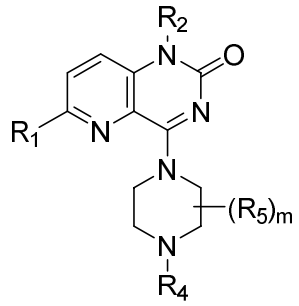
CLAIMS

1. An inhibitor of DGKα and/or DGKζ wherein the inhibitor is a compound of Formula (II):



(II)

or a salt thereof, wherein:

R_1 is H, F, Cl, Br, –CN, –OH, $C_{1–3}$ alkyl substituted with zero to 4 R_{1a}, $C_{3–4}$ cycloalkyl substituted with zero to 4 R_{1a}, $C_{1–3}$ alkoxy substituted with zero to 4 R_{1a}, $–NR_aR_a$, $–S(O)_nR_e$, or $–P(O)R_eR_e$;

each R_{1a} is independently F, Cl, –CN, –OH, $–OCH_3$, or $–NR_aR_a$;

each R_a is independently H or $C_{1–3}$ alkyl;

each R_e is independently $C_{3–4}$ cycloalkyl or $C_{1–3}$ alkyl substituted with zero to 4 R_{1a};

R_2 is H, $C_{1–3}$ alkyl substituted with zero to 4 R_{2a}, or $C_{3–4}$ cycloalkyl substituted with zero to 4 R_{2a};

each R_{2a} is independently F, Cl, –CN, –OH, $–O(C_{1–2}$ alkyl), $C_{3–4}$ cycloalkyl, $C_{3–4}$ alkenyl, or $C_{3–4}$ alkynyl;

R_4 is $–CH_2R_{4a}$, $–CH_2CH_2R_{4a}$, $–CH_2CHR_{4a}R_{4d}$, $–CHR_{4a}R_{4b}$, or $–CR_{4a}R_{4b}R_{4c}$;

R_{4a} and R_{4b} are independently:

(i) –CN or $C_{1–6}$ alkyl substituted with zero to 4 substituents independently selected from F, Cl, –CN, –OH, $–OCH_3$, $–SCH_3$, $C_{1–3}$ fluoroalkoxy, $–NR_aR_a$, $–S(O)_2R_e$, or $–NR_aS(O)_2R_e$;

(ii) $C_{3–6}$ cycloalkyl, 4- to 10-membered heterocyclyl, phenyl, or 5-to 10-membered heteroaryl, each substituted with zero to 4 substituents independently selected from F, Cl, Br, –CN, –OH, $C_{1–6}$ alkyl, $C_{1–3}$ fluoroalkyl, C_{1-2} bromoalkyl, C_{1-2} cyanoalkyl, $C_{1–4}$ hydroxyalkyl, $–(CH_2)_{1–2}O(C_{1–3}$ alkyl), $C_{1–4}$ alkoxy, $C_{1–3}$ fluoroalkoxy, $C_{1–3}$ cyanoalkoxy, $–O(C_{1–4}$ hydroxyalkyl), $–O(CR_xR_x)_{1–3}O(C_{1–3}$ alkyl), $C_{1–3}$

