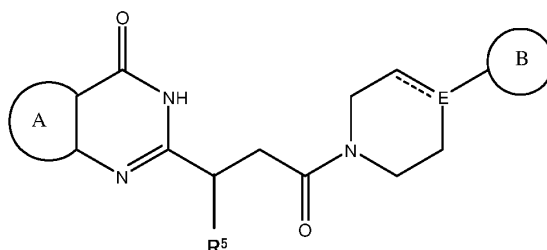


CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound represented by the following structural formula:



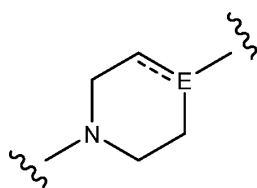
or a pharmaceutically acceptable salt thereof, wherein:

Ring A is optionally substituted phenyl or an optionally substituted 5-6 membered heteroaryl;

Ring B is aryl, 5-6 membered heteroaryl or 5-6 membered heterocyclyl, each optionally substituted with one or more substituents represented by R^3 ;

“-----” is absent or a bond;

E is N or CH when “-----” is absent or E is C when “-----” is a bond;



is optionally substituted with (C_1-C_5) alkyl or hydroxy (C_1-C_5) alkyl;

each R^3 is independently selected from the group consisting of -halogen, -CN, -NO₂, -OR^d, -NR^eR^f, -S(O)_iR^e, -C(=NR^e)NR^eR^f, -NR^eS(O)_iR^f, -S(O)_iNR^eR^f, -C(=O)OR^e, -OC(=O)OR^e, -C(=S)OR^e, -O(C=S)R^e, -C(=O)NR^eR^f, -NR^eC(=O)R^f, -C(=S)NR^eR^f, -NR^eC(=S)R^f, -NR^e(C=O)OR^f, -O(C=O)NR^eR^f, -NR^e(C=S)OR^f, -O(C=S)NR^eR^f, -NR^e(C=O)NR^eR^f, -NR^e(C=S)NR^eR^f, -C(=S)R^e, -C(=O)R^e, halo(C₁-C₅)alkyl, and (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl represented by R^3 is optionally substituted with -CN, -NO₂, -OR^e, -NR^eR^f, -S(O)_iR^e, -NR^eS(O)_iR^f, -S(O)_iNR^eR^f, -C(=O)OR^e, -OC(=O)OR^e, -C(=S)OR^e, -O(C=S)R^e, -C(=O)NR^eR^f, -NR^eC(=O)R^f, -C(=S)NR^eR^f, -NR^eC(=S)R^f, -NR^e(C=O)OR^f, -O(C=O)NR^eR^f, -NR^e(C=S)OR^f, -O(C=S)NR^eR^f, -NR^e(C=O)NR^eR^f, -NR^e(C=S)NR^eR^f, -C(=S)R^e, or -C(=O)R^e;

R^d is $-H$, halo(C_1-C_5)alkyl or (C_1-C_5)alkyl, wherein the (C_1-C_5)alkyl is optionally substituted with hydroxyl or (C_1-C_3)alkoxy;

each R^e is independently selected from the group consisting of $-H$ and (C_1-C_5)alkyl optionally substituted with hydroxyl or (C_1-C_3)alkoxy;

each R^f is independently selected from the group consisting of $-H$, (C_1-C_5)alkyl optionally substituted with hydroxyl or (C_1-C_3)alkoxy, (C_3-C_6)cycloalkyl optionally substituted with (C_1-C_2) alkyl, and 4-6 membered oxygen-containing heterocyclyl optionally substituted with (C_1-C_2) alkyl; or

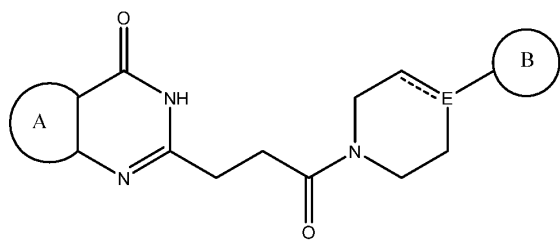
$-NR^eR^f$ taken together is a 4-6 membered heterocyclyl optionally substituted with (C_1-C_2) alkyl; or

$-C(=NR^e)NR^eR^f$ taken together is a 4-6 membered heterocyclyl optionally substituted with R^e ;

R^5 is $-H$ or (C_1-C_5)alkyl; and

i is 0, 1, or 2.

