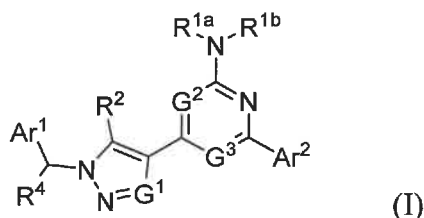


CLAIMS

1. A compound having the Formula (I)



or a pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein,

G^1 is N or CR^{3a} ;

G^2 is N or CR^{3b} ;

G^3 is N or CR^{3c} ;

R^{3a} , R^{3b} , and R^{3c} are each independently H, deuterium or C_{1-3} alkyl;

R^{1a} and R^{1b} are each independently selected from the group consisting of

i) H or deuterium,

ii) C_{1-8} alkyl optionally substituted with from 1-3 R^5 substituents,

iii) $-X^1-O-C_{1-8}$ alkyl optionally substituted with from 1-3 R^5 substituents,

iv) $-C(O)-R^6$,

v) Y optionally substituted with 1-3 R^7 substituents, and

vi) $-X^1-Y$ optionally substituted with 1-3 R^7 substituents; or

vii) R^{1a} and R^{1b} together with the nitrogen to which they are attached form a 5-6 membered heterocycloalkyl ring optionally substituted with from 1-3 R^8 substituents, wherein the heterocycloalkyl has 0-2 additional heteroatom ring vertices selected from the group consisting of O, N, and S;

each Y is C_{3-8} cycloalkyl or 4 to 6-membered heterocycloalkyl having 1-3 heteroatom ring vertices selected from the group consisting of O, N, and S;

R^2 and R^4 are each independently H, deuterium or C_{1-3} alkyl;

Ar^1 is phenyl or a 5 to 6-membered heteroaryl, each of which is optionally substituted with 1-3 R^9 ;

Ar^2 is phenyl or a 5 to 6-membered heteroaryl, each of which is optionally substituted with 1-3 R^{10} ;

26 wherein the 5 to 6-membered heteroaryl of Ar¹ and Ar² each independently have 1-3
 27 heteroatom ring vertices selected from the group consisting of O, N, N⁺-O⁻ and S;
 28 each X¹ is C₁₋₆ alkylene;
 29 each R⁵ is independently selected from the group consisting of hydroxyl, C₃₋₈ cycloalkyl,
 30 phenyl, -O-phenyl, -C(O)OR^a and oxo;
 31 each R⁶ is C₁₋₈ alkyl or Y, each of which is optionally substituted with 1-3 substituents
 32 selected from the group consisting of hydroxyl, -O-phenyl, phenyl, and -O-C₁₋₈ alkyl;
 33 each R⁷ is independently selected from the group consisting of C₁₋₈ alkyl, hydroxyl,
 34 -O-C₁₋₈ alkyl, oxo, and C(O)OR^a;
 35 each R⁸ is independently selected from the group consisting of C₁₋₈ alkyl, hydroxyl, and
 36 oxo;
 37 each R⁹ is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈
 38 deutoalkyl, -O-C₁₋₈ alkyl, -O-C₁₋₈ deutoalkyl, -X¹-O-C₁₋₈ alkyl, -O-X¹-O-C₁₋₈ alkyl, -X¹-O-
 39 X¹-O-C₁₋₈ alkyl, -C(O)OR^a, halogen, cyano, -NR^bR^c, Y, -X¹-C₃₋₈ cycloalkyl, and -X²-Z, wherein
 40 X² is selected from the group consisting of C₁₋₆ alkylene, -C₁₋₆ alkylene-O-, -C(O)-, and -S(O)₂-,
 41 Z is 4 to 6-membered heterocycloalkyl having 1-3 heteroatom ring vertices selected from the
 42 group consisting of O, N, and S, and wherein each of said R⁹ substituents is optionally
 43 substituted with 1-3 R¹¹;
 44 each R¹⁰ is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈
 45 deutoalkyl, halo, cyano, -O-C₁₋₈ alkyl, -O-C₁₋₈ deutoalkyl, -X¹-O-C₁₋₈ alkyl, -O-X¹-O-C₁₋₈
 46 alkyl, -S(O)₂-C₁₋₆ alkyl, -C(O)NR^dR^e, and 4-6-membered heteroaryl having from 1-3 heteroatom
 47 ring vertices selected from the group consisting of O, N, and S, wherein each of said R¹⁰
 48 substituents is optionally substituted with 1-3 R¹², or two R¹⁰ on adjacent ring vertices of Ar² are
 49 optionally combined to form a 5-membered heterocyclic ring optionally substituted with 1-2
 50 halogens;
 51 each R¹¹ is independently selected from the group consisting of hydroxyl, halo, cyano,
 52 -NR^dR^e, -C(O)OR^a, phenyl, C₃₋₈ cycloalkyl, and C₁₋₄ alkyl optionally substituted with C(O)OR^a;
 53 each R¹² is independently selected from the group consisting of halo, cyano, hydroxy,
 54 -C(O)OR^a; and
 55 each R^a is H, deuterium, or C₁₋₆ alkyl;

