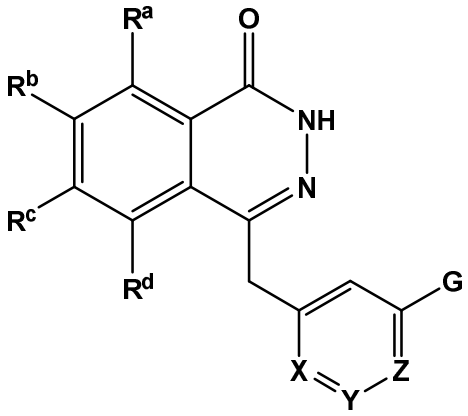
WHAT IS CLAIMED IS:

1. A compound of formula **(I)**:



(I)

or a tautomer thereof, prodrug thereof, N-oxide thereof, stereoisomer thereof, pharmaceutically acceptable ester thereof or pharmaceutically acceptable salt thereof, wherein

R^a, R^b, R^c and R^d are independently selected from hydrogen, halogen, or substituted or unsubstituted C_{1-3} alkyl;

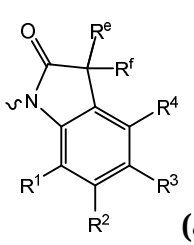
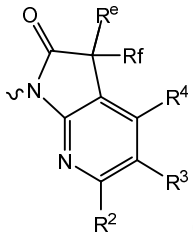
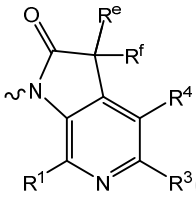
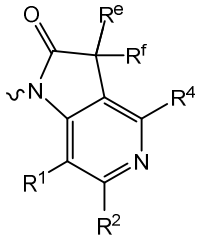
X is CR^x or N;

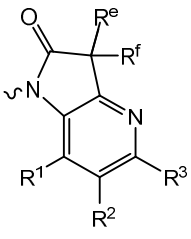
Y is CR^y or N;

Z is CR^z or N;

R^x, R^y and R^z are independently selected from hydrogen, halogen or substituted or unsubstituted C_{1-3} alkyl;

G is selected from

 **(a),**  **(b),**  **(c),**  **(d)** or

 **(e)**;

R^e and R^f are independently selected from hydrogen, halogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, -OR^g, or both R^e and R^f may be joined to form an C_{3-6} cycloalkyl or heterocyclic ring;

R^g is selected from hydrogen, substituted or unsubstituted C_{1-3} alkyl, or -$(CO)R^h$;

R^h is selected from hydrogen or substituted or unsubstituted alkyl; and

R^1, R^2, R^3 and R^4 are independently selected from hydrogen, halogen, and substituted or unsubstituted alkyl.

2. The compound of claim 1, wherein

R^a, R^b, R^c and R^d are independently selected from hydrogen, halogen or substituted or unsubstituted C_{1-3} alkyl;

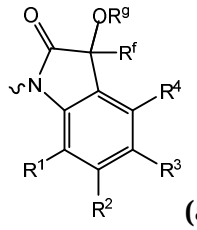
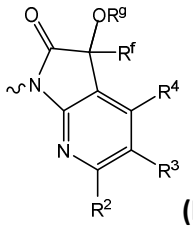
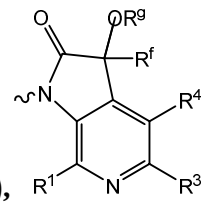
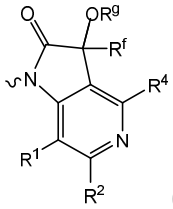
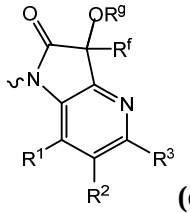
X is CR^x or N;

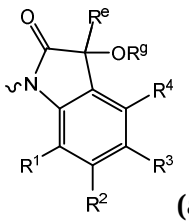
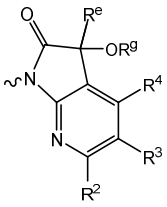
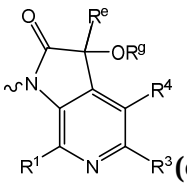
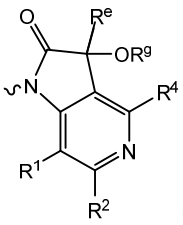
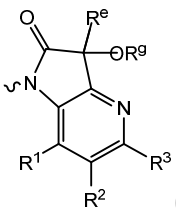
Y is CR^y or N;

Z is CR^z or N;

R^x, R^y and R^z are independently selected from hydrogen, halogen or substituted or unsubstituted C_{1-3} alkyl;