fluoroalkoxy, $-O(CH_2)_{1-3}NR_cR_c$, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-C(O)(C_{1-4}$ alkyl), $-C(O)OH$, $-C(O)O(C_{1-4}$ alkyl), $-NR_cR_c$, $-CH_2NR_aR_a$, $-NR_aS(O)_2(C_{1-3}$ alkyl), $-NR_aC(O)(C_{1-3}$ alkyl), $-(CR_xR_x)_{0-2}NR_aC(O)O(C_{1-4}$ alkyl), $-P(O)(C_{1-3}$ alkyl)$_2$, $-S(O)_2(C_{1-3}$ alkyl), $-(CR_xR_x)_{1-2}(C_{3-4}$ cycloalkyl), $-(CR_xR_x)_{1-2}$(morpholinyl), $-(CR_xR_x)_{1-2}$(difluoromorpholinyl), $-(CR_xR_x)_{1-2}$(dimethylmorpholinyl), $-(CR_xR_x)_{1-2}$(oxaazabicyclo[2.2.1]heptanyl), $(CR_xR_x)_{1-2}$(oxaazaspiro[3.3]heptanyl), $-(CR_xR_x)_{1-2}$(methylpiperazinonyl), $-(CR_xR_x)_{1-2}$(acetylpiperazinyl), $-(CR_xR_x)_{1-2}$(piperidinyl), $-(CR_xR_x)_{1-2}$(difluoropiperidinyl), $-(CR_xR_x)_{1-2}$(methoxypiperidinyl), $-(CR_xR_x)_{1-2}$(hydroxypiperidinyl), $-O(CR_xR_x)_{0-2}(C_{3-6}$ cycloalkyl), $-O(CR_xR_x)_{0-2}$(methylcyclopropyl), $-O(CR_xR_x)_{0-2}$((ethoxycarbonyl)cyclopropyl), $-O(CR_xR_x)_{0-2}$(oxetanyl), $-O(CR_xR_x)_{0-2}$(methylazetidinyl), $-O(CR_xR_x)_{0-2}$(tetrahydropyranyl), $-O(CR_xR_x)_{1-2}$(morpholinyl), $-O(CR_xR_x)_{0-2}$(thiazolyl), cyclopropyl, cyanocyclopropyl, methylazetidinyl, acetylazetidinyl, (*tert*-butoxycarbonyl)azetidinyl, triazolyl, tetrahydropyranyl, morpholinyl, thiophenyl, methylpiperidinyl, dioxolanyl, pyrrolidinonyl, and R_d; or

(iii) C_{1-4} alkyl substituted with one cyclic group selected from C_{3-6} cycloalkyl, 4- to 10-membered heterocyclyl, mono- or bicyclic aryl, or 5-to 10-membered heteroaryl, said cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, $-OH$, $-CN$, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, $-NR_aS(O)_2(C_{1-3}$ alkyl), $-NR_aC(O)(C_{1-3}$ alkyl), $-NR_aC(O)O(C_{1-4}$ alkyl), and C_{3-6} cycloalkyl;

or R_{4a} and R_{4b} together with the carbon atom to which they are attached form a C_{3-6} cycloalkyl or a 3- to 6-membered heterocyclyl, each substituted with zero to 3 R_f;

each R_f is independently F, Cl, Br, $-OH$, $-CN$, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, or a cyclic group selected from C_{3-6} cycloalkyl, 3- to 6-membered heterocyclyl, phenyl, monocyclic heteroaryl, and bicyclic heteroaryl, each cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, $-OH$, $-CN$, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, and $-NR_cR_c$;

R_{4c} is C_{1-6} alkyl or C_{3-6} cycloalkyl, each substituted with zero to 4 substituents

independently selected from F, Cl, –OH, $C_{1–2}$ alkoxy, $C_{1–2}$ fluoroalkoxy, and –CN;

R_{4d} is $–OCH_3$;

each R_c is independently H or $C_{1–2}$ alkyl;

R_d is phenyl substituted with zero to 1 substituent selected from F, Cl, –CN, $–CH_3$, and $–OCH_3$;

each R_5 is independently –CN, $C_{1–6}$ alkyl substituted with zero to 4 R_g, $C_{2–4}$ alkenyl substituted with zero to 4 R_g, $C_{2–4}$ alkynyl substituted with zero to 4 R_g, $C_{3–4}$ cycloalkyl substituted with zero to 4 R_g, phenyl substituted with zero to 4 R_g, oxadiazolyl substituted with zero to 3 R_g, pyridinyl substituted with zero to 4 R_g, $–(CH_2)_{1–2}$(4- to 10-membered heterocyclyl substituted with zero to 4 R_g), $–(CH_2)_{1–2}NR_cC(O)(C_{1–4}$ alkyl), $–(CH_2)_{1–2}NR_cC(O)O(C_{1–4}$ alkyl), $–(CH_2)_{1–2}NR_cS(O)_2(C_{1–4}$ alkyl), $–C(O)(C_{1–4}$ alkyl), –C(O)OH, $–C(O)O(C_{1–4}$ alkyl), $–C(O)O(C_{3–4}$ cycloalkyl), $–C(O)NR_aR_a$, or $–C(O)NR_a(C_{3–4}$ cycloalkyl);