each R^b and R^c are independently selected from the group consisting of H, deuterium, C_{1-8} alkyl, $-S(O)_2-C_{1-6}$ alkyl, $-C(O)OR^a$, and $-X^1-C(O)OR^a$;
 each R^d and R^e are independently selected from the group consisting of H, deuterium, C_{1-8} alkyl, $-S(O)_2-C_{1-6}$ alkyl; and
 provided that when G^1 and G^2 are each N, G^3 is CH, R^2 is CH_3 , and R^{1a} and R^{1b} are each H or deuterium, then Ar^2 is other than 2-thienyl, phenyl, 2-, 3- or 4-methoxyphenyl, 3- or 4-halophenyl, 2,4-dimethoxyphenyl, 2,4-dichlorophenyl or 2- or 4-methylphenyl.

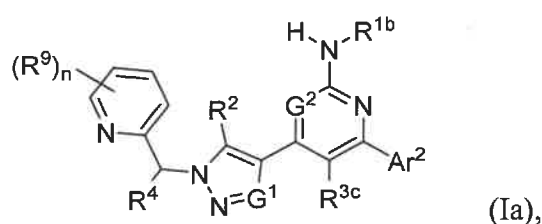
2. The compound of claim 1, wherein Ar^1 is a 5 to 6-membered heteroaryl optionally substituted with 1-3 R^9 .

3. The compound of claim 2, wherein Ar^1 is selected from the group consisting of pyridyl, pyridyl N-oxide, imidazolyl, pyrazolyl, and thiazolyl optionally substituted with 1-3 R^9 .

4. The compound of claim 3, wherein Ar^1 is pyridyl optionally substituted with 1-3 R^9 .

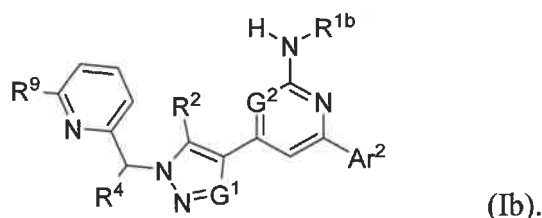
5. The compound of any one of claims 1-4, wherein the G^3 is CR^{3c} .

6. The compound of any one of claims 1-4, wherein the compound of Formula (I) is represented by Formula (Ia)



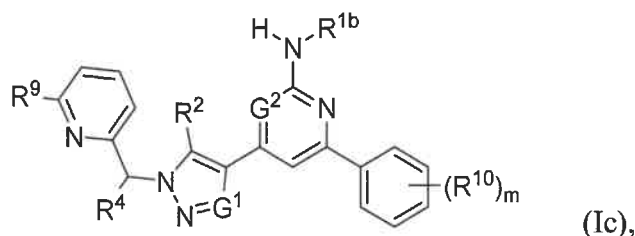
wherein, n is an integer from 0 to 2.

