, C₃₋₇ cycloalkyl, 4-7 membered heterocycloalkyl, C₆₋₁₀ aryl, and 5-6 membered heteroaryl, C₁₋₆ haloalkyl, halo, CN, OR^{a5}, SR^{a5}, C(O)R^{b5}, C(O)NR^{c5}R^{d5}, C(O)OR^{a5}, OC(O)R^{b5}, OC(O)NR^{c5}R^{d5}, NR^{c5}R^{d5}, NR^{c5}C(O)R^{b5}, NR^{c5}C(O)NR^{c5}R^{d5}, NR^{c5}C(O)OR^{a5}, C(=NR^{e5})NR^{c5}R^{d5}, NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}, S(O)R^{b5}, S(O)NR^{c5}R^{d5}, S(O)₂R^{b5}, NR^{c5}S(O)₂R^{b5}, NR^{c5}S(O)₂NR^{c5}R^{d5} and S(O)₂NR^{c5}R^{d5}, wherein said C₁₋₆ alkyl, C₃₋₇ cycloalkyl, 4-7 membered heterocycloalkyl, C₆₋₁₀ aryl and 5-6 membered heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected from halo, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ cyanoalkyl, CN, OR^{a5}, SR^{a5}, C(O)R^{b5}, C(O)NR^{c5}R^{d5}, C(O)OR^{a5}, OC(O)R^{b5}, OC(O)NR^{c5}R^{d5}, NR^{c5}R^{d5}, NR^{c5}C(O)R^{b5}, NR^{c5}C(O)NR^{c5}R^{d5}, NR^{c5}C(O)OR^{a5}, C(=NR^{e5})NR^{c5}R^{d5}, NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}, S(O)R^{b5}, S(O)NR^{c5}R^{d5}, S(O)₂R^{b5}, NR^{c5}S(O)₂R^{b5}, NR^{c5}S(O)₂NR^{c5}R^{d5} and S(O)₂NR^{c5}R^{d5};

or any R^{c3} and R^{d3} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6- or 7-membered heterocycloalkyl group optionally substituted with 1, 2 or 3 substituents independently selected from C₁₋₆ alkyl, C₃₋₇ cycloalkyl, 4-7 membered heterocycloalkyl, C₆₋₁₀ aryl, 5-6 membered heteroaryl, C₁₋₆ haloalkyl, halo, CN, OR^{a5}, SR^{a5}, C(O)R^{b5}, C(O)NR^{c5}R^{d5}, C(O)OR^{a5}, OC(O)R^{b5}, OC(O)NR^{c5}R^{d5}, NR^{c5}R^{d5}, NR^{c5}C(O)R^{b5}, NR^{c5}C(O)NR^{c5}R^{d5}, NR^{c5}C(O)OR^{a5}, C(=NR^{e5})NR^{c5}R^{d5}, NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}, S(O)R^{b5}, S(O)NR^{c5}R^{d5}, S(O)₂R^{b5}, NR^{c5}S(O)₂R^{b5}, NR^{c5}S(O)₂NR^{c5}R^{d5} and S(O)₂NR^{c5}R^{d5}, wherein said C₁₋₆ alkyl, C₃₋₇ cycloalkyl, 4-7 membered heterocycloalkyl, C₆₋₁₀ aryl, and 5-6 membered heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected from halo, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ cyanoalkyl, CN, OR^{a5}, SR^{a5}, C(O)R^{b5}, C(O)NR^{c5}R^{d5}, C(O)OR^{a5}, OC(O)R^{b5}, OC(O)NR^{c5}R^{d5}, NR^{c5}R^{d5}, NR^{c5}C(O)R^{b5}, NR^{c5}C(O)NR^{c5}R^{d5}, NR^{c5}C(O)OR^{a5}, C(=NR^{e5})NR^{c5}R^{d5}, NR^{c5}C(=NR^{e5})NR^{c5}R^{d5},