each R_g is independently F, Cl, –CN, –OH, $C_{1–3}$ alkoxy, $C_{1–3}$ fluoroalkoxy, $–O(CH_2)_{1–2}O(C_{1–2}$ alkyl), or $–NR_cR_c$;

each R_x is independently H or $–CH_3$;

m is zero, 1, 2, or 3; and

n is zero, 1, or 2,

for use in treating cancer in a subject,

wherein a therapeutically effective amount of the inhibitor of DGKα and/or DGKζ and a therapeutically effective amount of:

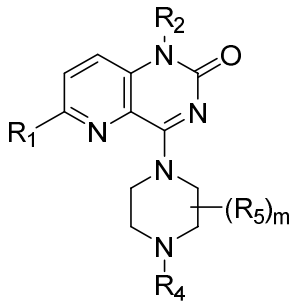
(a) an antagonist of the PD1/PD-L1 axis, wherein the antagonist is an antibody that binds to human PD1 or PD-L1;

(b) an antagonist of CTLA-4, wherein the antagonist is an antibody that binds to human CTLA-4; or

(c) an antagonist of the PD1/PD-L1 axis and an antagonist of CTLA4, wherein the antagonist of the PD1/PD-L1 axis is an antibody that binds to human PD1 or PD-L1 and the antagonist of CTLA-4 is an antibody that binds to human CTLA-4,

are to be administered to the subject.

2. Use of an inhibitor of DGKα and/or DGKζ wherein the inhibitor is a compound of Formula (II):



(II)

or a salt thereof, wherein:

R_1 is H, F, Cl, Br, –CN, –OH, $C_{1–3}$ alkyl substituted with zero to 4 R_{1a}, $C_{3–4}$ cycloalkyl substituted with zero to 4 R_{1a}, $C_{1–3}$ alkoxy substituted with zero to 4 R_{1a}, $–NR_aR_a$, $–S(O)_nR_e$, or $–P(O)R_eR_e$;

each R_{1a} is independently F, Cl, –CN, –OH, $–OCH_3$, or $–NR_aR_a$;

each R_a is independently H or $C_{1–3}$ alkyl;

each R_e is independently $C_{3–4}$ cycloalkyl or $C_{1–3}$ alkyl substituted with zero to 4 R_{1a};

R_2 is H, $C_{1–3}$ alkyl substituted with zero to 4 R_{2a}, or $C_{3–4}$ cycloalkyl substituted with zero to 4 R_{2a};

each R_{2a} is independently F, Cl, –CN, –OH, $–O(C_{1–2}$ alkyl), $C_{3–4}$ cycloalkyl, $C_{3–4}$ alkenyl, or $C_{3–4}$ alkynyl;

R_4 is $–CH_2R_{4a}$, $–CH_2CH_2R_{4a}$, $–CH_2CHR_{4a}R_{4d}$, $–CHR_{4a}R_{4b}$, or $–CR_{4a}R_{4b}R_{4c}$;

R_{4a} and R_{4b} are independently:

(i) –CN or $C_{1–6}$ alkyl substituted with zero to 4 substituents independently selected from F, Cl, –CN, –OH, $–OCH_3$, $–SCH_3$, $C_{1–3}$ fluoroalkoxy, $–NR_aR_a$, $–S(O)_2R_e$, or $–NR_aS(O)_2R_e$;

(ii) $C_{3–6}$ cycloalkyl, 4- to 10-membered heterocyclyl, phenyl, or 5-to 10-membered heteroaryl, each substituted with zero to 4 substituents independently selected from F, Cl, Br, –CN, –OH, $C_{1–6}$ alkyl, $C_{1–3}$ fluoroalkyl, C_{1-2} bromoalkyl, C_{1-2} cyanoalkyl, $C_{1–4}$ hydroxyalkyl, $–(CH_2)_{1–2}O(C_{1–3}$ alkyl), $C_{1–4}$ alkoxy, $C_{1–3}$ fluoroalkoxy, $C_{1–3}$ cyanoalkoxy, $–O(C_{1–4}$ hydroxyalkyl), $–O(CR_xR_x)_{1–3}O(C_{1–3}$ alkyl), $C_{1–3}$ fluoroalkoxy, $–O(CH_2)_{1–3}NR_cR_c$, $–OCH_2CH=CH_2$, $–OCH_2C≡CH$, $–C(O)(C_{1–4}$ alkyl), –C(O)OH, $–C(O)O(C_{1–4}$ alkyl), $–NR_cR_c$, $–CH_2NR_aR_a$, $–NR_aS(O)_2(C_{1–3}$