7. The compound of any one of claims 1-6, wherein the compound of Formula (I) is represented by Formula (Ib)



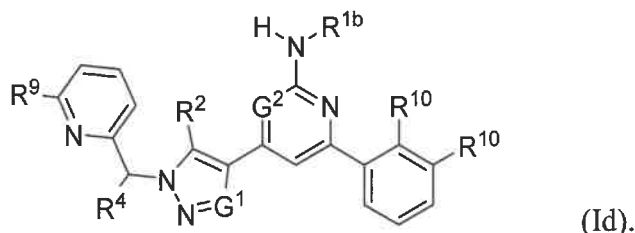
8. The compound of any one of claims 1-7, wherein Ar² is substituted with from 1-3 R¹⁰ and at least one R¹⁰ is cyano.

9. The compound any one of claims 1-8, wherein the compound of Formula (I) is represented by Formula (Ic)



wherein m is an integer from 0 to 2.

10. The compound of any one of claims 1-9, wherein the compound of Formula (I) is represented by Formula (Id)

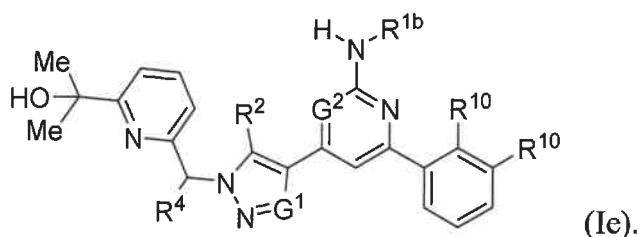


11. The compound of any one of claims 1-10, wherein each R⁹ is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈ deuterioalkyl, -O-C₁₋₈ alkyl, -O-C₁₋₈ deuterioalkyl, -X¹-O-C₁₋₈ alkyl, -O-X¹-O-C₁₋₈ alkyl, -X¹-O-X¹-O-C₁₋₈ alkyl, wherein each of said R⁹ substituents is optionally substituted with 1-3 R¹¹.

12. The compound of any one of claims 1-10, wherein each R⁹ is independently selected from the group consisting of -C(O)OR^a, -NR^bR^c, Y, -X¹-C₃₋₈ cycloalkyl, and -X²-Z, wherein X² is selected from the group consisting of C₁₋₆ alkylene, -C₁₋₆ alkylene-O-, -

C(O)-, and -S(O)₂-, Z is 4 to 6-membered heterocycloalkyl having 1-3 heteroatom ring vertices selected from the group consisting of O, N, and S, and wherein each of said R⁹ substituents is optionally substituted with 1-3 R¹¹.

