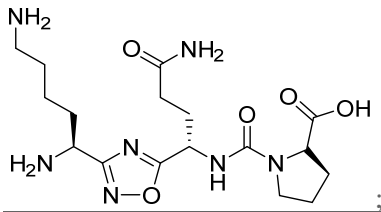
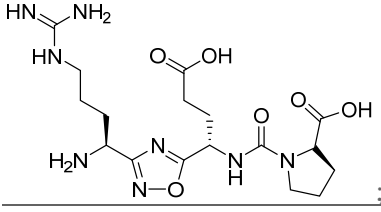
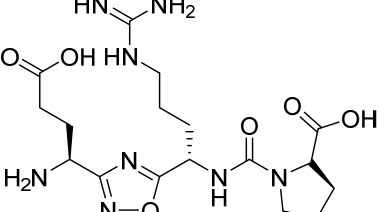
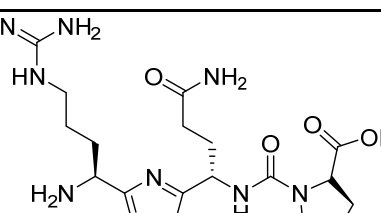
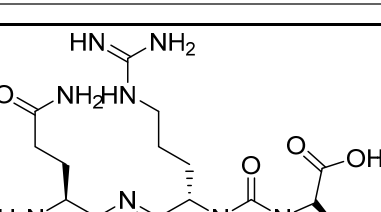


We claim:

1. A composition comprising a CD47-SIRP α blocking agent and one or more anti-cancer agent(s): wherein the CD47-SIRP α blocking agent is selected from the group consisting of represented by a compound of formula (I):

Compound	Structure
<u>1</u>	
<u>2</u>	
<u>3</u>	
<u>4</u>	
<u>5</u>	

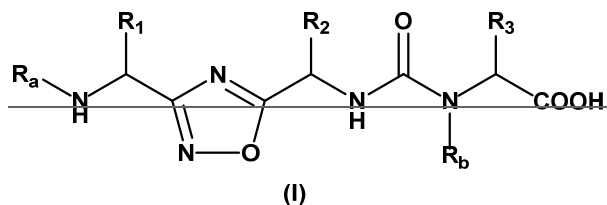
Compound	Structure
<u>6</u>	
<u>7</u>	
<u>8</u>	
<u>9</u>	
<u>10</u>	
<u>11</u>	

Compound	Structure
<u>12</u>	
<u>13</u>	
<u>14</u>	
<u>15</u>	
<u>16</u>	
<u>17</u>	
<u>18</u>	

Compound	Structure
<u>19</u>	
<u>20</u>	
<u>21</u>	
<u>22</u>	
<u>23</u>	
<u>24</u>	
<u>25</u>	

Compound	Structure
<u>26</u>	 ; and
<u>27</u>	 ;

or a pharmaceutically acceptable salt or an amide or an ester or a stereoisomer thereof.



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
 wherein;

R_a is hydrogen; and R_1 represents hydrogen, $(CH_2)_2CONH_2$, $(CH_2)_2COOH$, $(CH_2)_3NHC(=NH)NH_2$, $(CH_2)_4NH_2$, CH_2CONH_2 , CH_2 -aryl, or CH_2 -heteroaryl; or R_a and R_1 , together with the atoms to which they are attached form pyrrolidine ring;

R_2 represents hydrogen, $(CH_2)_3NHC(=NH)NH_2$, $(CH_2)_2CONH_2$, $(CH_2)_2COOH$, CH_2 -aryl, or CH_2 -heteroaryl;

R_b is hydrogen; and R_3 represents hydrogen, CH_2 -aryl, $(CH_2)_3NHC(=NH)NH_2$, $(CH_2)_2CONH_2$, $(CH_2)_2COOH$, $(CH_2)_4NH_2$ or CH_2 -heteroaryl; or R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