G is selected from


(a1),

(b1),

(c1),

(d1),

(e1),


(a2),

(b2),

(c2),

(d2) or

(e2);

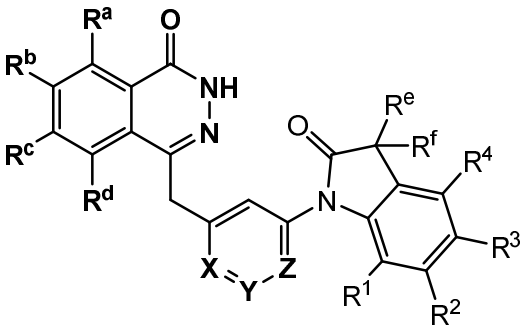
R^e and R^f are independently selected from hydrogen, halogen, hydroxy, substituted or unsubstituted C_{1-3} alkyl, substituted or unsubstituted C_{1-3} alkoxy or -$O(CO)R^h$;

R^g is selected from hydrogen, substituted or unsubstituted C_{1-3} alkyl, or -$(CO)R^h$;

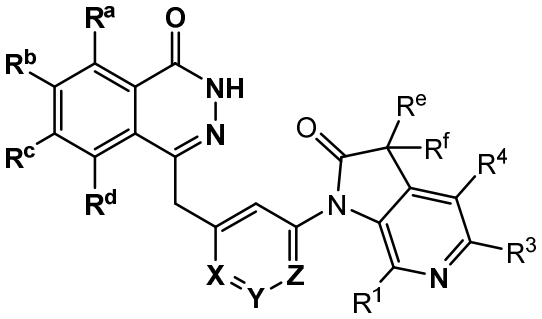
R^h is selected from hydrogen or substituted or unsubstituted alkyl; and

R^1, R^2, R^3 and R^4 are independently selected from hydrogen, halogen, and substituted or unsubstituted C_{1-3} alkyl.

3. The compound of claim 1, wherein the compound is of the formula **(IA)** or **(IB)**:



(IA)



(IB)

or a tautomer thereof, prodrug thereof, N-oxide thereof, stereoisomer thereof, pharmaceutically acceptable ester thereof or pharmaceutically acceptable salt thereof.

4. The compound of any one of claims 1-3, wherein

(i) any one or more of R^a, R^b, R^c and R^d are independently selected from hydrogen and halogen;

(ii) R^a, R^c and R^d is hydrogen and R^b is halogen; or

(iii) R^a, R^b and R^d is hydrogen and R^c is halogen

5. The compound of claim 4, wherein R^b is fluorine or chlorine

6. The compound of claim 4, wherein R^c is fluorine or chlorine

7. The compound of any one of claims 1-6, wherein X, Y and Z are independently selected from CH or N.

8. The compound of claim 7, wherein

(i) Y and Z is CH and X is N;

(ii) X and Z is CH and Y is N; or

(iii) X and Y is CH and Z is N.

9. The compound of any one of claims 1-8, wherein X and Y is CH and Z is CR^z.

10. The compound of claim 9, wherein R^z is hydrogen or halogen.

11. The compound of claim 10, wherein R^z is fluorine.

12. The compound of any one of claims 1-11, wherein R^e and R^f are independently selected from hydrogen, hydroxy, substituted or unsubstituted C_{1-3} alkyl, substituted or unsubstituted C_{1-3} alkoxy, and acetyloxy.

13. The compound of claim 12, wherein R^e is hydroxy, substituted or unsubstituted C_{1-3} alkoxy, or acetyloxy.

14. The compound of claim 13, wherein R^e is hydroxy.

15. The compound of claim 12, wherein R^f is substituted or unsubstituted C_{1-3} alkyl.

16. The compound of claim 15, wherein R^f is methyl, ethyl or CF_3.

17. The compound of claim 12, wherein R^e is hydroxy and R^f is substituted or unsubstituted C_{1-3} alkyl.

18. The compound of claim 1, wherein

(i) both R^e and R^f are hydrogen;

(ii) both R^e and R^f are independently selected from substituted or unsubstituted C_{1-3} alkyl; or

(iii) both R^e and R^f are joined to form a C_{3-6} cycloalkyl.

