CLAIMS

1. Use of a TLR7 agonist in manufacture of a medicament for inducing effector memory T cell to treat a cancer or an infection, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6 methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and is used with an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

2. Use of a TLR7 agonist in manufacture of a medicament for inducing MHC class I to treat a cancer or an infection, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6 methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and is used with an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is an

anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

3. The use according to claim 1 or 2, wherein the medicament is for treating a cancer.

4. The use according to claim 3, wherein the cancer is selected from the group consisting of non-small-cell lung cancer; small cell lung cancer; pancreatic cancer; malignant melanoma; renal cell carcinoma; gastric cancer; colon cancer; rectal cancer; small intestinal cancer; breast cancer; germ cell cancer; bladder cancer; prostate cancer; endometrial cancer; cervical cancer; ovarian cancer; liver cancer; Merkel cell carcinoma; bone cancer; head and neck cancer; cutaneous or intraorbital malignant melanoma; anal cancer; testicular cancer; esophageal cancer; endocrine system cancer; thyroid cancer; parathyroid cancer; adrenal cancer; soft tissue sarcoma; urothelial cancer; penile cancer; glioblastoma multiforme; brain tumor; chronic or acute leukemia including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, and chronic lymphocytic leukemia; malignant lymphoma including Hodgkin's lymphoma and non-Hodgkin's lymphoma; myelodysplastic syndrome; and multiple myeloma.

5. The use according to any one of claims 1 to 4, wherein the medicament is to be administered to a patient having refractoriness to the immune checkpoint inhibitor.

6. The use according to any one of claims 1 to 5, wherein the medicament is to be administered to a patient who has relapsed with cancer.

7. The use according to any one of claims 1 to 6, wherein the medicament has a long-term anticancer immunity.

8. The use according to any one of claims 1 to 7, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, or a pharmaceutically acceptable salt thereof.

~~9. The use according to any one of claims 1 to 8, wherein the immune checkpoint inhibitor is at least one medicament that can inhibit the function of a molecular which is selected from the group consisting of~~

~~(1) CTLA-4,~~

~~(2) PD-1,~~

~~(3) LAG-3,~~

~~(4) BTLA,~~

~~(5) KIR,~~

~~(6) TIM-3,~~

~~(7) PD-L1,~~

~~(8) PD-L2,~~

~~(9) B7-H3,~~

~~(10) B7-H4,~~

~~(11) HVEM,~~

~~(12) GAL9,~~

~~(13) CD160,~~

~~(14) VISTA,~~

~~(15) BTNL2,~~

~~(16) TIGIT,~~

~~(17) PVR,~~

~~(18) BTN1A1,~~

~~(19) BTN2A2,~~

~~(20) BTN3A2, and~~

~~(21) CSF-1R.~~

~~10. The use according to claim 9, wherein the immune checkpoint inhibitor is at least one medicament that can inhibit the function of a molecular which is selected from the group consisting of CTLA-4, PD-1, LAG-3, TIM-3, BTLA, VISTA, HVEM, TIGIT, PVR, PD-L1, and CD160.~~

~~11. The use according to claim 10, wherein the immune checkpoint inhibitor is a medicament which can inhibit the function of a molecular of PD-1 or PD-L1.~~

~~12. The use according to any one of claims 9 to 11, wherein the immune checkpoint inhibitor is an antibody against the molecular.~~

~~13. The use according to claim 12, wherein the immune checkpoint inhibitor is anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA-4 antibody.~~

~~14~~9. The use ~~agent~~ of ~~claim 12~~any one of claims 1 to 8, wherein the immune checkpoint inhibitor is anti-PD-1 antibody or anti-PD-L1 antibody.

~~15~~10. The use according to ~~claim 12~~any one of claims 1 to 8, wherein the immune checkpoint inhibitor is anti-PD-1 antibody.

~~16~~11. The use according to ~~claim 12~~any one of claims 1 to 8, wherein the immune checkpoint inhibitor is anti-CTLA-4 antibody.

~~17~~12. The use according to ~~claim 13 or 14~~any one of claims 1 to 10, wherein the anti-PD-1 antibody is nivolumab, pembrolizumab, cemiplimab, tislelizumab, dostarlimab, spartalizumab, camrelizumab, genolimzumab, sintilimab, JNJ-3283, BI-754091, INCMGA-00012, ABBV-181, CC-90006, AGEN-

2034w, GSL-010, LZM-009, Sym-021, AB-122, AK-105, CS-1003, HLX-10, or BCD-100.

~~18~~13. The use according to any one of claims 1 to 9~~claim 13 or 14~~, wherein the anti-PD-L1 antibody is durvalumab, atezolizumab, avelumab, STI-1014, CK-301, BMS-986189, LY-3300054, CX-072, CBT-502, FAZ-053, FS-118, HTI-1088, MSB-2311, BGB-A333, IMC-001, HLX-20, A-167, or BMS-936559.