2. The pharmaceutical composition of claim 1, wherein the compound is represented by the following structural formula:



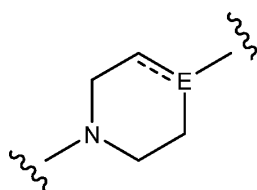
or a pharmaceutically acceptable salt thereof, wherein:

Ring A is optionally substituted phenyl or an optionally substituted 5-6 membered heteroaryl;

Ring B is aryl, 5-6 membered heteroaryl or 5-6 membered heterocyclyl, each optionally substituted with one or more substituents represented by R^3 ;

“-----” is absent or a bond;

E is N or CH when “-----” is absent or E is C when “-----” is a bond;



is optionally substituted with (C₁-C₅)alkyl or hydroxy (C₁-C₅)alkyl;

each R³ is independently selected from the group consisting of -halogen, -CN, -NO₂, -OR^d, -NR^eR^f, -S(O)_iR^e, -C(=NR^e)NR^eR^f, -NR^eS(O)_iR^f, -S(O)_iNR^eR^f, -C(=O)OR^e, -OC(=O)OR^e, -C(=S)OR^e, -O(C=S)R^e, -C(=O)NR^eR^f, -NR^eC(=O)R^f, -C(=S)NR^eR^f, -NR^eC(=S)R^f, -NR^e(C=O)OR^f, -O(C=O)NR^eR^f, -NR^e(C=S)OR^f, -O(C=S)NR^eR^f, -NR^e(C=O)NR^eR^f, -NR^e(C=S)NR^eR^f, -C(=S)R^e, -C(=O)R^e, halo(C₁-C₅)alkyl and (C₁-C₅)alkyl, wherein the (C₁-C₅)alkyl represented by R³ is optionally substituted with -CN, -NO₂, -OR^e, -NR^eR^f, -S(O)_iR^e, -NR^eS(O)_iR^f, -S(O)_iNR^eR^f, -C(=O)OR^e, -OC(=O)OR^e, -C(=S)OR^e, -O(C=S)R^e, -C(=O)NR^eR^f, -NR^eC(=O)R^f, -C(=S)NR^eR^f, -NR^eC(=S)R^f, -NR^e(C=O)OR^f, -O(C=O)NR^eR^f, -NR^e(C=S)OR^f, -O(C=S)NR^eR^f, -NR^e(C=O)NR^eR^f, -NR^e(C=S)NR^eR^f, -C(=S)R^e, or -C(=O)R^e;

R^d is -H, halo(C₁-C₅)alkyl or (C₁-C₅)alkyl, wherein the (C₁-C₅)alkyl is optionally substituted with hydroxyl or (C₁-C₃)alkoxy;

each R^e is independently selected from the group consisting of -H and (C₁-C₅)alkyl optionally substituted with hydroxyl or (C₁-C₃)alkoxy;

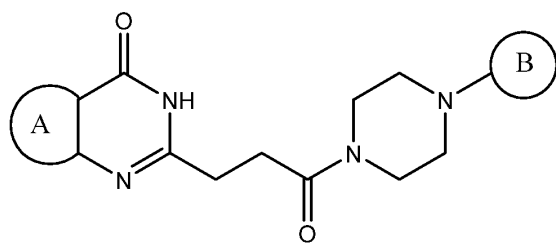
each R^f is independently selected from the group consisting of -H, (C₁-C₅)alkyl optionally substituted with hydroxyl or (C₁-C₃)alkoxy, (C₃-C₆)cycloalkyl optionally substituted with (C₁-C₂) alkyl, and 4-6 membered oxygen-containing heterocyclyl optionally substituted with (C₁-C₂) alkyl; or

-NR^eR^f taken together is a 4-6 membered heterocyclyl optionally substituted with (C₁-C₂) alkyl; or

-C(=NR^e)NR^eR^f taken together is a 4-6 membered heterocyclyl optionally substituted with R^e; and

i is 0, 1, or 2.