13. The compound of any one of claims 1-11, wherein the compound of Formula (I) is represented by Formula (Ie)



14. The compound of any one of claims 1-13, wherein G² is N.

15. The compound of any one of claims 1-14, wherein G¹ is N.

16. The compound of any one of claims 1-14, wherein G¹ is CR^{3a}.

17. The compound of any one of claims 1-16, wherein R² is H.

18. The compound of any one of claims 1-17, wherein R⁴ is H.

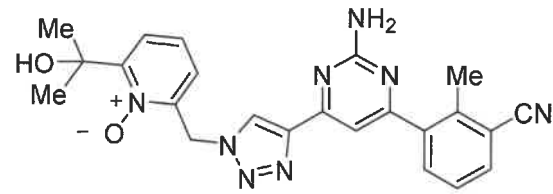
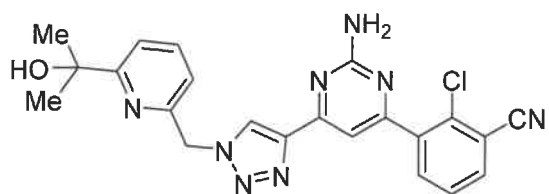
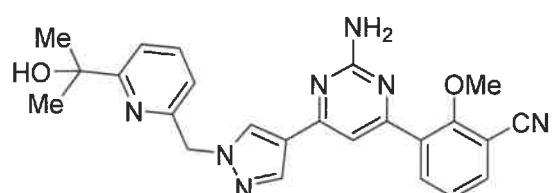
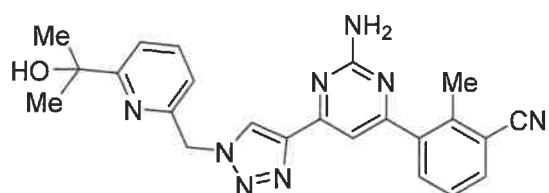
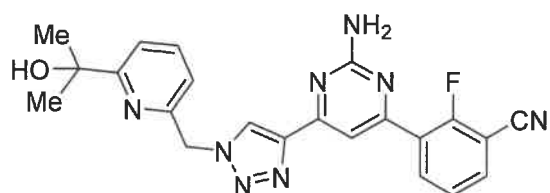
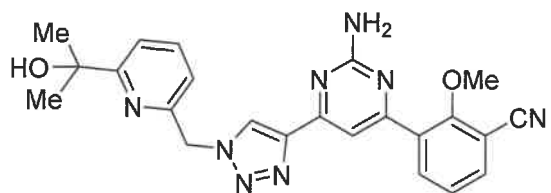
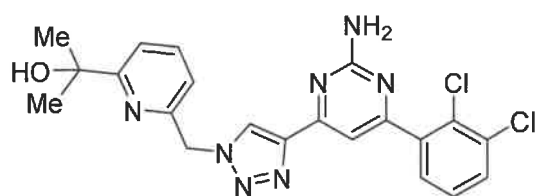
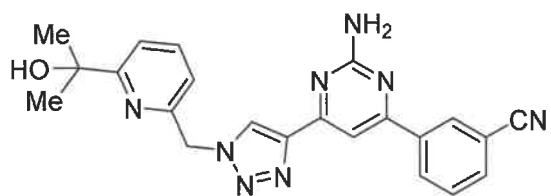
19. The compound of any one of claims 6-18, wherein R^{1b} is H.

20. The compound of any one of claims 6-19, wherein each R¹⁰ is independently selected from the group consisting of C₁₋₈ alkyl, halo, cyano, -O-C₁₋₈ alkyl, -X¹-O-C₁₋₈ alkyl, -O-X¹-O-C₁₋₈ alkyl, wherein each of said R¹⁰ substituents is optionally substituted with 1-3 R¹²,

21. The compound of claim 19, wherein each R¹⁰ is independently selected from the group consisting of C₁₋₈ alkyl, halo, cyano, -O-C₁₋₈ alkyl.

22. The compound of claim 1, selected from the compound of Table 1.

23. The compound of claim 1, selected from the group consisting of



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24. The compound of claim **Error! Reference source not found.**, having the Formula



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Compound I.

1 **25.** A pharmaceutical composition comprising a compound of any one of
2 claims **1-24** and a pharmaceutically acceptable excipient.

1 **26.** Use of a compound of any one of claims **1-24** for the preparation of a
2 medicament for treating a disease, disorder, or condition, mediated at least in part by the
3 adenosine A_{2A} receptor (A_{2A}R) or the adenosine A_{2B} receptor (A_{2B}R).

1 **27.** The use of claim **26**, wherein said disease, disorder, or condition is
2 mediated at least in part by A_{2A}R.

1 **28.** The use of claim **26**, wherein said disease, disorder, or condition is
2 mediated at least in part by A_{2B}R.

3 **29.** The use of claim **26**, wherein said disease, disorder, or condition is
4 mediated at least in part by both the A_{2A}R and A_{2B}R receptors.

1 **30.** The use of claim **27**, wherein the medicament comprises an amount of
2 said compound effective to reverse or stop the progression of A_{2A}R-mediated
3 immunosuppression.

