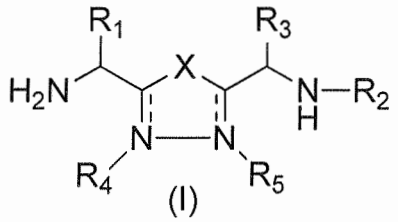
CLAIMS

1. A compound of formula (I)



(I)

wherein,

R_1 represents a side chain of an amino acid selected from Ser, Thr, Phe, Ala and Asn;

X is S or O;

R_2 is hydrogen or -CO-Aaa;

Aaa is an amino acid residue selected from Ser, Asn ~~or~~ and Thr; wherein a C-terminus thereof is a free terminus, is amidated or is esterified;

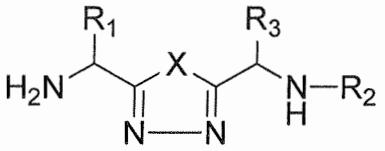
R_3 represents a side chain of an amino acid selected from Ser, Ala, Glu, Gln, Asn and Asp;

---- is an optional bond;

R_4 and R_5 independently are hydrogen or absent;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, having a structure of formula (IA):



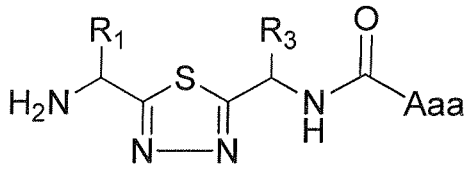
(IA).

3. The compound according to claim 1 or 2, wherein X is S.

4. The compound according to claim 1 or 2, wherein X is O.

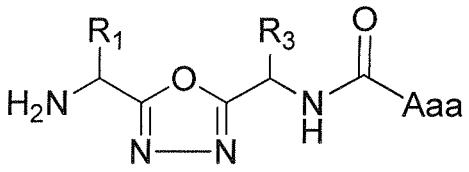
5. The compound according to any one of claims 1 to 4, wherein R_2 is hydrogen.

6. The compound according to claim 1 or 2, having the structure of formula (IB):



(IB).

7. The compound according to claim 1 or 2, having the structure of formula (IC):



(IC).

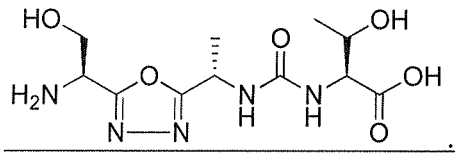
8. The compound according to any one of claims 1 to 4, 6, and 7, wherein R_2 is -CO-Aaa.

9. The compound according to any one of claims 1 to 4 and 6 to 8, wherein Aaa is an amino acid residue Ser or Thr; wherein the C-terminus is a free terminus.

10. The compound according to any one of claims 1 to 9, wherein R_1 represents the side chain of an amino acid residue Ser or Thr.

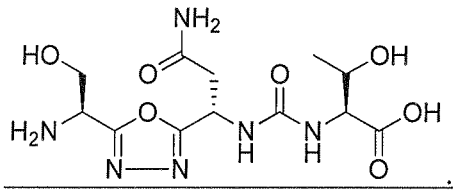
11. The compound according to any one of claims 1 to 10, wherein R_3 represents the side chain of the amino acid residue selected from Glu, Gln, Asn, and Asp.

12. The compound according to claim 1, having the following structure:

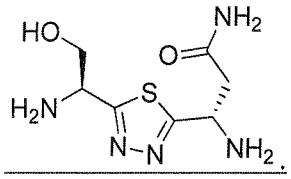


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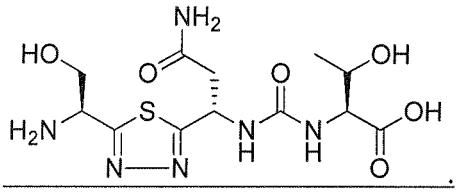
13. The compound according to claim 1, having the following structure:



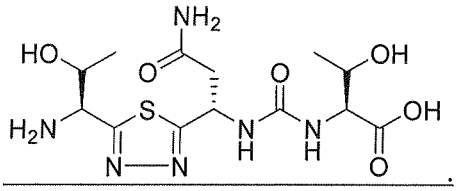
14. The compound according to claim 1, having the following structure:



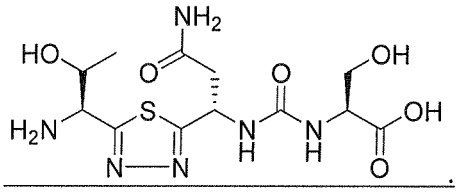
15. The compound according to claim 1, having the following structure:



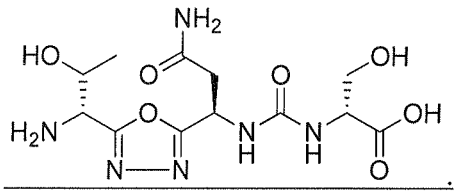
16. The compound according to claim 1, having the following structure:



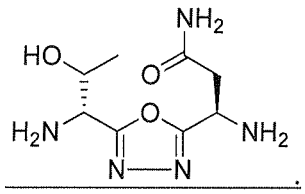
17. The compound according to claim 1, having the following structure:



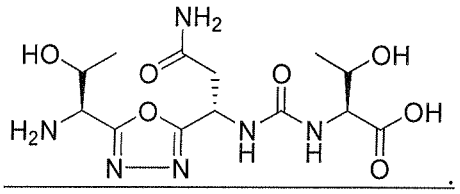
18. The compound according to claim 1, having the following structure:



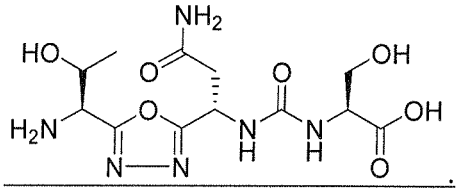
19. The compound according to claim 1, having the following structure:



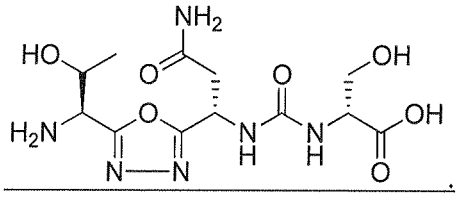
20. The compound according to claim 1, having the following structure:



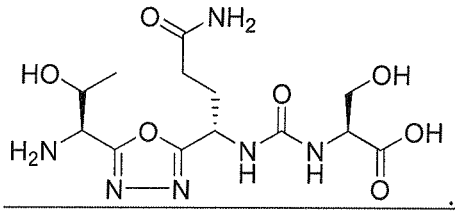
21. The compound according to claim 1, having the following structure:



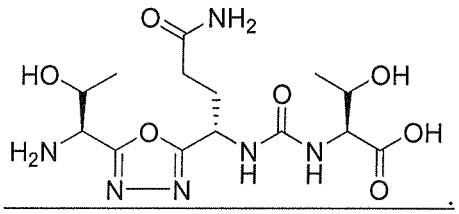
22. The compound according to claim 1, having the following structure:



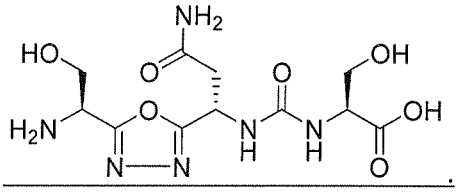
23. The compound according to claim 1, having the following structure:



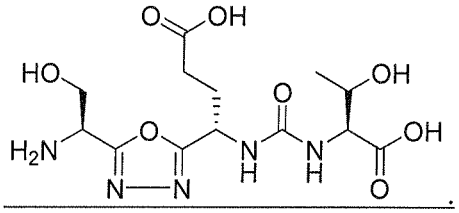
24. The compound according to claim 1, having the following structure:



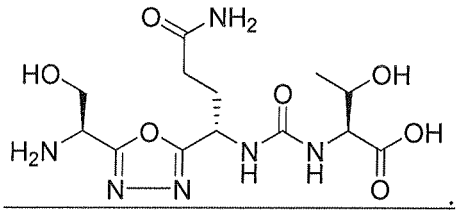
25. The compound according to claim 1, having the following structure:



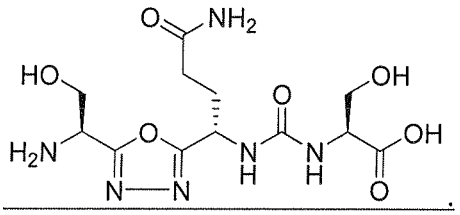
26. The compound according to claim 1, having the following structure:



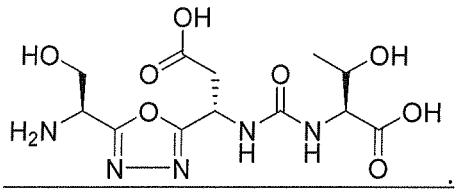
27. The compound according to claim 1, having the following structure:



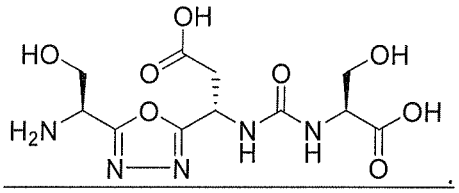
28. The compound according to claim 1, having the following structure:



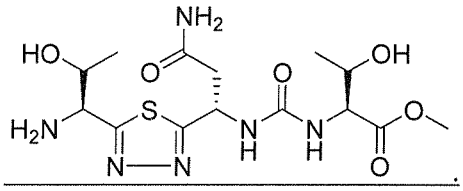
29. The compound according to claim 1, having the following structure:



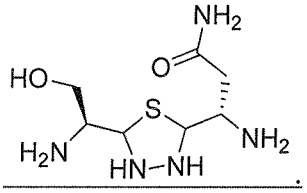
30. The compound according to claim 1, having the following structure:



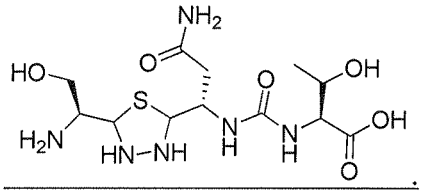
31. The compound according to claim 1, having the following structure:



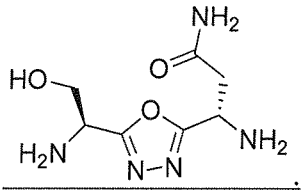
32. The compound according to claim 1, having the following structure:



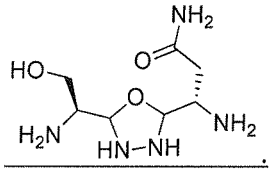
33. The compound according to claim 1, having the following structure:



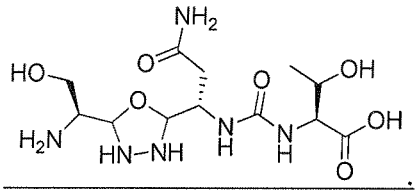
34. The compound according to claim 1, having the following structure:



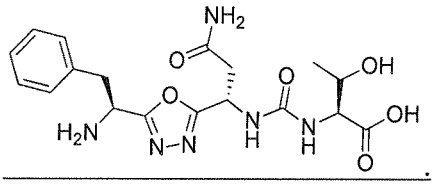
35. The compound according to claim 1, having the following structure:



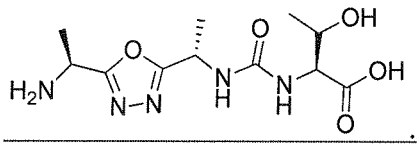
36. The compound according to claim 1, having the following structure:



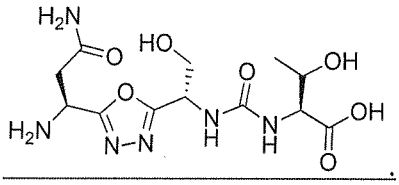
37. The compound according to claim 1, having the following structure:



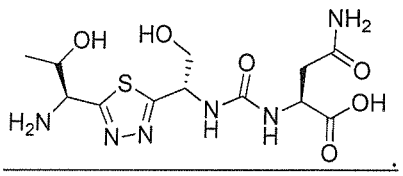
38. The compound according to claim 1, having the following structure:



39. The compound according to claim 1, having the following structure:



40. The compound according to claim 1, having the following structure:



.

41. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and at least one compound according to any one of claims 1 to 40 or a pharmaceutically acceptable salt thereof.

42. The pharmaceutical composition according to claim 41, further comprising at least one agent selected from an anticancer agent, a chemotherapy agent, and an antiproliferative compound.

43. Use of a compound according to any one of claims 1 to 40 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for modulating an immune response mediated by PD-1 signaling pathway.

44. Use of a compound according to any one of claims 1 to 40 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of cancer.

45. Use according to claim 44, wherein the cancer is selected from breast cancer, colon cancer, lung cancer, melanoma, prostate cancer, and renal cancer.

46. Use according to claim 44, wherein the cancer is selected from bone cancer, cancer of the head or neck, pancreatic cancer, skin cancer, cutaneous or intraocular malignant melanoma, 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, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors 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), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

47. Use of a compound according to any one of claims 1 to 40 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of infectious disease.