$S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$ and $S(O)_2NR^{c5}R^{d5}$;

or any R^{c4} and R^{d4} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6- or 7-membered heterocycloalkyl group optionally substituted with 1, 2 or 3 substituents independently selected from C_{1-6} alkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, C_{6-10} aryl, 5-6 membered heteroaryl, C_{1-6} haloalkyl, halo, CN, OR^{a5} , SR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$, $NR^{c5}C(O)OR^{a5}$, $C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$ and $S(O)_2NR^{c5}R^{d5}$, wherein said C_{1-6} alkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, C_{6-10} aryl, and 5-6 membered heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected from halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} cyanoalkyl, CN, OR^{a5} , SR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$, $NR^{c5}C(O)OR^{a5}$, $C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$ and $S(O)_2NR^{c5}R^{d5}$;

each R^{a5} , R^{b5} , R^{c5} and R^{d5} is independently selected from H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkenyl and C_{2-4} alkynyl, wherein said C_{1-4} alkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl, is optionally substituted with 1, 2 or 3 substituents independently selected from OH, CN, amino, halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

or any R^{c5} and R^{d5} attached to the same N atom, together with the N atom to which they are attached, form a 3-, 4-, 5-, 6-, or 7-membered heterocycloalkyl group optionally substituted with 1, 2 or 3 substituents independently selected from OH, CN, amino, halo, C_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{1-4} haloalkyl and C_{1-4} haloalkoxy; and

each R^{e1} , R^{e3} , R^{e4} and R^{e5} is independently selected from H, C_{1-4} alkyl and CN.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:-

a) n is 0; or

b) n is 1.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:-
- a) each R^B is independently selected from halo, C_{1-6} alkyl, C_{1-6} haloalkyl, CN, OR^{a1} and oxo; or
- b) each R^B is independently selected from halo, C_{1-6} alkyl, C_{1-6} haloalkyl, CN, and OR^{a1} ; or
- c) each R^B is independently selected from CN, OH, methoxy and oxo; or
- d) each R^B is independently selected from CN, OH and methoxy.
4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein a nitrogen atom of ring D forms the bond to the remainder of the molecule.
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:-
- a) each R^D is independently selected from halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a2} , SR^{a2} , $C(O)R^{b2}$, $C(O)NR^{c2}R^{d2}$, $C(O)OR^{a2}$, $NR^{c2}R^{d2}$, $S(O)R^{b2}$, $S(O)NR^{c2}R^{d2}$, $S(O)_2R^{b2}$, and $S(O)_2NR^{c2}R^{d2}$; or
- b) each R^D is independently selected from C_{1-6} alkyl, OR^{a2} , and $NR^{c2}R^{d2}$.
6. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein each R^D is independently selected from methyl, OH, and NH_2 .
7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein ring D is a piperidin-1-yl ring substituted at the 3-position by an amino group.
8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:-
- a) the configuration of the carbon atom at the 3-position of the piperidin-1-yl ring forming ring D is (S); or
- b) the configuration of the carbon atom at the 3-position of the piperidin-1-yl ring forming ring D is (R).