alkyl), $-NR_aC(O)(C_{1-3}$ alkyl), $-(CR_xR_x)_{0-2}NR_aC(O)O(C_{1-4}$ alkyl), $-P(O)(C_{1-3}$ alkyl)$_2$, $-S(O)_2(C_{1-3}$ alkyl), $-(CR_xR_x)_{1-2}(C_{3-4}$ cycloalkyl), $-(CR_xR_x)_{1-2}$(morpholinyl), $-(CR_xR_x)_{1-2}$(difluoromorpholinyl), $-(CR_xR_x)_{1-2}$(dimethylmorpholinyl), $-(CR_xR_x)_{1-2}$(oxaazabicyclo[2.2.1]heptanyl), $(CR_xR_x)_{1-2}$(oxaazaspiro[3.3]heptanyl), $-(CR_xR_x)_{1-2}$(methylpiperazinonyl), $-(CR_xR_x)_{1-2}$(acetylpiperazinyl), $-(CR_xR_x)_{1-2}$(piperidinyl), $-(CR_xR_x)_{1-2}$(difluoropiperidinyl), $-(CR_xR_x)_{1-2}$(methoxypiperidinyl), $-(CR_xR_x)_{1-2}$(hydroxypiperidinyl), $-O(CR_xR_x)_{0-2}(C_{3-6}$ cycloalkyl), $-O(CR_xR_x)_{0-2}$(methylcyclopropyl), $-O(CR_xR_x)_{0-2}$((ethoxycarbonyl)cyclopropyl), $-O(CR_xR_x)_{0-2}$(oxetanyl), $-O(CR_xR_x)_{0-2}$(methylazetidinyl), $-O(CR_xR_x)_{0-2}$(tetrahydropyranyl), $-O(CR_xR_x)_{1-2}$(morpholinyl), $-O(CR_xR_x)_{0-2}$(thiazolyl), cyclopropyl, cyanocyclopropyl, methylazetidinyl, acetylazetidinyl, (*tert*-butoxycarbonyl)azetidinyl, triazolyl, tetrahydropyranyl, morpholinyl, thiophenyl, methylpiperidinyl, dioxolanyl, pyrrolidinonyl, and R_d; or

(iii) C_{1-4} alkyl substituted with one cyclic group selected from C_{3-6} cycloalkyl, 4- to 10-membered heterocyclyl, mono- or bicyclic aryl, or 5-to 10-membered heteroaryl, said cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, –OH, –CN, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, $-NR_aS(O)_2(C_{1-3}$ alkyl), $-NR_aC(O)(C_{1-3}$ alkyl), $-NR_aC(O)O(C_{1-4}$ alkyl), and C_{3-6} cycloalkyl;

or R_{4a} and R_{4b} together with the carbon atom to which they are attached form a C_{3-6} cycloalkyl or a 3- to 6-membered heterocyclyl, each substituted with zero to 3 R_f;

each R_f is independently F, Cl, Br, –OH, –CN, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, or a cyclic group selected from C_{3-6} cycloalkyl, 3- to 6-membered heterocyclyl, phenyl, monocyclic heteroaryl, and bicyclic heteroaryl, each cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, –OH, –CN, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, and $-NR_cR_c$;

R_{4c} is C_{1-6} alkyl or C_{3-6} cycloalkyl, each substituted with zero to 4 substituents independently selected from F, Cl, –OH, C_{1-2} alkoxy, C_{1-2} fluoroalkoxy, and –CN;

R_{4d} is $-OCH_3$;

each R_c is independently H or $C_{1–2}$ alkyl;