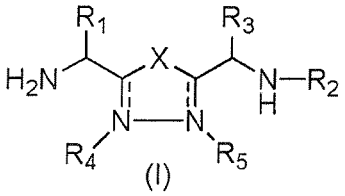
48. Use of a compound according to any one of claims 1 to 40 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a bacterial infectious disease, a viral infectious disease or a fungal infectious disease.

49. Use according to claim 47, wherein the infectious disease is selected from HIV, Influenza, Herpes, *Giardia*, Malaria, *Leishmania*, the pathogenic infection by the virus Hepatitis (A, B, & C), herpes virus (e.g., VZV, HSV-I, HAV-6, HSV-II, and CMV, Epstein Barr virus), adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, cornovirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus and arboviral encephalitis virus, pathogenic infection by the bacteria *chlamydia*, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci and conococci, *klebsiella, proteus, serratia, pseudomonas, E. coli, legionella*, diphtheria, *salmonella*, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lyme's disease bacteria, pathogenic infection by the fungi *Candida* (*albicans, krusei, glabrata, tropicalis*, etc.), *Cryptococcus neoformans, Aspergillus* (*fumigatus, niger*, etc.), Genus *Mucorales* (*mucor, absidia, rhizophus*), *Sporothrix schenkii, Blastomyces dermatitidis, Paracoccidioides brasiliensis, Coccidioides immitis* and *Histoplasma capsulatum*, and pathogenic infection by the parasites *Entamoeba histolytica, Balantidium coli, Naegleria fowleri, Acanthamoeba* sp., *Giardia lambia,*

Cryptosporidium sp., *Pneumocystis carinii*, *Plasmodium vivax*, *Babesia microti*, *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania donovani*, *Toxoplasma gondi*, or *Nippostrongylus brasiliensis*.

We claim:

1. A compound of formula (I)



(I)

wherein,

R_1 is side chain of an amino acid selected from Ser, Thr, Phe, Ala or Asn;

X is S or O;

R_2 is hydrogen or -CO-Aaa;

Aaa is an amino acid residue selected from Ser, Asn or Thr; wherein a C-terminus thereof is a free terminus, is amidated or is esterified;

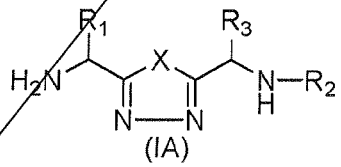
R_3 is side chain of an amino acid selected from Ser, Ala, Glu, Gln, Asn or Asp;

---- is an optional bond;

R_4 and R_5 independently are hydrogen or absent;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

2. The compound according to claim 1 is a compound of formula (IA):



(IA)

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein,

R_1 is side chain of an amino acid selected from Ser, Thr, Phe, Ala or Asn;

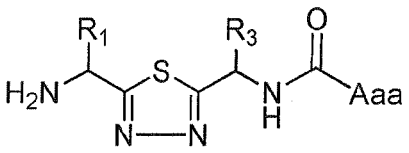
X is S or O;

R_2 is hydrogen or -CO-Aaa;

R_3 is side chain of an amino acid selected from Ser, Ala, Glu, Gln, Asn or Asp;

Aaa is an amino acid residue selected from Ser, Asn or Thr; wherein a C-terminus thereof is a free terminus, is amidated or is esterified.

3. The compound according to any one of claims 1 to 2, is a compound of formula (IB):



(IB)

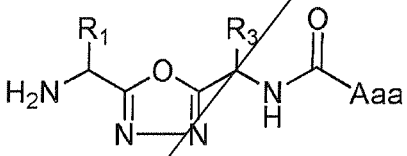
or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein,

R_1 is side chain of an amino acid selected from Ser, Thr, Phe, Ala or Asn;

R_3 is side chain of an amino acid selected from Ser, Ala, Glu, Gln, Asn or Asp;

Aaa is an amino acid residue selected from Ser, Asn or Thr; wherein a C-terminus thereof is a free terminus, is amidated or is esterified.

4. The compound according to any one of claims 1 to 2, is a compound of formula (IC):



(IC)

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein,

R_1 is side chain of an amino acid selected from Ser, Thr, Phe, Ala or Asn;

R_3 is side chain of an amino acid selected from Ser, Ala, Glu, Gln, Asn or Asp;

Aaa is an amino acid residue selected from Ser, Asn or Thr; wherein a C-terminus thereof is a free terminus, is amidated or is esterified.