~~19~~14. The use according to any one of claims 1 to 8 and 11~~claim 13 or 16~~, wherein the anti-CTLA-4 antibody is ipilimumab, tremelimumab, BMS-986218, MK-1308, ADU-1604, BMS-986249, CS-1002, BCD-145, or REGN-4659.

~~20~~15. The use according to any one of claims 1 to ~~19~~14, wherein the TLR7 agonist and the immune checkpoint inhibitor are to be simultaneously administered.

~~21~~16. The use according to any one of claims 1 to ~~19~~14, wherein the TLR7 agonist and the immune checkpoint inhibitor are to be separately administered.

~~22~~17. The use according to any one of claims 1 to ~~19~~14, wherein the TLR7 agonist is to be administered prior to the immune checkpoint inhibitor.

~~23~~18. The use according to any one of claims 1 to ~~19~~14, wherein the TLR7 agonist is to be administered posterior to the immune checkpoint inhibitor.

~~24~~19. The use according to any one of claims 1 to ~~23~~18, wherein the medicament further comprises a pharmaceutically acceptable carrier.

~~25~~20. A kit of an agent for inducing effector memory T cell, comprising a TLR7 agonist and an immune checkpoint inhibitor, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

~~26~~21. A kit of an agent for inducing MHC class I, comprising a TLR7 agonist and an immune checkpoint inhibitor, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine,

N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

~~27~~22. Use of a TLR7 agonist in manufacture of a medicament for inducing effector memory T cell to treat a cancer or an infection, wherein the TLR7 agonist is to be administered simultaneously, separately, or sequentially with an immune checkpoint inhibitor, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

~~28~~23. Use of a TLR7 agonist in manufacture of a medicament for inducing MHC class I to treat a cancer or an infection, wherein the TLR7 agonist is to be administered simultaneously, separately, or sequentially with an immune checkpoint inhibitor, wherein the TLR7 agonist is N-{4-[(2-

amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

~~29~~24. Use of a TLR7 agonist comprising N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, in manufacture of a medicament for treating or preventing a cancer, wherein the medicament is to be used with an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA-4 antibody.

~~30~~25. The use according to claim ~~29~~24, wherein the TLR7 agonist is N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, or a pharmaceutically acceptable salt thereof.

~~31. The use according to claim 29, wherein the immune checkpoint inhibitor is anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA-4 antibody.~~

~~32~~26. The use according to claim ~~29~~24, wherein the immune checkpoint inhibitor is anti-PD-1 antibody or anti-PD-L1 antibody.

~~33~~27. The use according to claim ~~29~~24, wherein the immune checkpoint inhibitor is anti-PD-1 antibody.

~~34~~28. The use according to claim ~~29~~24, wherein the immune checkpoint inhibitor is anti-CTLA-4 antibody.

~~35~~29. The use according to ~~claim 31 or 32~~any one of claims 24 to 27, wherein the anti-PD-1 antibody is nivolumab, pembrolizumab, cemiplimab, tislelizumab, dostarlimab, spartalizumab, camrelizumab, genolimzumab, sintilimab, JNJ-3283, BI-754091, INCMGA-00012, ABBV-181, CC-90006, AGEN-2034w, GSL-010, LZM-009, Sym-021, AB-122, AK-105, CS-1003, HLX-10, or BCD-100.

~~36~~30. The use according to ~~claim 31 or 32~~any one of claims 24 to 26, wherein the anti-PD-L1 antibody is durvalumab, atezolizumab, avelumab, STI-1014, CK-301, BMS-

986189, LY-3300054, CX-072, CBT-502, FAZ-053, FS-118, HTI-1088, MSB-2311, BGB-A333, IMC-001, HLX-20, A-167, or BMS-936559.

~~37~~31. The use according to any one of claims 24, 25 and 28~~claim 31 or 33~~, wherein the anti-CTLA-4 antibody is ipilimumab, tremelimumab, BMS-986218, MK-1308, ADU-1604, BMS-986249, CS-1002, BCD-145, or REGN-4659.

~~38~~32. The use according to any one of claims ~~29~~ 24 to ~~37~~31, wherein the medicament is to be administered to a patient who is resistant to the immune checkpoint inhibitor.

~~39~~33. The use according to any one of claims ~~29~~ 24 to ~~37~~31, wherein the medicament is to be administered to a patient who suffers relapse of cancer.

~~40~~34. The use according to any one of claims ~~29~~ 24 to ~~37~~31, wherein the medicament has a long-term anticancer immunity.

~~41~~35. The use according to any one of claims ~~29~~ 24 to ~~37~~31, wherein the medicament further comprises a pharmaceutically acceptable carrier.

~~42~~36. A kit of an agent for treating or preventing a cancer, comprising N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine, N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof, and an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA-4 antibody.

~~43~~37. Use of a TLR7 agonist comprising N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2,2-trifluoroethyl)glycine,N-{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxybenzyl}-N-(2,2-difluoroethyl)glycine, or a pharmaceutically acceptable salt thereof in manufacture of a medicament for treating or preventing a cancer, wherein the TLR7 agonist is to be administered simultaneously, separately, or sequentially with an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA-4 antibody.