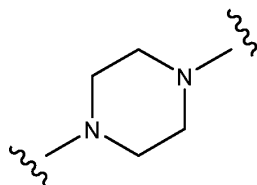
3. The pharmaceutical composition of claim 2, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

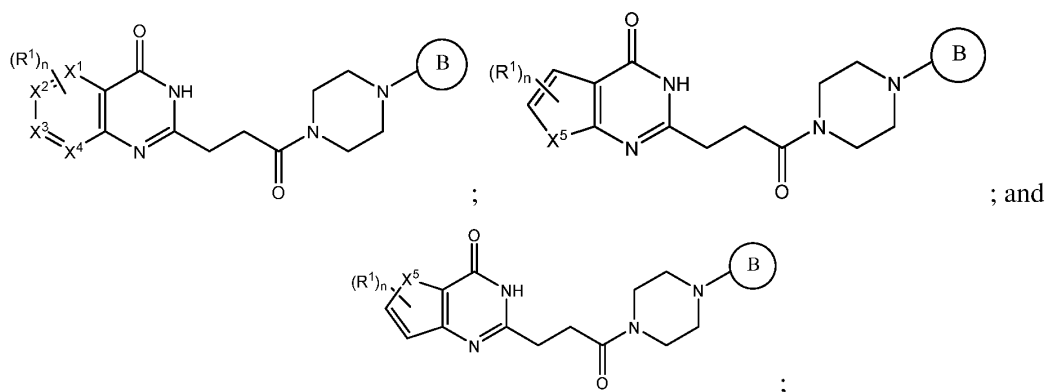
Ring A is optionally substituted phenyl or an optionally substituted 5-6 membered heteroaryl;

Ring B is aryl, 5-6 membered heteroaryl or 5-6 membered heterocyclyl, each optionally substituted with one or more substituents represented by R^3 ; and



is optionally substituted with (C_1-C_5) alkyl or hydroxy (C_1-C_5) alkyl.

4. The pharmaceutical composition of claims 1, 2 or 3, wherein the compound is represented by a structural formula selected from the group consisting of:

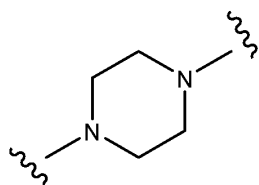


or a pharmaceutically acceptable salt thereof, wherein:

X^1 , X^2 , X^3 and X^4 are each independently selected from the group consisting of N and CH, provided no more than two of X^1 , X^2 , X^3 and X^4 is N;

X^5 is NR^2 , O, or S;

Ring B is aryl, 5-6 membered heteroaryl or 5-6 membered heterocyclyl, each optionally substituted with one or more substituents represented by R^3 ;



is optionally substituted with (C_1-C_5) alkyl or hydroxy (C_1-C_5) alkyl;

each R^1 is independently selected from the group consisting of -halogen, -CN, -NO₂, -OR^c, -NR^aR^b, -S(O)_iR^a, -NR^aS(O)_iR^b, -S(O)_iNR^aR^b, -C(=O)OR^a, -OC(=O)OR^a, -C(=S)OR^a, -O(C=S)R^a, -C(=O)NR^aR^b, -NR^aC(=O)R^b, -C(=S)NR^aR^b, -NR^aC(=S)R^b, -NR^a(C=O)OR^b, -O(C=O)NR^aR^b, -NR^a(C=S)OR^b, -O(C=S)NR^aR^b, -NR^a(C=O)NR^aR^b, -NR^a(C=S)NR^aR^b, -C(=S)R^a, -C(=O)R^b, halo (C_1-C_5) alkyl and (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl represented by R^1 is optionally substituted with -CN, -NO₂, -OR^c, -NR^aR^b, -S(O)_iR^a, -NR^aS(O)_iR^b, -S(O)_iNR^aR^b, -C(=O)OR^a, -OC(=O)OR^a, -C(=S)OR^a, -O(C=S)R^a, -C(=O)NR^aR^b, -NR^aC(=O)R^b, -C(=S)NR^aR^b, -NR^aC(=S)R^b, -NR^a(C=O)OR^b, -O(C=O)NR^aR^b, -NR^a(C=S)OR^b, -O(C=S)NR^aR^b, -NR^a(C=O)NR^aR^b, -NR^a(C=S)NR^aR^b, -C(=S)R^a, or -C(=O)R^a;