2. The composition of claim 1, wherein the anti-cancer agent is a chemotherapeutic agent, or an immunomodulatory agent.

3. ~~—The composition of claim 1, wherein the anticancer agent is a therapeutic antibody targeting tumor antigens that stimulate activating Fc receptors (FcRs).~~
4. ~~—The composition of claim 3, wherein the antibody is selected from the group capable of triggering efficient phagocytosis.~~
- 5 5. ~~—The composition of claim 4, wherein the group capable of triggering efficient phagocytosis comprises anti CD20 (rituximab, tiuxetan, tositumomab), which combination finds particular use in the treatment of non Hodgkin's B cell lymphomas and chronic lymphocytic leukemia (CLL); anti CD22, (Epratuzumab) which combination finds particular use in the treatment of B cell leukemia and hairy cell leukemia; anti CD52, (alemtuzumab)~~
10 ~~which combination finds particular use in the treatment of B cell and T cell leukemia, (chronic lymphocytic leukemia); anti CD33 (gemtuzumab ozogomicin) which combination finds particular use in the treatment of myeloid leukemia (acute myelogenous leukemia); trastuzumab which combination finds particular use in the treatment of breast cancer; bevacizumab which combination finds particular use in the treatment of certain type of brain~~
15 ~~tumor, and certain types of cancers of kidney, lung, colon, rectum, cervix, ovary, or fallopian tube; cetuximab which combination finds particular use in the treatment of colon and head and neck cancer; panitumumab which combination finds particular use in the treatment of colorectal cancer; anti CD38 (daratumumab) which combination finds particular use in the treatment of multiple myeloma; CD96, anti CD44, anti CD123 which combination finds~~
20 ~~particular use in the treatment of myelogenous leukemias; ofatumumab which combination finds particular use in the treatment of chronic lymphocytic leukemia; obinutuzumab which combination finds particular use in the treatment of follicular lymphoma; alemtuzumab which combination finds particular use in the treatment of B cell chronic lymphocytic leukaemia; Ibritumomab tiuxetan which combination finds particular use in the treatment of B cell non-~~
25 ~~Hodgkin lymphomas; dinutuximab which combination finds particular use in the treatment of neuroblastoma; and necitumumab which combination finds particular use in the treatment of lung cancer.~~
6. ~~—The composition of any one of claims 1 to 5, wherein the anticancer agent is anti CD20 antibody selected from rituximab, tiuxetan, and tositumomab.~~
- 30 37. The composition of claim 2, wherein the chemotherapeutic agent is azacitidine or a
proteasome inhibitor (bortezomib, ixazomib and carfilzomib), Anthracyclines (Doxorubicin,
Epirubicin, Daunorubicin, Idarubicin, Mitoxantrone) Oxaliplatin, Cyclophosphamide,

~~Bleomycin, Vorinostat, Paclitaxel, 5-Fluorouracil, Cytarabine, BRAF inhibitory drugs (Dabrafenib, Vemurafenib), PI3K inhibitor, Docetaxel, Mitomycin C, Sorafenib, or Tamoxifen; or a combination thereof.~~

8. ~~The composition of any one of claims 1 to 2, wherein the anticancer agent is proteasome inhibitor.~~

9. ~~The composition of claim 8, wherein the anticancer agent is bortezomib, ixazomib, or carfilzomib, or derivative thereof.~~

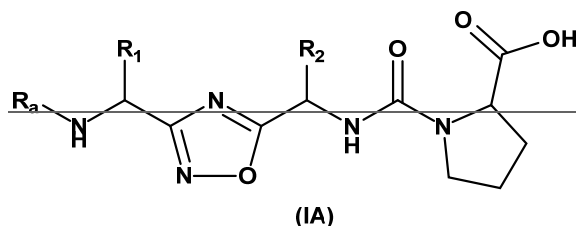
10. ~~The composition of claim 2, wherein the chemotherapeutic agent is Abiraterone acetate, Afatinib, Aldesleukin, Alemtuzumab, Anastrozole, Axitinib, Belinostat, Bendamustine, Bicalutamide, Blinatumomab, Bosutinib, Brentuximab, Busulfan, Cabazitaxel, Capecitabine, Carboplatin, Carfilzomib, Carmustine, Ceritinib, Clofarabine, Crizotinib, Dacarbazine, Dactinomycin, Dasatinib, Degarelix, Denileukin, Denosumab, Enzalutamide, Eribulin, Erlotinib, Everolimus, Exemestane, Exemestane, Fludarabine, Fulvestrant, Gefitinib, Goserelin, Ibritumomab, Imatinib, Ipilimumab, Irinotecan, Ixabepilone, Lapatinib, Lenalidomide, Letrozole, Leucovorin, Leuprolide, Lomustine, Mechlorethamine, Megestrol, Nelarabine, Nilotinib, Nivolumab, Olaparib, Omacetaxine, Palbociclib, Pamidronate, Panitumumab, Panobinostat, Pazopanib, Pegaspargase, Pembrolizumab, Pemetrexed Disodium, Pertuzumab, Plerixafor, Pomalidomide, Ponatinib, Pralatrexate, Procarbazine, Radium 223, Ramucirumab, Regorafenib, rIFN α 2b, Romidepsin, Sunitinib, Temozolomide, Temsirolimus, Thiotepa, Tositumomab, Trametinib, Vinorelbine, abarelix, aldesleukin, alitretinoin, allopurinol, altretamine, arsenic trioxide, asparaginase, azacitidine, bexarotene, baricitinib, bortezomib, busulfan intravenous, busulfan oral, calusterone, cetuximab, chlorambucil, cisplatin, cladribine, dalteparin sodium, decitabine, diftitox, disulfiram, dexrazoxane, dromostanolone propionate, eculizumab, estramustine, etoposide phosphate, etoposide, fentanyl citrate, filgrastim, floxuridine, gemcitabine, histrelin acetate, fosfamide, interferon alfa 2a, lapatinib ditosylate, levamisole, marizomib, meclorothamine, melphalan, mercaptopurine, methotrexate, methoxsalen, mitotane, nandrolone phenpropionate, nofetumomab, oprozomib, pegfilgrastim, pentostatin, pipobroman, plicamycin, procarbazine, quinaerine, rasburicase, ruxolitinib, rucaparib, streptozocin, teniposide, testolactone, thalidomide, thioguanine, topotecan, toremifene, tretinoin, uracil mustard, valrubicin, vinblastine, vincristine, niraparib, veliparib, talazoparib, zoledronate, Ibrutinib, Aflibercept and Idelalisib.~~