5. The compound according to any one of claims 1 to 2, wherein X is O.

6. The compound according to any one of claims 1 to 2, wherein X is S.

7. The compound according to claim 1, wherein

R_1 is side chain of Ser or Thr;

R_2 is -CO-Aaa;

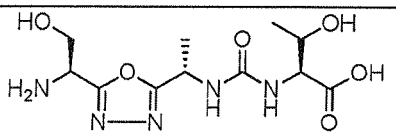
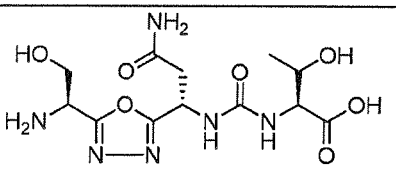
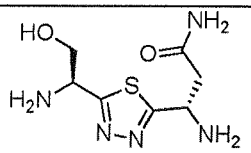
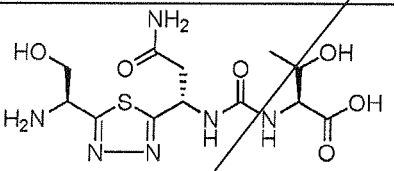
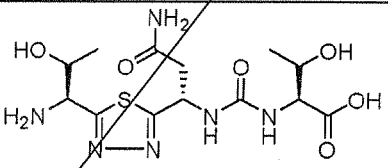
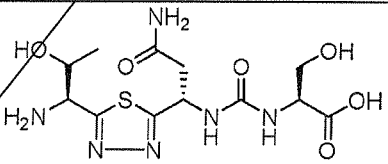
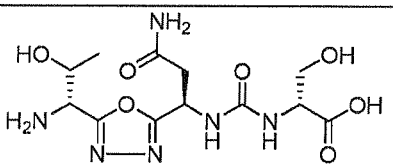
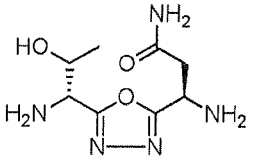
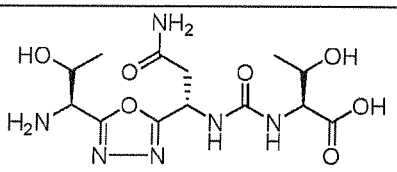
Aaa is an amino acid residue Ser or Thr; wherein the C-terminus is free;

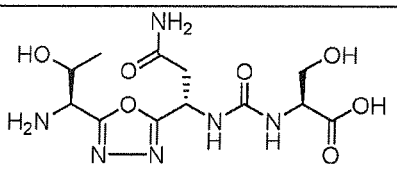
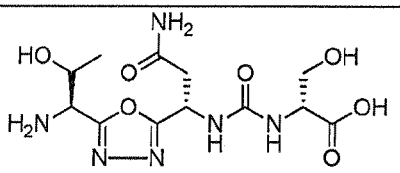
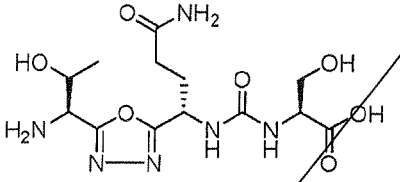
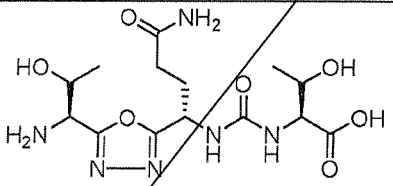
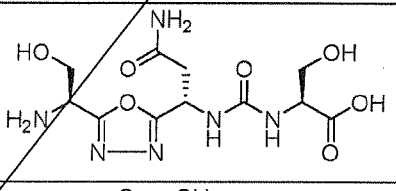
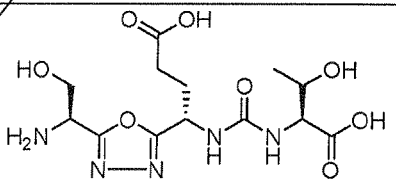
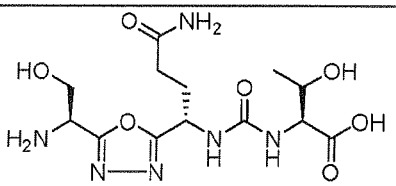
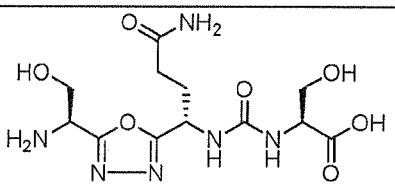
R_3 is side chain of Asn, Gln, Glu or Asp.