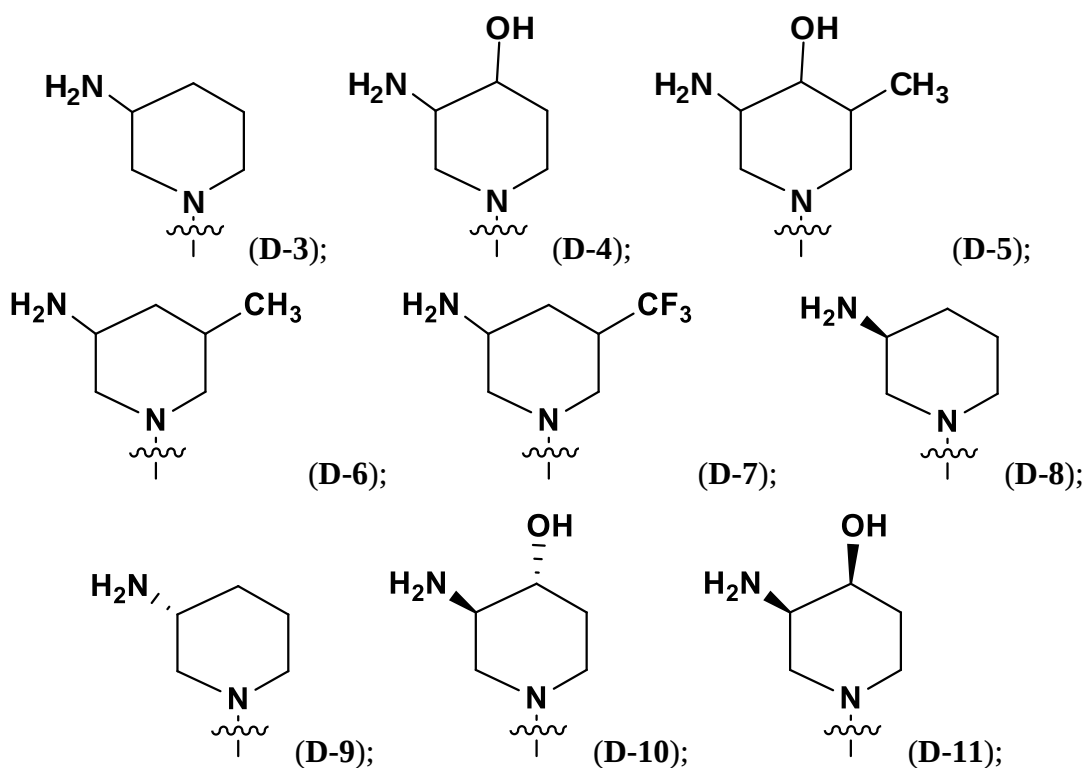
9. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:-

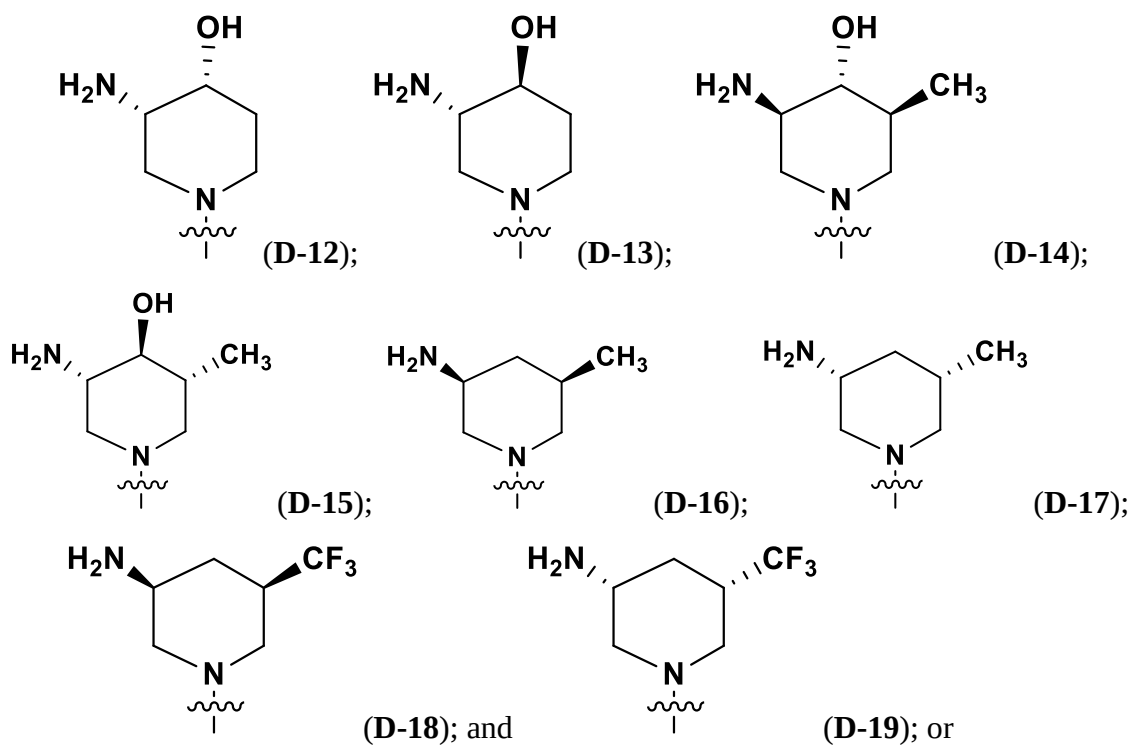
a) ring D is (3*S*)-aminopiperidin-1-yl, (3*R*,4*R*)-3-amino-4-hydroxypiperidinyl, (3*R*,4*S*)-3-amino-4-hydroxypiperidinyl, (3*R*,4*R*,5*R*)-3-amino-4-hydroxy-5-methylpiperidinyl, (3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidinyl, (3*R*,4*S*,5*R*)-3-amino-4-hydroxy-5-methylpiperidinyl or (3*R*,4*S*,5*S*)-3-amino-4-hydroxy-5-methylpiperidinyl; or