411. The composition of claim 2, wherein the immunomodulatory agent is a costimulatory molecule or a coinhibitory molecule comprising ~~CTLA-4 (e.g., ipilimumab), 4-1BB (e.g., urelumab, and utomilumab), antibodies to PD-1 and PD-L1 (e.g., nivolumab, pembrolizumab, atezolizumab, Durvalumab and Camrelizumab), antibodies to cytokines (IL-10, TGF- β),~~
5 ~~antibodies to TIM-3, antibodies to LAG3, antibodies to B7H3, antibodies to B7H4 or antibodies to B7H6; or a combination thereof.~~
5. The composition of claim 1, wherein the anticancer agent is a therapeutic antibody targeting tumor antigens that stimulate activating Fc receptors (FcRs).
6. The composition of claim 5, wherein the therapeutic antibody is selected from the group
10 capable of triggering efficient phagocytosis comprising anti CD-20 (rituximab, tiuxetan, and tositumomab).
12. ~~The composition of claim 1, wherein CD47-SIRP α blocking agent is an agent that blocks the interaction between CD47 and SIRP α .~~
13. ~~The composition of claim 1, wherein blocking the interaction between CD47 and SIRP α~~
15 ~~induces macrophage phagocytosis of tumor cells expressing CD47.~~
14. ~~The composition of claim 1, wherein R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂CONH₂, CH₂-phenyl, or CH₂-imidazolyl.~~
15. ~~The composition of claim 1, wherein R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂,~~
20 ~~(CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-phenyl, or CH₂-imidazolyl.~~
16. ~~The composition of claim 1, wherein R₃ represents hydrogen, CH₂-phenyl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₄NH₂ or CH₂-imidazolyl.~~
17. ~~The composition of claim 16, wherein R₃ represents hydrogen, CH₂-phenyl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, or (CH₂)₄NH₂.~~
18. ~~The composition of any one claim 1 to 17, wherein~~
25 ~~R_a is hydrogen; and R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂CONH₂, CH₂-phenyl, or CH₂-imidazolyl; or R_a and R₁, together with the atoms to which they are attached form pyrrolidine ring;~~

~~—R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-phenyl, or CH₂-imidazolyl;~~

~~—R_b is hydrogen; and R₃ represents hydrogen, CH₂-phenyl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₄NH₂ or CH₂-imidazolyl; or R_b and R₃, together with the atoms to which they are attached form pyrrolidine ring.~~

19. The composition of claim 1, represented by compound of formula (IA)



~~or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R₁, R_a and R₂ are as defined in claim 1.~~

20. The composition of claim 19, wherein R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂-phenyl, or CH₂-imidazolyl.

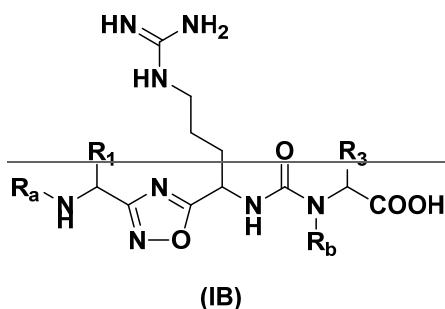
21. The composition of claim 19, wherein R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-phenyl, or CH₂-imidazolyl.