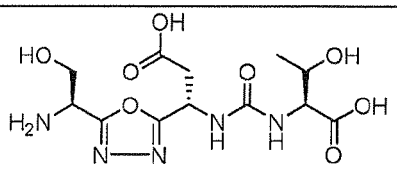
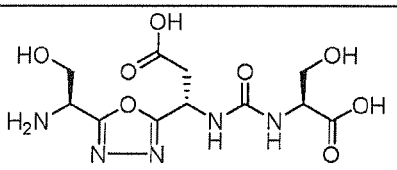
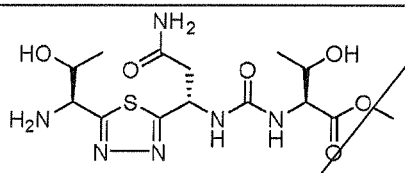
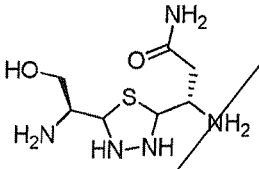
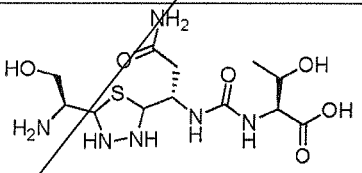
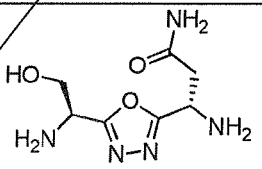
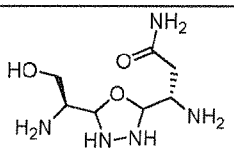
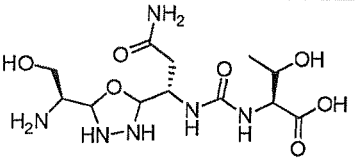
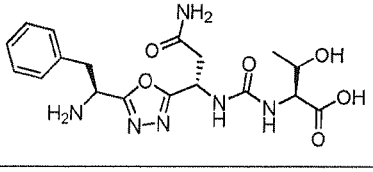
8. The compound according to any one of claims 1 to 2, wherein R_2 is hydrogen.

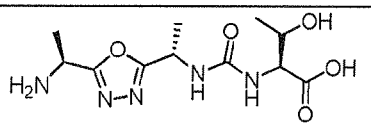
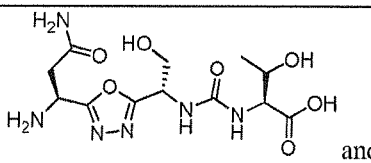
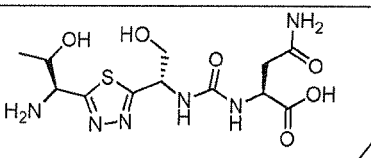
9. A compound according to claim 1 is selected from the group consisting of

Compound No.	Structure

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27.	
28.	 and
29.	

or a pharmaceutically acceptable salt or a stereoisomer thereof.

10. A pharmaceutical composition comprising at least one compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt or a stereoisomer thereof, and a pharmaceutically acceptable carrier or excipient.

11. The pharmaceutical composition according to claim 10, comprising at least one additional pharmaceutical agent wherein the said additional pharmaceutical agent is an anticancer agent, chemotherapy agent, or antiproliferative compound.

12. A compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt or a stereoisomer thereof, for use as a medicament.

13. A compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt or a stereoisomer thereof, for use as a medicament for the treatment of cancer or infectious disease.

14. A compound for use according to claim 13, wherein the cancer is selected from bone cancer, cancer of the head or neck, pancreatic cancer, skin cancer, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine 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, 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), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

15. A compound for use according to claim 13, wherein the infectious disease is a bacterial infectious disease, a viral infectious disease or a fungal infectious disease.

16. A method of modulating an immune response mediated by PD-1 signaling pathway in a subject, comprising administering to the subject therapeutically effective amount of a compound according to any one of claims 1 to 9.

17. A method of inhibiting growth of tumour cells and/or metastasis in a subject, comprising administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 9.

18. The method of claim 15, wherein the tumour cells are of a cancer selected from the group consisting of breast cancer, colon cancer, lung cancer, melanoma, prostate cancer and renal cancer.

19. The method of claim 15, wherein the tumour cells are of a cancer selected from the list consisting of bone cancer, cancer of the head or neck, pancreatic cancer, skin cancer, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine 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, 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), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

20. A method of treating an infectious disease in a subject comprising administering to the subject a therapeutically effective amount of compound according to any one of claims 1 to 9.

21. A method of treating bacterial, viral and fungal infections in a subject comprising administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 9.