tolerance and control of T cell activation. Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway contributes to inhibition of active T-cell immune surveillance of tumors. Inhibition of PD-1 or PD-L1, has been shown to restore immune mediated destruction of tumors. Clinical research has found that targeting PD-1or PD-L1 with antagonist antibodies releases the PD-1 pathway mediated inhibition of the immune response, including the anti-tumor response.

Notch pathway signaling is reported to be a regulator of PD-1 expression by activated $CD8^+$ T cells, Mathieu et al, *Immunology and Cell Biology*, 2013, 91: 82-88. Despite existing treatment options for patients with cancer, there continues to be a need for new and different therapies affording one or both of enhanced efficacy and lower toxicity. Current immunotherapies have shown a benefit in a subset of cancer types and only in a subset of patients. Novel therapies or combination strategies are needed to improve the overall response against specific cancers or to facilitate extension of these treatments into cancers that may currently be less responsive to either agent alone.

It is believed the present invention provides beneficial therapeutic effects from the combined activity of Compound A and anti-PD-1 or PD-L1 monoclonal antibody inhibitor activity against T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumors, soft tissue sarcoma, and adenoid cystic carcinoma as compared to the therapeutic effects provided by either agent alone.

Disclosed is a method of treating T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia,

acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, or adenoid cystic carcinoma in a patient comprising administering to a patient in need of treatment an effective amount of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, and an effective amount of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

Disclosed is a method of treating colorectal cancer in a patient, comprising administering to the patient in need of treatment an effective amount of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, and an effective amount of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

Disclosed is a method of treating T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, or adenoid cystic carcinoma in a patient, comprising administering to a patient in need of treatment, simultaneously, separately, or sequentialy, an effective amount of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-

hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, and an effective amount of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

Disclosed is a method of treating colorectal cancer in a patient, comprising administering to a patient in need of treatment, simultaneously, separately, or sequentialy, an effective amount of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, and an effective amount of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

Disclosed is a compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof; and a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab; for simultaneous, separate, or sequential use in the treatment of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, or adenoid cystic carcinoma.

In one aspect, there is provided a compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, for use in treating a cancer, wherein said cancer is selected from the group consisting of T-cell acute

lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma, wherein the compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered in combination with a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

In another aspect, there is provided a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab, for use in treating a cancer, wherein said cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma, wherein the PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab is to be administered in combination with 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof.

In another aspect, there is provided a combination of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof; and a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab for use in the treatment of a cancer selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma.

Disclosed is a compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof; and a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab,

durvalumab, and avelumab; for simultaneous, separate, or sequential use in the treatment of colorectal cancer.

Disclosed is use of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof for the manufacture of a medicament; and use of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab for the manufacture of a medicament;
for the simultaneous, separate, or sequential treatment of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, or adenoid cystic carcinoma.

In another aspect, there is provided use of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof in the manufacture of a first medicament; and
use of a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab in the independent manufacture of a second medicament; for the treatment of a cancer selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver

cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor soft tissue sarcoma, and adenoid cystic carcinoma, wherein the first medicament and the second medicament are to be administered in combination.

Disclosed is use of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof for the manufacture of a medicament; and use of a PD-1 or PD-L1 inhibitor selected from pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab for the manufacture of a medicament;
for the simultaneous, separate, or sequential treatment of colorectal cancer.

Disclosed is a commercial package comprising a separate composition of each of the therapeutic agents together with instructions for simultaneous, separate or sequential administration for use in treating T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple

negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, or adenoid cystic carcinoma.

Disclosed is a commercial package comprising a separate composition of each of the therapeutic agents together with instructions for simultaneous, separate or sequential administration for use in treating colorectal cancer.

The compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, (Compound A) has the CAS registry number 142138-81-4. Alternativly, the compound may be named: N-[(1S)-2-[[(7S)-6,7-dihydro-5-(2-hydroxyethyl)-6-oxo-5H-pyrido[3,2-a][3]benzazepin-7-yl]amino]-1-methyl-2-oxoethyl]-4,4,4-trifluorobutanamide. Other names may be used to unambiguously identify Compound A.

The terms, as used herein, "PD-1 inhibitor" and PD-L1 inhibitor" mean a fully human, or humanized IgG, , optionally optimized, monoclonal antibody.

PD-1 inhibitors include nivolumab and pembrolizumab. Nivolumab, (Opdivo®) is also known as iMDX- 1106, MDX-1106-04, ONO-4538, or BMS-936558 and has a CAS Registry Number: of 946414-94-4. Nivolumab is a fully human IgG4 monoclonal antibody which specifically blocks PD-1. Nivolumab (clone 5C4) and other human monoclonal antibodies that specifically bind to PD-1 are disclosed in US 8,008,449 and WO2006/121168. Pembrolizumab, (Keytruda®) (formerly lambrolizumab), also known as Merck 3745, MK-3475 or SCH-900475, is a humanized IgG4 monoclonal antibody that binds to PD-1. Pembrolizumab is disclosed in Hamid, O. et al., *New England Journal of Medicine*, 2013, 369(2): 134-44; WO2009/114335; and US 8,354,509. Other anti- PD-1 antibodies are disclosed in US 8,609,089; US 2010028330; and/or US 20120114649.