22. The composition of claim 19, 20 or 21, wherein

R_a is hydrogen; and R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂-phenyl, or CH₂-imidazolyl;

R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂COOH, CH₂-phenyl, or CH₂-imidazolyl.

23. The composition of claim 1, represented by compound of formula (IB)



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein, R_1 , R_a , R_b and R_3 are as defined in claim 1.

24. The composition of claim 23, wherein R_1 represents hydrogen, $(CH_2)_2CONH_2$, $(CH_2)_2COOH$, $(CH_2)_3NHC(=NH)NH_2$, $(CH_2)_4NH_2$, or CH_2 phenyl.

25. The composition of claim 23, wherein R_3 represents hydrogen, CH_2 phenyl, $(CH_2)_2CONH_2$, or $(CH_2)_2COOH$.

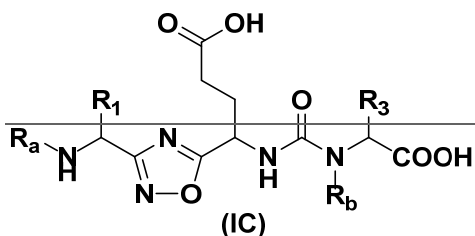
26. The composition of claim 23 wherein R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

27. The composition of any one of claims 23 to 26, wherein

R_1 represents $(CH_2)_2CONH_2$, or $(CH_2)_2COOH$;

R_b is hydrogen; and R_3 represents hydrogen, or CH_2 phenyl; or R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

28. The composition of claim 1, represented by compound of formula (IC), wherein



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein, R_1 , R_a , R_3 and R_b are as defined in claim 1.

29. The composition of claim 28, wherein, R_1 represents $(CH_2)_4NH_2$, $(CH_2)_3NHC(=NH)NH_2$ or $(CH_2)_2CONH_2$.

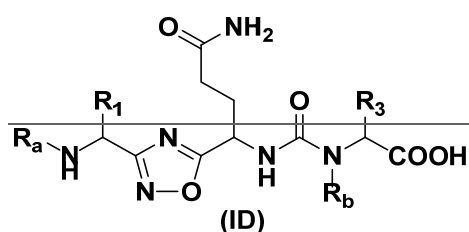
30. — The composition of claim 28, wherein R_b is hydrogen; R_3 represents hydrogen, CH_2 -phenyl, or CH_2 -heteroaryl; or R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

31. — The composition of any one of claims 28 to 30, wherein:

5 — R_1 represents $(\text{CH}_2)_4\text{NH}_2$, $(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$ or $(\text{CH}_2)_2\text{CONH}_2$;

— R_b is hydrogen; R_3 represents hydrogen, CH_2 -phenyl, or CH_2 -heteroaryl; or R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

32. — The composition of claim 1, represented by compound of formula (ID), wherein



10 or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_1 , R_a , R_3 and R_b are as defined in claim 1.

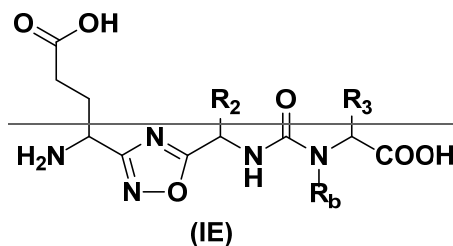
33. — The composition of claim 32, wherein, R_1 represents CH_2CONH_2 , $(\text{CH}_2)_4\text{NH}_2$, or $(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$.

34. — The composition of any one of claims 32 to 33, wherein:

15 — R_1 represents $(\text{CH}_2)_4\text{NH}_2$, or $(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$;

— R_b is hydrogen; R_3 represents hydrogen, $(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$, or $(\text{CH}_2)_4\text{NH}_2$; or R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

35. — The composition of claim 1, represented by compound of formula (IE), wherein



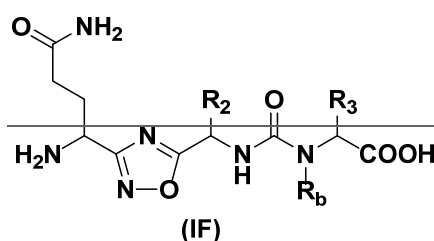
or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein, R_2 , R_3 and R_b are as defined in claim 1.