b) ring D is (3*R*)-aminopiperidin-1-yl, (3*S*,4*S*)-3-amino-4-hydroxypiperidinyl, (3*S*,4*R*)-3-amino-4-hydroxypiperidinyl, (3*S*,4*R*,5*R*)-3-amino-4-hydroxy-5-methylpiperidinyl, (3*S*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidinyl, (3*S*,4*S*,5*R*)-3-amino-4-hydroxy-5-methylpiperidinyl or (3*S*,4*S*,5*S*)-3-amino-4-hydroxy-5-methylpiperidinyl.

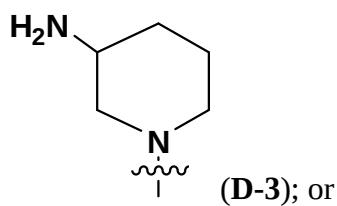
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein:-

a) ring D is a group selected from formula (D-3)-(D-19):

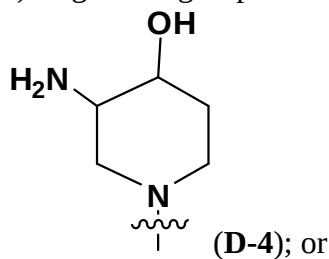




5 b) ring D is a group of formula (D-3):

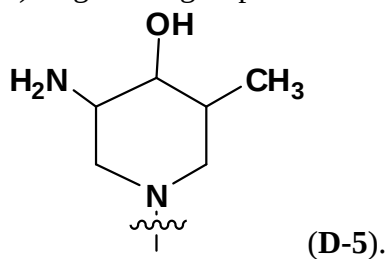


c) ring D is a group of formula (D-4):

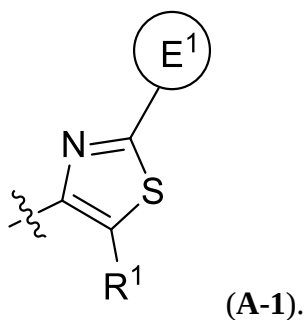


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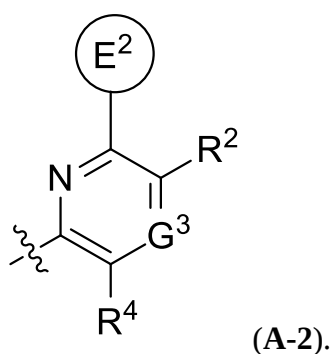
d) ring D is a group of formula (D-5):



11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein ring A is of the formula (A-1):