19. The compound of claim 18, wherein both R^e and R^f are hydrogen.

20. The compound of claim 18, wherein both R^e and R^f are methyl.

21. The compound of claim 18, wherein R^e and R^f are joined to form a C_{3-6} cycloalkyl ring or heterocyclic ring.

22. The compound of any one of claims 1-21, wherein

(i) R^1, R^2, R^3 and R^4 are independently selected from hydrogen or halogen;

(ii) R^1, R^2, R^3 and R^4 are hydrogen;

(iii) R^1, R^2, R^3 and R^4 are independently selected from halogen;

(iv) R^1, R^3 and R^4 are hydrogen and R^2 is halogen; or

(v) R^1, R^2 and R^4 are hydrogen and R^3 is halogen.

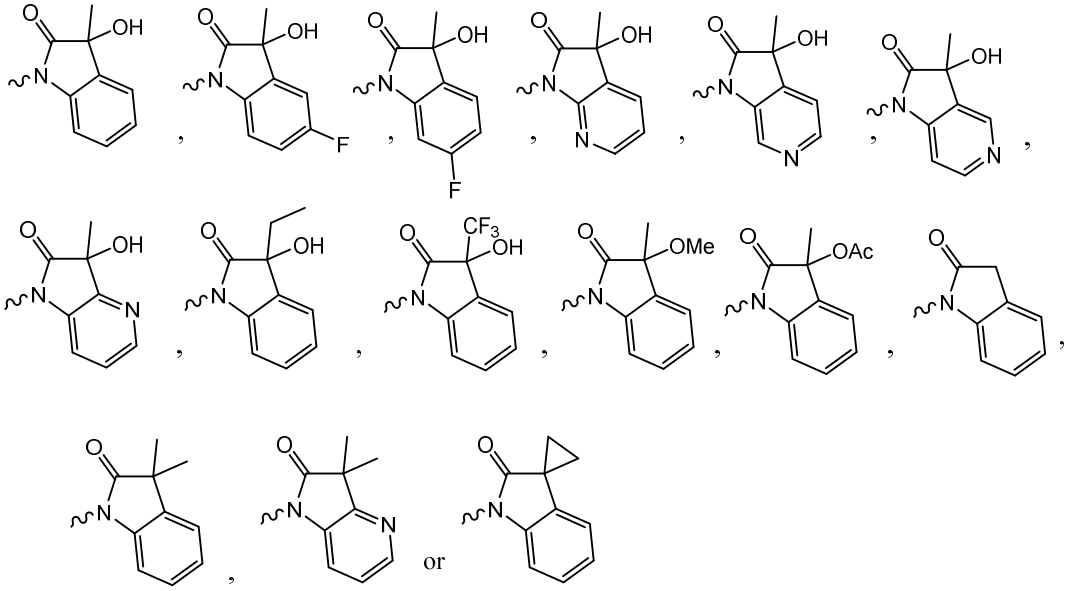
23. The compound of claim 1, wherein

(i) any one or more of R^1, R^2, R^3 and R^4 is fluorine or chlorine;

(ii) R^1, R^3 and R^4 is hydrogen and R^2 is fluorine; or

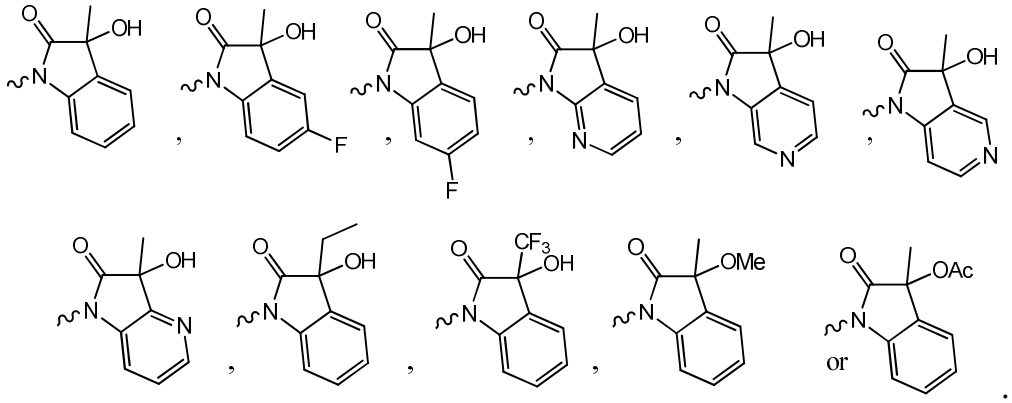
(iii) R^1, R^2 and R^4 is hydrogen and R^3 is fluorine.

24. The compound of any one of claims 1-23, wherein G is selected from



.