WE CLAIM:

1. A compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof, for use in treating a cancer, wherein said cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma, wherein the compound 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered in combination with a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab.

2. A PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab, for use in treating a cancer, wherein said cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic

cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma, wherein the PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab is to be administered in combination with 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof.

3. A combination of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof; and a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab for use in the treatment of a cancer selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor, soft tissue sarcoma, and adenoid cystic carcinoma.

4. The compound for use according to claim 1, the PD-1 or PD-L1 inhibitor for use according to claim 2, or the combination for use according to Claim 3, wherein said cancer is colorectal cancer.

5. The compound for use according to claim 1 or claim 4, the PD-1 or PD-L1 inhibitor for use according to claim 2 or claim 4, or the combination for use according to claim 3 or claim 4, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-

hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof, and the PD-1 or PD-L1 inhibitor are to be administered simultaneously, separately, or sequentially.

6. The compound for use according to any of claims 1, 4, and 5, the PD-1 or PD-L1 inhibitor for use according to any of claims 2, 4, and 5, or the combination for use according to any of claims 3-5, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered in an amount between 2.5 mg and 75 mg.

7. The compound for use according to any of claims 1 and claim 4-6, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and claim 4-6, or the combination for use according to any of claims 3-6, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered in an amount between 10 mg and 50 mg.

8. The compound for use according to any of claims 1 and 4-7, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and 4-7, or the combination for use according to any of claims 3-7, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered once per day every other day over a five day period followed by two days without dosing (T.I.W.).

9. The compound for use according to any of claims 1 and 4-8, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and 4-8, or the combination for use according to any of claims 3-8, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof is to be administered orally.

10. The compound for use according to any of claims 1 and 4-9, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and 4-9, or the combination for use according to any of claims 3-9, wherein the PD-1 or PD-L1 inhibitor is to be administered of between 1 mg/kg and 3 mg/kg.

11. The compound for use according to any of claims 1 and 4-10, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and 4-10, or the combination for use according to any of claims 3-10, wherein the PD-1 or PD-L1 inhibitor is to be administered once every 14 to 21 days.

12. The compound for use according to any of claims 1 and 4-11, the PD-1 or PD-L1 inhibitor for use according to any of claims 2 and 4-11, or the combination for use according to any of claims 3-11, wherein the PD-1 or PD-L1 inhibitor is to be administered parenterally.

13. The compound for use according to claim 12, the PD-1 or PD-L1 inhibitor for use according to claim 12, or the combination for use according to claim 12, wherein the parenteral administration is intravenous infusion.

14. Use of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof in the manufacture of a first medicament; and use of a PD-1 or PD-L1 inhibitor selected from the group consisting of pembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab in the independent manufacture of a second medicament; for the treatment of a cancer selected from the group consisting of T-cell acute lymphoblastic leukemia, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, erythroleukemia, triple negative breast cancer, breast cancer, ovarian cancer, melanoma, lung cancer, non small-cell lung cancer, pancreatic cancer, glioblastoma, colorectal cancer, head and neck cancer, cervical cancer, prostate cancer, liver cancer, oral squamous cell carcinoma, skin cancer, medulloblastoma, hepatocellular carcinoma, intrahepatic and extrahepatic cholangiocarcinoma, desmoid tumor soft tissue sarcoma, and adenoid cystic carcinoma, wherein the first medicament and the second medicament are to be administered in combination.

15. The use of Claim 14, wherein said cancer is colorectal cancer.

16. The use of claim 14 or claim 15, wherein the 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or the pharmaceutically acceptable salt or hydrate thereof, and the PD-1 or PD-L1 inhibitor are to be administered simultaneously, separately, or sequentially.

17. The use of any of claims 14-16, wherein the first medicament comprises between 2.5 mg and 75 mg of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof.

18. The use of claim 17, wherein the first medicament comprises between 10 mg and 50 mg of 4,4,4-trifluoro-N-[(1S)-2-[[(7S)-5-(2-hydroxyethyl)-6-oxo-7H-pyrido[2,3-d][3]benzazepin-7-yl]amino]-1-methyl-2-oxo-ethyl]butanamide, or a pharmaceutically acceptable salt or hydrate thereof.

19. The use of any of claims 14-18, wherein the first medicament is to be administered once per day every other day over a five day period followed by two days without dosing (T.I.W.).

20. The use of any of claims 14-19, wherein the first medicament is to be administered orally.

21. The use of any of claims 14-20, wherein the second medicament is to be administered in an amount between 1 mg/kg and 3 mg/kg.

22. The use of any of claims 14-21, wherein the second medicament is to be administered once every 14 to 21 days.

23. The use of any of claims 14-22, wherein the second medicament is to be administered parenterally.

24. The use of claim 23, wherein the parenteral administration is intravenous infusion.