12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from H and NH₂.
13. The compound of claim 11 or 12, or a pharmaceutically acceptable salt thereof,
5 wherein ring E¹ is phenyl that is 2,6-disubstituted by substituents independently selected from R^E.
14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein each R^E is independently selected from halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, CN, OR^{a3}, C(O)R^{b3}, C(O)NR^{c3}R^{d3}, C(O)OR^{a3}, NR^{c3}R^{d3}, S(O)R^{b3},
10 S(O)NR^{c3}R^{d3}, S(O)₂R^{b3}, and S(O)₂NR^{c3}R^{d3}.
15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein each R^E is independently selected from halo.
16. The compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein:-
a) ring E¹ is phenyl that is 2,6-dihalo-substituted; or
15 b) ring E¹ is 2,6-difluorophenyl.
17. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt thereof, wherein:-
a) G³ is CR³; or
b) G³ is N.
- 20 18. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein ring A is of the formula (A-2):

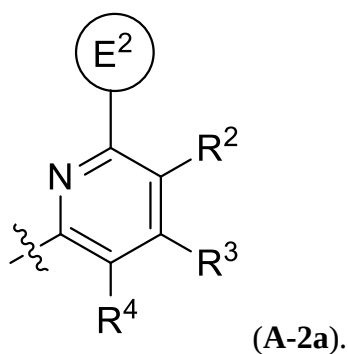


19. The compound of claim 18, or a pharmaceutically acceptable salt thereof, wherein:-

a) G^3 is CR^3 ; or

b) G^3 is N.

5 20. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein ring A is of the formula (A-2a):



21. The compound of any one of claims 18 to 20, or a pharmaceutically acceptable salt thereof, wherein:-

10 a) R^2 is H or halogen; or

b) R^2 is F.

22. The compound of any one of claims 18 to 21, or a pharmaceutically acceptable salt thereof, wherein R^3 is H.

15 23. The compound of any one of claims 18 to 22, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from H and NH_2 .

24. The compound of any one of claims 18 to 23, or a pharmaceutically acceptable salt thereof, wherein ring E² is phenyl that is 2,6-disubstituted by substituents independently selected from R^E.
- 5 25. The compound of any one of claims 18 to 24, or a pharmaceutically acceptable salt thereof, wherein each R^E is independently selected from halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, CN, OR^{a3}, C(O)R^{b3}, C(O)NR^{c3}R^{d3}, C(O)OR^{a3}, NR^{c3}R^{d3}, S(O)R^{b3}, S(O)NR^{c3}R^{d3}, S(O)₂R^{b3}, and S(O)₂NR^{c3}R^{d3}.
26. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein each R^E is independently selected from halo.
- 10 27. The compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein:-
 a) ring E² is phenyl that is 2,6-dihalo-substituted; or
 b) ring E² is 2,6-difluorophenyl.
28. The compound of any one of claims 1 to 27, wherein:-
 a) R^{a1}, R^{b1}, R^{c1}, R^{d1}, R^{a2}, R^{c2}, R^{d2}, R^{a3}, R^{b3}, R^{c3} and R^{d3} are each independently H or C₁₋₆ alkyl; and/or
 15 b) R^{a4}, R^{b4}, R^{c4} and R^{d4} are each independently H or C₁₋₆ alkyl; and/or
 c) R^{a5}, R^{b5}, R^{c5} and R^{d5} are each independently H or C₁₋₆ alkyl.
29. The compound of any one of claims 1 to 28, wherein:-
 a) R^{e1}, R^{e3}, R^{e4} and R^{e5} are each independently H or C₁₋₆ alkyl; or
 20 b) R^{e1}, R^{e3}, R^{e4} and R^{e5} are each H.
30. The compound of claim 1:-
 a) selected from the following compounds, or a pharmaceutically acceptable salt thereof:
 25 5-amino-N-{4-[3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5 3-amino-*N*-{4-[3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

10 3-amino-*N*-{4-[3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

15 *N*-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[3-amino-5-(trifluoromethyl)piperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