R^2 is -H, C_{1-5} alkyl, phenyl, -C(O) $(C_{1-5}$ alkyl), -C(O)(phenyl), -C(O)O $(C_{1-5}$ alkyl), -C(O)O(phenyl), -S(O)₂ $(C_{1-5}$ alkyl) or -S(O)₂(phenyl), wherein each alkyl in the groups represented by R^2 independently is optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, cyano, phenyl, 5-6 membered heteroaryl, (C_1-C_5) alkoxy, and halo (C_1-C_5) alkoxy, and wherein each phenyl in the groups represented by R^2 independently is optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, nitro, cyano, amino, (C_1-C_5) alkyl, halo (C_1-C_5) alkyl, (C_1-C_5) alkoxy and halo (C_1-C_5) alkoxy;

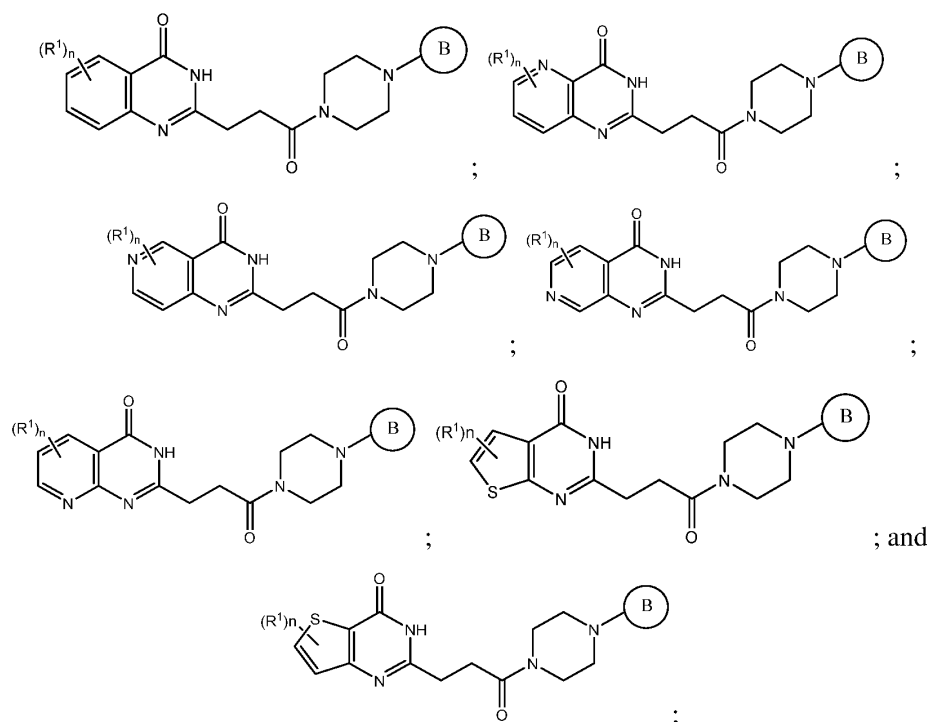
each R^a and each R^b are independently selected from -H and (C_1-C_5) alkyl optionally substituted with hydroxyl or (C_1-C_3) alkoxy;

R^c is -H, halo (C_1-C_5) alkyl or (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl is optionally substituted with hydroxyl or (C_1-C_3) alkoxy;

i is 0, 1, or 2; and

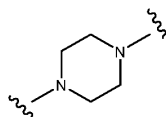
n is 0, 1 or 2.