1 **31.** The use of any one of claims 26-30, wherein said disease, disorder, or
2 condition is cancer.

1 **32.** The use of claim **31**, wherein said cancer is a cancer of the prostate, colon,
2 rectum, pancreas, cervix, stomach, endometrium, brain, liver, bladder, ovary, testis, head, neck,
3 skin (including melanoma and basal carcinoma), mesothelial lining, white blood cell (including
4 lymphoma and leukemia), esophagus, breast, muscle, connective tissue, lung (including small-
5 cell lung carcinoma and non-small-cell lung carcinoma), adrenal gland, thyroid, kidney, or bone;
6 or is glioblastoma, mesothelioma, renal cell carcinoma, gastric carcinoma, sarcoma (including
7 Kaposi's sarcoma), choriocarcinoma, cutaneous basocellular carcinoma, or testicular seminoma.

1 **33.** The use of claim **31**, wherein said cancer is selected from the group
2 consisting of melanoma, colorectal cancer, pancreatic cancer, breast cancer, prostate cancer, lung

cancer, leukemia, a brain tumor, lymphoma, ovarian cancer, Kaposi's sarcoma, renal cell carcinoma, head and neck cancer, and esophageal cancer.

34. The use of any one of claims **26-30**, wherein said disease, disorder, or condition is an immune-related disease, disorder or condition.

35. The use of claim **34**, wherein said immune-related disease, disorder, or condition is selected from the group consisting of selected from the group consisting of rheumatoid arthritis, kidney failure, lupus, asthma, psoriasis, colitis, pancreatitis, allergies, fibrosis, anemia fibromyalgia, Alzheimer's disease, congestive heart failure, stroke, aortic valve stenosis, arteriosclerosis, osteoporosis, Parkinson's disease, infections, Crohn's disease, ulcerative colitis, allergic contact dermatitis and other eczemas, systemic sclerosis and multiple sclerosis.

36. A combination comprising a compound of claims 1-24, and at least one additional therapeutic agent.

37. A combination of claim **36**, wherein the at least one additional therapeutic agent is a chemotherapeutic agent, an immune- and/or inflammation-modulating agent, an anti-hypercholesterolemia agent, an anti-infective agent or radiation.

38. A combination of claim **36**, wherein the at least one additional therapeutic agent is an immune checkpoint inhibitor.

39. A combination of claim **38**, wherein said immune checkpoint inhibitor blocks the activity of at least one of PD1, PDL1, CTLA4, TIGIT or TIM3.

40. A combination of claim **39**, wherein said immune checkpoint inhibitor blocks the activity of PD1 or PDL1.

41. A combination of claim **40**, wherein said immune checkpoint inhibitor is selected from the group consisting of nivolumab, pembrolizumab, lambrolizumab, avelumab, atezolizumab, and durvalumab.

- 1 **42.** A combination of claim 36 for use in treating a subject before, undergoing
2 or after radiation.
- 1 **43.** A combination of claim **40** or **41**, further comprising an additional
2 therapeutic agent that blocks the activity of TIGIT.
- 1 **44.** A combination of claim **43**, wherein the additional therapeutic agent
2 blocks the activity of TIGIT by activating its ligand.
- 1 **45.** A combination of claim **38**, wherein said immune checkpoint inhibitor
2 blocks the activity of TIGIT.
- 1 **46.** A combination of claim **45**, wherein said immune checkpoint inhibitor
2 blocks the activity of TIGIT by activating its ligand.
- 1 **47.** A combination of any one of claims **38** to **46**, further comprising a
2 chemotherapeutic agent.
- 1 **48.** A combination of claim **47**, wherein the chemotherapeutic agent
2 comprises a platinum-based or anthracycline-based chemotherapeutic agent.
- 1 **49.** A combination of claim **48**, wherein the chemotherapeutic agent is
2 selected from the group consisting of cisplatin, carboplatin, oxaliplatin, and doxorubicin.
- 1 **50.** A combination of any one of claims **38** to **49**, for use in treating
2 a subject before, undergoing or after radiation.
- 1 **51.** A combination of claim **36**, wherein the at least one additional therapeutic
2 agent is a chemotherapeutic agent.
- 1 **52.** A combination of claim **51**, wherein the chemotherapeutic agent is a
2 platinum-based or anthracycline-based chemotherapeutic agent.
- 1 **53.** A combination of claim **52**, wherein the chemotherapeutic agent is
2 selected from the group consisting of cisplatin, carboplatin, oxaliplatin, and doxorubicin.
- 1 **54.** A combination of claim **52** or **53**, for use in treating a subject before,
2 undergoing or after radiation.