20 *N*-{4-[3-amino-5-(trifluoromethyl)piperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-[2,6-difluoro-4-(1-hydroxy-1-methylethyl)phenyl]-5-fluoropyridine-2-carboxamide;

25 *N*-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-[2,6-difluoro-4-(tetrahydro-2H-pyran-3-yloxy)phenyl]-5-fluoropyridine-2-carboxamide;

3-amino-*N*-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

30 *N*-{4-[3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[3-amino-4-hydroxy-4,5-dimethylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;
and

5-amino-*N*-{4-[3-amino-4-hydroxy-4,5-dimethylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide.
or

b) selected from the following compounds, or a pharmaceutically acceptable salt thereof:

5-amino-*N*-{4-[(3*S*)-3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[(3*S*)-3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[(3*S*)-3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

3-amino-*N*-{4-[(3*S*)-3-aminopiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[(3*S*,5*R*)-3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

3-amino-*N*-{4-[(3*S*,5*R*)-3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[(3*S*,5*R*)-3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[(3*S*,5*R*)-3-amino-5-(trifluoromethyl)piperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide;

N-{4-[(3*S*,5*R*)-3-amino-5-(trifluoromethyl)piperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-[2,6-difluoro-4-(1-hydroxy-1-methylethyl)phenyl]-5-fluoropyridine-2-carboxamide;

N-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-[2,6-difluoro-4-(tetrahydro-2*H*-pyran-3-yloxy)phenyl]-5-fluoropyridine-2-carboxamide;

3-amino-*N*-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluorophenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[(3*S*,5*R*)-3-amino-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxamide;

N-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-5-methylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-6-(2,6-difluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxamide;

5-amino-*N*-{4-[(3*R*,4*S*,5*S*)-3-amino-4-hydroxy-4,5-dimethylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide; and

5-amino-*N*-{4-[(3*R*,4*R*,5*S*)-3-amino-4-hydroxy-4,5-dimethylpiperidin-1-yl]-2,3-dihydrofuro[2,3-*b*]pyridin-5-yl}-2-(2,6-difluorophenyl)-1,3-thiazole-4-carboxamide.

31. A composition comprising a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

32. A method of inhibiting Pim1, Pim2, or Pim3 enzyme comprising contacting the enzyme *in vitro* with a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof.

33. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease or condition that is associated with an elevated level of expression or activity at least one of Pim1, Pim2 and Pim3.

34. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer.

35. The compound, or pharmaceutically acceptable salt thereof, for use according to claim 34, wherein:-

a) the cancer is a cancer wherein the expression or activity of at least one of Pim1, Pim2 and Pim3 is upregulated; and/or

5 b) the cancer is a cancer wherein an oncogene is activated; and/or

c) the cancer is a cancer wherein Myc or BCL2 is activated; and/or

d) the cancer is a solid tumor or a hematological cancer; and/or

10 e) the cancer is prostate cancer, colon cancer, esophageal cancer, endometrial cancer, ovarian cancer, uterine cancer, renal cancer, hepatic cancer, pancreatic cancer, gastric cancer, breast cancer, lung cancer, cancer of the head or neck, thyroid cancer, glioblastoma, sarcoma, bladder cancer, lymphoma, leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, diffuse large-B cell lymphoma, mantle cell lymphoma, non-Hodgkin lymphoma, Hodgkin lymphoma or multiple myeloma; or

15 f) the cancer is prostate cancer, pancreatic cancer, acute myelogenous leukemia, diffuse large-B cell lymphoma or multiple myeloma; or

g) the cancer is prostate cancer; or

h) the cancer is pancreatic cancer; or

i) the cancer is acute myelogenous leukemia; or

20 j) the cancer is diffuse large-B cell lymphoma; or

k) the cancer is multiple myeloma.

36. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in:-

a) the treatment of a myeloproliferative disorder; or

b) the treatment of a myeloproliferative disorder, wherein the myeloproliferative disorder is polycythemia vera, essential thrombocythemia, chronic myelogenous leukemia, myelofibrosis, primary myelofibrosis, myelofibrosis with myeloid metaplasia, post polycythemia vera/essential thrombocythemia myelofibrosis, post-essential thrombocythemia myelofibrosis or post polycythemia vera myelofibrosis.

37. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in:

a) the treatment of an immune disorder; or

b) the treatment of an immune disorder, wherein the immune disorder is an autoimmune disease; or

c) the treatment of an immune disorder, wherein the immune disorder is multiple sclerosis, rheumatoid arthritis, allergy, food allergy, asthma, lupus, inflammatory bowel disease or ulcerative colitis, Crohn's disease, irritable bowel syndrome, pancreatitis, diverticulosis, Grave's disease, juvenile rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, myasthenia gravis, vasculitis, autoimmune thyroiditis, dermatitis, psoriasis, scleroderma, systemic sclerosis, vitiligo, graft versus host disease, Sjogren's syndrome, glomerulonephritis, or type I diabetes mellitis.

38. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in the treatment of atherosclerosis.

39. A compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, for use in the reduction of angiogenesis or tumor metastasis.

40. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disease or condition that is associated with an elevated level of expression or activity at least one of Pim1, Pim2 and Pim3.

41. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer.

42. The use according to claim 41, wherein:

a) the cancer is a cancer wherein the expression or activity of at least one of Pim1, Pim2 and Pim3 is upregulated; and/or

b) the cancer is a cancer wherein an oncogene is activated; and/or

5 c) the cancer is a cancer wherein Myc or BCL2 is activated; and/or

d) the cancer is a solid tumor or a hematological cancer; and/or

e) the cancer is prostate cancer, colon cancer, esophageal cancer, endometrial cancer, ovarian cancer, uterine cancer, renal cancer, hepatic cancer, pancreatic cancer, gastric cancer, breast cancer, lung cancer, cancer of the head or neck, thyroid cancer,

10 glioblastoma, sarcoma, bladder cancer, lymphoma, leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, diffuse large-B cell lymphoma, mantle cell lymphoma, non-Hodgkin lymphoma, Hodgkin lymphoma or multiple myeloma; or

15 f) the cancer is prostate cancer, pancreatic cancer, acute myelogenous leukemia, diffuse large-B cell lymphoma or multiple myeloma; or

g) the cancer is prostate cancer; or

h) the cancer is pancreatic cancer; or

i) the cancer is acute myelogenous leukemia; or

j) the cancer is diffuse large-B cell lymphoma; or

20 k) the cancer is multiple myeloma.

43. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for:

a) the treatment of a myeloproliferative disorder; or

25 b) the treatment of a myeloproliferative disorder, wherein the myeloproliferative disorder is polycythemia vera, essential thrombocythemia, chronic myelogenous

leukemia, myelofibrosis, primary myelofibrosis, myelofibrosis with myeloid metaplasia, post polycythemia vera/essential thrombocythemia myelofibrosis, post-essential thrombocythemia myelofibrosis or post polycythemia vera myelofibrosis.

44. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for:

a) the treatment of an immune disorder; or

b) the treatment of an immune disorder, wherein the immune disorder is an autoimmune disease; or

c) the treatment of an immune disorder, wherein the immune disorder is multiple sclerosis, rheumatoid arthritis, allergy, food allergy, asthma, lupus, inflammatory bowel disease or ulcerative colitis, Crohn's disease, irritable bowel syndrome, pancreatitis, diverticulosis, Grave's disease, juvenile rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, myasthenia gravis, vasculitis, autoimmune thyroiditis, dermatitis, psoriasis, scleroderma, systemic sclerosis, vitiligo, graft versus host disease, Sjogren's syndrome, glomerulonephritis, or type I diabetes mellitis.

45. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of atherosclerosis.

46. Use of a compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the reduction of angiogenesis or tumor metastasis.