5. The pharmaceutical composition of claim 4, wherein the compound is represented by a structural formula selected from the group consisting of:



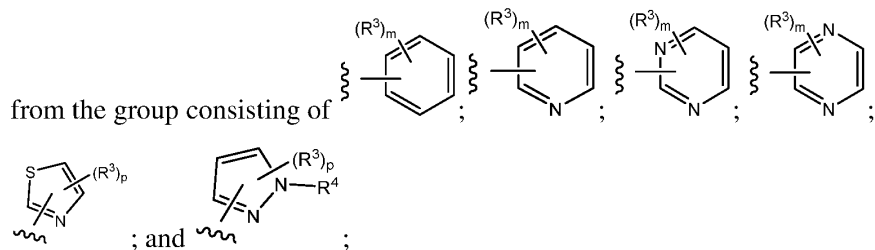
or a pharmaceutically acceptable salt thereof, wherein:

Ring B is aryl, 5-6 membered heteroaryl or 5-6 membered heterocyclyl, each optionally substituted with one or more substituents represented by R^3 ; and



is optionally substituted with (C_1-C_5) alkyl or hydroxy (C_1-C_5) alkyl.

6. The pharmaceutical composition of any one of claims 1-5, wherein Ring B is selected

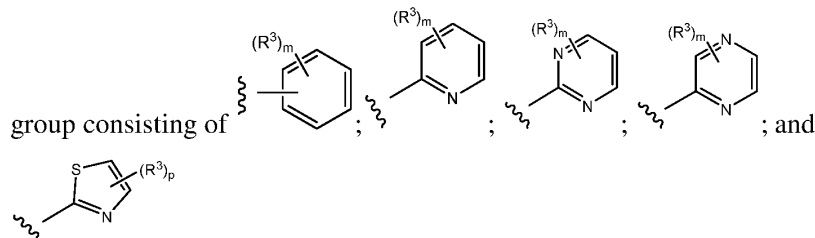


each R^4 is $-H$, (C_1-C_5) alkyl, or hydroxy (C_1-C_5) alkyl;

each p is independently 0 or 1; and

each m is 0 or 1, or 2.

7. The pharmaceutical composition of claim 6, wherein Ring B is selected from the



8. The pharmaceutical composition of any one of claims 4-7, wherein:

each R^1 is independently halogen, (C_1-C_5) alkyl, halo (C_1-C_5) alkyl, (C_1-C_5) alkoxy, halo (C_1-C_5) alkoxy or cyano;

each R^3 is independently selected from the group consisting of -halogen, -CN, $-C(=NR^d)NHR^f$, $-C(=NR^d)NR^eR^f$, $-S(O)_iNR^eR^f$, $-C(=O)NR^eR^f$, $-C(=S)NR^eR^f$, $-O(C=O)NR^eR^f$, $-O(C=S)NR^eR^f$, $-NR^d(C=O)NR^eR^f$, $-NR^d(C=S)NR^eR^f$, and (C_1-C_5) alkyl.

9. The pharmaceutical composition of any one of claims 4-8, wherein:

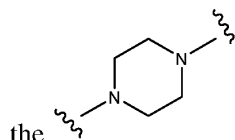
each R^1 is independently halogen or (C_1-C_5) alkyl;

each R^3 is independently selected from the group consisting of -halogen, -CN, $-C(=NR^d)NR^eR^f$, $-C(=O)NR^eR^f$, $-C(=NR^e)NHR^f$ and (C_1-C_5) alkyl.

10. The pharmaceutical composition of any one of claims 4-8, wherein:

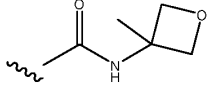
each R^1 is independently chloro, fluoro or methyl;

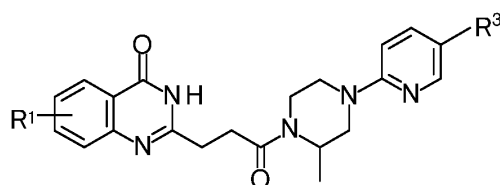
each R^3 is independently selected from the group consisting of chloro, fluoro, -CN, $-C(=NR^d)NR^eR^f$, $-C(=O)NR^eR^f$ and methyl;



group is optionally substituted with methyl or hydroxymethyl.