36. The composition of claim 35, wherein, R_2 represents hydrogen, or $(CH_2)_3NHC(=NH)NH_2$.

5 37. The composition of any one of claims 34 to 35, wherein:

— R_1 represents hydrogen or $(CH_2)_3NHC(=NH)NH_2$; and R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

38. The composition of claim 1, represented by compound of formula (IF), wherein



10 or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein, R_2 , R_3 and R_b are as defined in claim 1.

39. The composition of claim 38, wherein, R_2 represents hydrogen, CH_2 -phenyl, $(CH_2)_2COOH$, or $(CH_2)_3NHC(=NH)NH_2$.

40. The composition of any one of claims 38 to 39, wherein:

15 — R_2 represents hydrogen, CH_2 -phenyl, $(CH_2)_2COOH$, or $(CH_2)_3NHC(=NH)NH_2$;

— R_b is hydrogen; and R_3 represents CH_2 -phenyl, $(CH_2)_2CONH_2$, $(CH_2)_4NH_2$ or $(CH_2)_2COOH$; R_b and R_3 , together with the atoms to which they are attached form pyrrolidine ring.

41. The composition of any one of claims 1 to 40, wherein the compound is selected from

Compound	Structure
1	

Compound	Structure
2	
3	
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5	
6	
7	

Compound	Structure
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13	

Compound	Structure
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20	

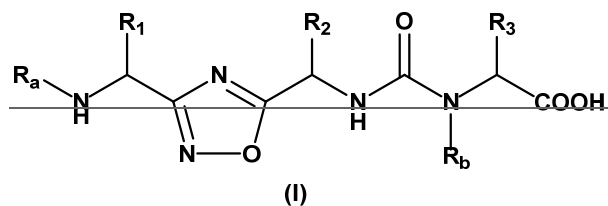
Compound	Structure
21	
22	
23	
24	
25	
26	

Compound	Structure
27	

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof.

742. A pharmaceutical composition comprising the CD47-SIRPα blocking agent and one or more anti-cancer agent(s) as claimed in ~~any one of claims 1,~~ and a pharmaceutically acceptable carrier—41 for use as a medicament.

- 5 43. —A method for treating cancer in a subject presenting a dysregulated CD47 pathway, the ~~method comprising administering to the subject a therapeutically effective amount of a CD47-SIRPα blocking agent in combination with a therapeutically effective amount of one or more anti-cancer agent(s); wherein the CD47-SIRPα blocking agent is represented by compound of formula (I):~~



10

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein,

- ~~R_a is hydrogen; and R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂CONH₂, CH₂-aryl, or CH₂-heteroaryl; or R_a and R₁, together with the atoms to which they are attached form pyrrolidine ring;~~
- 15

~~R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-aryl, or CH₂-heteroaryl;~~

- ~~R_b is hydrogen; and R₃ represents hydrogen, CH₂-aryl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₄NH₂ or CH₂-heteroaryl; or R_b and R₃, together with the atoms to which they are attached form pyrrolidine ring.~~
- 20

44. The method of claim 43, wherein the subject presenting a dysregulated CD47 pathway is a subject presenting with CD47+ disease cells.

45. The method of claim 44, wherein CD47+ disease cells are CD47+ cancer cells.

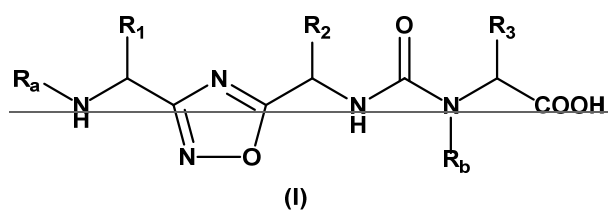
46. The method of claim 43, wherein the treatment with one or more anti-cancer agent(s) is prior to, concomitant with, or following treatment with a compound of formula (I) or a pharmaceutically acceptable salt thereof.