25. The compound of claim 24, wherein G is selected from



26. A compound selected from:

4-((5-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(R)-(+)-4-((5-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(S)-(-)-4-((5-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

4-(4-Fluoro-3-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)benzyl)phthalazin-1(2H)-one;

4-((5-(3-Ethyl-3-hydroxy-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

7-Fluoro-4-((5-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(+)-7-Fluoro-4-((5-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(-)-7-Fluoro-4-((5-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

6-Fluoro-4-((5-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

7-Fluoro-4-((5-(5-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(+)-7-Fluoro-4-((5-(5-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(-)-7-Fluoro-4-((5-(5-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

4-((5-(5-Fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(+)-4-((5-(5-Fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

(-)-4-((5-(5-Fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
7-Fluoro-4-((5-(6-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
7-Fluoro-4-((5-(6-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
4-((2-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
(-)-4-((2-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
(+)-4-((2-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
7-Fluoro-4-((2-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
(-)-7-Fluoro-4-((2-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
(+)-7-Fluoro-4-((2-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
7-Fluoro-4-((2-(5-fluoro-3-hydroxy-3-methyl-2-oxoindolin-1-yl)pyridin-4-yl)methyl)phthalazin-1(2H)-one;
4-((5-(3-Hydroxy-2-oxo-3-(trifluoromethyl)indolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
(+)-4-((5-(3-Hydroxy-2-oxo-3-(trifluoromethyl)indolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
(-)-4-((5-(3-Hydroxy-2-oxo-3-(trifluoromethyl)indolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
4-(3-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)benzyl)phthalazin-1(2H)-one;
7-Fluoro-4-(4-fluoro-3-(3-hydroxy-3-methyl-2-oxoindolin-1-yl)benzyl)phthalazin-1(2H)-one;
4-((5-(3-methoxy-3-methyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
4-(3-(3-Hydroxy-3-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-1-yl)benzyl)phthalazin-1(2H)-one;
3-Methyl-2-oxo-1-(5-((4-oxo-3,4-dihydrophthalazin-1-yl)methyl)pyridin-3-yl)indolin-3-yl acetate;
4-(4-Fluoro-3-(2-oxoindolin-1-yl)benzyl)phthalazin-1(2H)-one;
4-(3-(3,3-Dimethyl-2-oxoindolin-1-yl)-4-fluorobenzyl)phthalazine-1(2H)-one;
4-((5-(3,3-Dimethyl-2-oxoindolin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;

4-((5-(3,3-Dimethyl-2-oxo-2,3-dihydro-1H-pyrrolo[3,2-b]pyridin-1-yl)pyridin-3-yl)methyl)phthalazin-1(2H)-one;
4-(3-(3,3-Dimethyl-2-oxo-2,3-dihydro-1H-pyrrolo[3,2-b]pyridin-1-yl)-4-fluorobenzyl)phthalazin-1(2H)-one; and
1'-(5-((4-Oxo-3,4-dihydrophthalazin-1-yl)methyl)pyridin-3-yl)spiro[cyclopropane-1,3'-indolin]-2'-one;
and pharmaceutically acceptable salts thereof.

27. A pharmaceutical composition comprising a compound of any one of claims 1-26 and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of claim 27, further comprising one or more additional therapeutic agents.

29. The pharmaceutical composition of claim 28, wherein the one or more additional therapeutic agents is an anti-cancer agent, anti-inflammatory agent, immunosuppressive agent, steroid, non-steroidal anti-inflammatory agent, antihistamine, analgesic, or any combination of any of the foregoing.

30. ~~A method of inhibiting a catalytic activity of a PARP enzyme present in a cell comprising contacting the cell with an effective amount of a~~ Use of the compound of any one of claims 1-26 in the manufacture of a medicament for inhibiting a catalytic activity of a PARP enzyme present in a cell, wherein an effective amount of the medicament is to be contacted with the cell.

31. The ~~method~~ use of claim 30, wherein the inhibition takes place in a subject suffering from a disease or disorder which is cancer, bone disorder, inflammatory disease, immune disease, nervous system disease, metabolic disease, respiratory disease, thrombosis, or cardiac disease.

32. Use of ~~a~~ the compound of any one of claims 1-26 in the manufacture of a medicament for the treatment of a disease, disorder, or condition that would benefit from inhibiting catalytic activity of an enzyme.

33. The use of ~~a compound of~~ claim 32, wherein the enzyme is PARP.

34. ~~A method for the treatment of a PARP associated disease or disorder comprising administering to a subject in need thereof an effective amount of~~ Use of the compound of any one of claims 1-26 in the manufacture of a medicament for the treatment of a PARP associated disease or disorder, wherein an effective amount of the medicament is to be administered to a subject in need thereof.