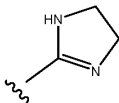
11. The pharmaceutical composition of any one of claims 6-10, wherein:
 each R^e and each R^f are independently selected from the group consisting of -H and methyl; or R^e is -H and R^f is $-(C_3-C_6)\text{cycloalkyl}$ or 4-6 membered oxygen-containing heterocyclyl each optionally substituted with (C_1-C_2) alkyl.
12. The pharmaceutical composition of any one of claims 6-10, wherein:
 each R^e and each R^f are independently selected from the group consisting of -H and methyl; or R^e is -H and R^f is cyclopropyl, cyclobutyl or oxetanyl each optionally substituted with methyl.
13. The pharmaceutical composition of any one of claims 6-10, wherein each R^3 is independently selected from the group consisting of chloro, fluoro, -CN, -C(O)NH(cyclopropyl), -C(O)NH₂, -C(O)NH(CH₃), -C(O)N(CH₃)₂,

 -C(O)NH(cyclobutyl),

 -C(=NH)NHCH₃, and methyl.
14. The pharmaceutical composition of claim 4, wherein R^2 is -H or $(C_1-C_5)\text{alkyl}$, preferably, -H or methyl.
15. The pharmaceutical composition of claim 1 or 2, wherein the compound is 6-[(3S)-4-[3-(6-fluoro-4-oxo-3H-quinazolin-2-yl)propanoyl]-3-methyl-piperazin-1-yl]pyridine-3-carbonitrile or a pharmaceutically acceptable salt thereof.
16. The pharmaceutical composition of claim 1 or 2, wherein the compound is 6-[(3S)-4-[3-(5-fluoro-4-oxo-3H-quinazolin-2-yl)propanoyl]-3-methyl-piperazin-1-yl]pyridine-3-carbonitrile or a pharmaceutically acceptable salt thereof.
17. A compound of the following structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is F or methyl; and

R³ is -CN, -C(=NH)NHCH₃,  or methyl.

18. The compound of claim 17, wherein:
R¹ is F; and
R³ is -CN.
19. The compound of claim 18, wherein the compound is 6-[(3S)-4-[3-(6-fluoro-4-oxo-3H-quinazolin-2-yl)propanoyl]-3-methyl-piperazin-1-yl]pyridine-3-carbonitrile or a pharmaceutically acceptable salt thereof.
20. The compound of claim 18, wherein the compound is 6-[(3S)-4-[3-(5-fluoro-4-oxo-3H-quinazolin-2-yl)propanoyl]-3-methyl-piperazin-1-yl]pyridine-3-carbonitrile or a pharmaceutically acceptable salt thereof.
21. A method of treating a subject with a disease which can be ameliorated by inhibition of poly(ADP-ribose)polymerase (PARP), comprising administering to the subject an effective amount of the pharmaceutical composition of any one of claims 1-16, or compound or a pharmaceutical acceptable salt thereof of any one of claims 17-20.
22. A method of treating a subject with acute kidney injury, comprising administering to the subject an effective amount of the pharmaceutical composition of any one of claims 1-16, or compound or a pharmaceutical acceptable salt thereof of any one of claims 17-20.
23. A method of treating a subject with cancer, comprising administering to the subject an effective amount of the pharmaceutical composition of any one of claims 1-16, or compound or a pharmaceutical acceptable salt thereof of any one of claims 17-20.
24. The method of claim 21, wherein with the disease which can be ameliorated by inhibition of PARP is a muscle structure disorder, a neuronal activation disorder, a muscle fatigue disorder, a muscle mass disorder, a beta oxidation disease, a metabolic

disease, a cancer, a vascular disease, an ocular vascular disease, a muscular eye disease, or a renal disease.

25. The method of claim 24, wherein:

the muscle structure disorder is selected from Bethlem myopathy, central core disease, congenital fiber type disproportion, distal muscular dystrophy (MD), Duchenne & Becker MD, Emery-Dreifuss MD, facioscapulohumeral MD, hyaline body myopathy, limb-girdle MD, a muscle sodium channel disorders, myotonic chondrodystrophy, myotonic dystrophy, myotubular myopathy, nemaline body disease, oculopharyngeal MD, and stress urinary incontinence;

the neuronal activation disorder is selected from amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, Guillain-Barre syndrome, Lambert-Eaton syndrome, multiple sclerosis, myasthenia gravis, nerve lesion, peripheral neuropathy, spinal muscular atrophy, tardy ulnar nerve palsy, and toxic myoneural disorder;