1 **55.** Use of a compound of any one of claims **1-24** for the preparation of a
2 medicament for treating cancer in a subject , wherein the treating comprises said compound and
3 at least one additional therapeutic agent to be administered to a subject.

4 **56.** The use of claim **55**, wherein the at least one additional thereapeutic agent
5 is a chemotherapeutic agent, an immune- and/or inflammation-modulating agent, an anti-
6 hypercholesterolemia agent, an anti-infective agent or radiation.

7
8 **57.** The use of claim **55**, wherein the medicament is for treating a subject
9 before, undergoing or after radiation.

1 **58.** The use of claim **55**, wherein the at least one additional thereapeutic agent
2 is an immune checkpoint inhibitor.

1 **59.** The use of claim **58**, wherein said immune checkpoint inhibitor blocks the
2 activity of at least one of PD1, PDL1, CTLA4, TIGIT or TIM3.

1 **60.** The use of claim **59**, wherein said immune checkpoint inhibitor blocks the
2 activity of PD1 or PDL1.

1 **61.** The use of claim **60**, wherein said immune checkpoint inhibitor is selected
2 from the group consisting of nivolumab, pembrolizumab, lambrolizumab, avelumab,
3 atezolizumab, and durvalumab.

1 **62.** The use of claim **60** or **61**, further comprising an additional therapeutic
2 agent that blocks the activity of TIGIT.

1 **63.** The use of claim **62**, wherein the additional therapeutic agent blocks the
2 activity of TIGIT by activating its ligand.

1 **64.** The use of claim **58**, wherein said immune checkpoint inhibitor blocks the
2 activity of TIGIT.

1 **65.** The use of claim **64**, wherein said immune checkpoint inhibitor blocks the
2 activity of TIGIT by activating its ligand.

1 **66.** The use of any one of claims **58** to **65**, further comprising a
2 chemotherapeutic agent.

1 **67.** The use of claim **66**, wherein the chemotherapeutic agent comprises a
2 platinum-based or anthracycline-based chemotherapeutic agent.

1 **68.** The use of claim **67**, wherein the chemotherapeutic agent is selected from
2 the group consisting of cisplatin, carboplatin, oxaliplatin, and doxorubicin.

1 **69.** The use of any one of claims **58** to **68**, for treating a subject before,
2 undergoing or after radiation.

1 **70.** The use of claim **56**, wherein the at least one additional therapeutic agent
2 is a chemotherapeutic regimen.

1 **71.** The use of claim **70**, wherein the chemotherapeutic regimen includes a
2 platinum-based or anthracycline-based chemotherapeutic agent.

1 **72.** The use of claim **71**, wherein the chemotherapeutic agent is selected from
2 the group consisting of cisplatin, carboplatin, oxaliplatin, and doxorubicin.

1 **73.** The use of claim **71** or **70**, for trating a subject before, undergoing or after.

1 **74.** The use of any one of claims **55** to **73**, wherein said compound and said at
2 least one additional therapeutic agent are to be administered in combination.

1 **75.** The use of any one of claims **55** to **73**, wherein said compound and said at
2 least one additional therapeutic agent are to be administered sequentially.

76. The use of any one of claims 55 to 73, wherein the treatment periods for the administration of the compound and the at least one additional therapeutic agent overlap.