35. The ~~method~~ use of claim 34, ~~further comprising the step of administering simultaneously or sequentially to the subject~~ wherein at least one other anti-cancer agent, anti-inflammatory agent, immunosuppressive agent, steroid, non-steroidal anti-inflammatory agent, antihistamine, analgesic, or any combination of any of the foregoing is to be administered simultaneously or sequentially to the subject.

36. The ~~method~~ use of claim 34 or claim 35, wherein the PARP associated disease, disorder or condition is an immune system-related disease, a disease or disorder involving inflammation, cancer or other proliferative disease, a hepatic disease or disorder, or a renal disease or disorder.

37. The ~~method~~ use of claim 34 or claim 35, wherein the PARP associated disease, disorder or condition is selected from inflammation, glomerulonephritis, uveitis, hepatic diseases or disorders, renal diseases or disorders, chronic obstructive pulmonary disease, rheumatoid arthritis, inflammatory bowel disease, vasculitis, dermatitis, osteoarthritis, inflammatory muscle disease, allergic rhinitis, vaginitis, interstitial cystitis, scleroderma, osteoporosis, eczema, allogeneic or xenogeneic transplantation, graft rejection, graft-versus-host disease, lupus erythematosus, pulmonary fibrosis, dermatomyositis, thyroiditis, myasthenia gravis, autoimmune hemolytic anemia, cystic fibrosis, chronic relapsing hepatitis, primary biliary cirrhosis, allergic conjunctivitis, hepatitis, atopic dermatitis, asthma, Sjogren's syndrome, organ transplant rejection, multiple sclerosis, Guillain-Barre, autoimmune uveitis, autoimmune hemolytic anemia, pernicious anemia, autoimmune thrombocytopenia, temporal arteritis, anti-phospholipid syndrome, vasculitides, Wegener's granulomatosis, Behcet's disease, psoriasis, dermatitis herpetiformis, pemphigus vulgaris, vitiligo, Crohn's disease, colitis, ulcerative colitis, primary biliary cirrhosis, autoimmune hepatitis, Type 1 or immune-mediated diabetes mellitus, Grave's disease, Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, autoimmune disorder of the adrenal gland, systemic lupus erythematosus, polymyositis, dermatomyositis, ankylosing spondylitis, transplant rejection, skin graft rejection, arthritis, bone diseases associated with increased bone resorption, ileitis, Barrett's syndrome, adult respiratory distress syndrome, chronic obstructive airway disease; corneal dystrophy,

trachoma, onchocerciasis, sympathetic ophthalmitis, endophthalmitis, gingivitis, periodontitis, tuberculosis, leprosy, uremic complications, nephrosis, sclerodermatitis, psoriasis, chronic demyelinating diseases of the nervous system, AIDS-related neurodegeneration, Alzheimer's disease, infectious meningitis, encephalomyelitis, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis viral or autoimmune encephalitis, autoimmune disorders, immune-complex vasculitis, systemic lupus and erythematodes, systemic lupus erythematosus (SLE), cardiomyopathy, ischemic heart disease hypercholesterolemia, atherosclerosis, preeclampsia, chronic liver failure, brain and spinal cord trauma, and cancer.

38. The ~~method~~ use of claim 34 or claim 35, wherein the PARP associated disease, disorder or condition is selected from hematopoietic tumors of lymphoid lineage, leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma, hematopoietic tumors of myeloid lineage, acute myelogenous leukemias, chronic myelogenous leukemias, myelodysplastic syndrome, promyelocytic leukemia, carcinoma of the bladder, carcinoma of the breast, carcinoma of the colon, carcinoma of the kidney, carcinoma of the liver, carcinoma of the lung, small cell lung cancer, esophageal cancer, gall bladder cancer, ovarian cancer, pancreatic cancer, stomach cancer, cervical cancer, thyroid cancer, prostate cancer, skin cancer, squamous cell carcinoma, tumors of mesenchymal origin, fibrosarcoma, rhabdomyosarcoma, tumors of the central and peripheral nervous system, astrocytoma, neuroblastoma, glioma, schwannoma, melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

39. The ~~method~~ use of claim 34 or claim 35, wherein the PARP associated disease, disorder or condition is selected from carcinoma of the breast, ovarian cancer, carcinoma of the liver, carcinoma of the lung, small cell lung cancer, esophageal cancer, gall bladder cancer, pancreatic cancer or stomach cancer.

40. The ~~method~~ use of claim 34 or claim 35, wherein the PARP associated disease, disorder or condition is carcinoma of the breast or ovarian cancer.

41. The compound of any one of claims 1-26 for use in therapy.