the muscle fatigue disorder is selected from chronic fatigue syndrome, diabetes (type I or II), glycogen storage disease, fibromyalgia, Friedreich's ataxia, intermittent claudication, lipid storage myopathy, MELAS, mucopolysaccharidosis, Pompe disease, and thyrotoxic myopathy;

the muscle mass disorder is cachexia, cartilage degeneration, cerebral palsy, compartment syndrome, critical illness myopathy, inclusion body myositis, muscular atrophy (disuse), sarcopenia, steroid myopathy, and systemic lupus erythematosus;

the beta oxidation disease is selected from systemic carnitine transporter, carnitine palmitoyltransferase (CPT) II deficiency, very long-chain acyl-CoA dehydrogenase (LCHAD or VLCAD) deficiency, trifunctional enzyme deficiency, medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, short-chain acyl-CoA dehydrogenase (SCAD) deficiency, and riboflavin-responsive disorders of β -oxidation (RR - MADD);

the metabolic disease is selected from hyperlipidemia, dyslipidemia, hypercholesterolemia, hypertriglyceridemia, HDL hypocholesterolemia, LDL hypercholesterolemia and/or HLD non-cholesterolemia, VLDL hyperproteinemia, dyslipoproteinemia, apolipoprotein A-I hypoproteinemia, atherosclerosis, disease of

arterial sclerosis, disease of cardiovascular systems, cerebrovascular disease, peripheral circulatory disease, metabolic syndrome, syndrome X, obesity, diabetes (type I or II), hyperglycemia, insulin resistance, impaired glucose tolerance, hyperinsulinism, diabetic complication, cardiac insufficiency, cardiac infarction, cardiomyopathy, hypertension, Non-alcoholic fatty liver disease (NAFLD), Nonalcoholic steatohepatitis (NASH), thrombus, Alzheimer disease, neurodegenerative disease, demyelinating disease, multiple sclerosis, adrenal leukodystrophy, dermatitis, psoriasis, acne, skin aging, trichosis, inflammation, arthritis, asthma, hypersensitive intestine syndrome, ulcerative colitis, Crohn's disease, and pancreatitis;

the vascular disease is selected from peripheral vascular insufficiency, peripheral vascular disease, intermittent claudication, peripheral vascular disease (PVD), peripheral artery disease (PAD), peripheral artery occlusive disease (PAOD), and peripheral obliterative arteriopathy;

the ocular vascular disease is selected from age-related macular degeneration (AMD), stargardt disease, hypertensive retinopathy, diabetic retinopathy, retinopathy, macular degeneration, retinal haemorrhage, and glaucoma;

the muscular eye disease is selected from strabismus, progressive external ophthalmoplegia, esotropia, exotropia, a disorder of refraction and accommodation, hypermetropia, myopia, astigmatism, anisometropia, presbyopia, a disorders of accommodation, and internal ophthalmoplegia; and

the renal disease is selected from glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, acute nephritis, recurrent hematuria, persistent hematuria, chronic nephritis, rapidly progressive nephritis, acute renal failure, chronic renal failure, diabetic nephropathy, and Bartter's syndrome.

26. The method of claim 21, wherein with the disease which can be ameliorated by inhibition of PARP is selected from genetic lipodystrophy, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), renal ischemia/reperfusion injury (IRI), Duchenne & Becker muscular dystrophy, diabetes (type I or type II), obesity, and sarcopenia.

27. The method of claim 21, wherein the disease which can be ameliorated by inhibition of PARP is selected from Alpers's Disease, CPEO-Chronic progressive external ophthalmoplegia, Kearns-Sayra Syndrome (KSS), Leber Hereditary Optic Neuropathy (LHON), MELAS-Mitochondrial myopathy, encephalomyopathy, lactic acidosis, and stroke-like episodes, MERRF-Myoclonic epilepsy and ragged-red fiber disease, NARP-neurogenic muscle weakness, ataxia, and retinitis pigmentosa, Pearson Syndrome, platinum-based chemotherapy induced ototoxicity, Cockayne syndrome, xeroderma pigmentosum A, Wallerian degeneration, and HIV-induced lipodystrophy.