47. The method of claim 43, wherein the anticancer agent is anti-CD20 antibody.

48. The method of claim 43, wherein the anticancer agent is proteasome inhibitor.

49. The method of claim 43, wherein the anticancer agent is bortezomib or any derivative thereof.

850. Use of a therapeutically effective amount of the composition of claim 1 in the manufacture of a medicament A method for treating or delaying progression of diseases or disorders mediated by deregulated CD47-SIRPα pathway in a subject, the method comprising administering to the subject in need thereof a therapeutically effective amount of an agent blocking CD47-SIRPα pathway in combination with a therapeutically effective amount of one or more anti-cancer agent(s); wherein the agent blocking CD47-SIRPα pathway is represented by compound of formula (I):



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein,

R_a is hydrogen; and R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂CONH₂, CH₂-aryl, or CH₂-heteroaryl; or R_a and R₁, together with the atoms to which they are attached form pyrrolidine ring;

R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-aryl, or CH₂-heteroaryl;

~~R₁ is hydrogen; and R₃ represents hydrogen, CH₂-aryl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₄NH₂ or CH₂-heteroaryl; or R₁ and R₃, together with the atoms to which they are attached form pyrrolidine ring.~~

9. The use of claim 8, wherein the subject presenting a dysregulated CD47 pathway is a subject presenting with CD47+ disease cells.

~~1051. The method-use of claim 850, wherein the disease or disorder is cancer mediated by dysregulated CD47-SIRPα pathway is cancer.~~

~~1152. The method-use of claim 1051, wherein the cancer is selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), non-small cell lung cancer (NSCLC), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, B-cell lymphomas, myeloproliferative disorder/neoplasm (MPDS); myelodysplastic syndrome; giant cell myeloma, heavy-chain myeloma, light chain myeloma and Bence- Jones myeloma, multiple myeloma, environmentally induced cancers including those induced by asbestos (e.g., mesothelioma), and combinations of said cancers.~~

~~53. Use of a composition comprising CD47-SIRPα blocking agent and one or more anti-cancer agent(s) as claimed in claim 1 to 41, in the manufacture of a medicament for the treatment of cancer in a subject presenting a dysregulated CD47 pathway.~~

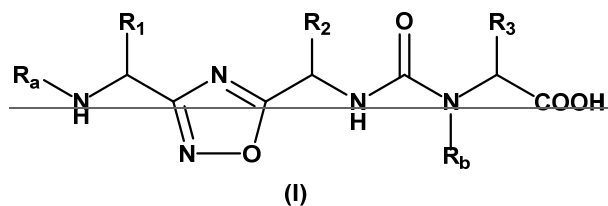
~~54. The use of claim 53, wherein the cancer is selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine~~

cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), non-small cell lung cancer (NSCLC), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain-stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T cell lymphoma, B cell lymphomas, environmentally induced cancers including those induced by asbestos (e.g., mesothelioma), and combinations of said cancers.

55. — A kit comprising a composition of any one of claims 1 to 41 and a package insert comprising instructions for administration of the medicament to treat the subject presenting a dysregulated CD47 pathway.

56. — A pharmaceutical composition comprising CD47-SIRPα blocking agent and one or more anti-cancer agent(s) as claimed in any one of claims 1 to 41 and a pharmaceutically acceptable carrier.

57. — A combination comprising CD47-SIRPα blocking agent and one or more anti-cancer agent(s); wherein the CD47-SIRPα blocking agent is represented by compound of formula (I):



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;
wherein,

R_a is hydrogen; and R₁ represents hydrogen, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₃NHC(=NH)NH₂, (CH₂)₄NH₂, CH₂CONH₂, CH₂-aryl, or CH₂-heteroaryl; or R_a and R₁, together with the atoms to which they are attached form pyrrolidine ring;

~~R₂ represents hydrogen, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, CH₂-aryl, or CH₂-heteroaryl;~~

~~R_b is hydrogen; and R₃ represents hydrogen, CH₂-aryl, (CH₂)₃NHC(=NH)NH₂, (CH₂)₂CONH₂, (CH₂)₂COOH, (CH₂)₄NH₂ or CH₂-heteroaryl; or R_b and R₃, together with the atoms to which they are attached form pyrrolidine ring.~~

12. The composition of claim 1, for use as a medicament.

13. The composition of claim 1, for use in treating or delaying progression of diseases or disorders mediated by deregulated CD47-SIRP α pathway in a subject.

14. The composition for use of claim 13, wherein the subject presenting a dysregulated CD47 pathway is a subject presenting with CD47+ disease cells.

15. The composition for use of claim 13, wherein the disease or disorder is cancer mediated by dysregulated CD47-SIRP α pathway.

16. The composition for use of claim 15, wherein the cancer is selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), non-small cell lung cancer (NSCLC), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, B-cell lymphomas, myeloproliferative disorder/neoplasm (MPDS); myelodysplastic syndrome; giant cell myeloma, heavy-chain myeloma, light chain myeloma and Bence- Jones myeloma, multiple myeloma, environmentally induced cancers including those induced by asbestos (e.g., mesothelioma), and combinations of said cancers.