R_d is phenyl substituted with zero to 1 substituent selected from F, Cl, –CN, $–CH_3$, and $–OCH_3$;

each R_5 is independently –CN, $C_{1–6}$ alkyl substituted with zero to 4 R_g, $C_{2–4}$ alkenyl substituted with zero to 4 R_g, $C_{2–4}$ alkynyl substituted with zero to 4 R_g, $C_{3–4}$ cycloalkyl substituted with zero to 4 R_g, phenyl substituted with zero to 4 R_g, oxadiazolyl substituted with zero to 3 R_g, pyridinyl substituted with zero to 4 R_g, $–(CH_2)_{1–2}$(4- to 10-membered heterocyclyl substituted with zero to 4 R_g), $–(CH_2)_{1–2}NR_cC(O)(C_{1–4}$ alkyl), $–(CH_2)_{1–2}NR_cC(O)O(C_{1–4}$ alkyl), $–(CH_2)_{1–2}NR_cS(O)_2(C_{1–4}$ alkyl), $–C(O)(C_{1–4}$ alkyl), –C(O)OH, $–C(O)O(C_{1–4}$ alkyl), $–C(O)O(C_{3–4}$ cycloalkyl), $–C(O)NR_aR_a$, or $–C(O)NR_a(C_{3–4}$ cycloalkyl);

each R_g is independently F, Cl, –CN, –OH, $C_{1–3}$ alkoxy, $C_{1–3}$ fluoroalkoxy, $–O(CH_2)_{1–2}O(C_{1–2}$ alkyl), or $–NR_cR_c$;

each R_x is independently H or $–CH_3$;

m is zero, 1, 2, or 3; and

n is zero, 1, or 2,

in the manufacture of a medicament for treating cancer in a subject,

wherein a therapeutically effective amount of the inhibitor of DGKα and/or DGKζ and a therapeutically effective amount of:

(a) an antagonist of the PD1/PD-L1 axis, wherein the antagonist is an antibody that binds to human PD1 or PD-L1;

(b) an antagonist of CTLA-4, wherein the antagonist is an antibody that binds to human CTLA-4; or

(c) an antagonist of the PD1/PD-L1 axis and an antagonist of CTLA4, wherein the antagonist of the PD1/PD-L1 axis is an antibody that binds to human PD1 or PD-L1 and the antagonist of CTLA-4 is an antibody that binds to human CTLA-4,

are to be administered to the subject.

3. The inhibitor for use of claim 1 or the use of claim 2, wherein the antibody that binds to human PD-1 is nivolumab or pembrolizumab.

4. The inhibitor for use of claim 1 or the use of claim 2, wherein the antibody that binds to human PD-L1 is atezolizumab.

5. The inhibitor for use of claim 1 or the use of claim 2, wherein the antibody that binds to human CTLA4 is ipilimumab.

6. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) or a pharmaceutically acceptable salt thereof, wherein:

R_1 is H, F, Cl, Br, –CN, –OH, $C_{1–3}$ alkyl substituted with zero to 4 R_{1a}, cyclopropyl substituted with zero to 3 R_{1a}, $C_{1–3}$ alkoxy substituted with zero to 3 R_{1a}, $–NR_aR_a$, $–S(O)_nCH_3$, or $–P(O)(CH_3)_2$;

R_2 is H or $C_{1–2}$ alkyl substituted with zero to 2 R_{2a};

each R_{2a} is independently F, Cl, –CN, –OH, $–O(C_{1–2}$ alkyl), cyclopropyl, $C_{3–4}$ alkenyl, or $C_{3–4}$ alkynyl;

R_{4a} and R_{4b} are independently:

(i) –CN or $C_{1–4}$ alkyl substituted with zero to 4 substituents independently selected from F, Cl, –CN, –OH, $–OCH_3$, $–SCH_3$, $C_{1–3}$ fluoroalkoxy, and $–NR_aR_a$;

(ii) $C_{3–6}$ cycloalkyl, 4- to 10-membered heterocyclyl, phenyl, or 5-to 10-membered heteroaryl, each substituted with zero to 4 substituents independently selected from F, Cl, Br, –CN, –OH, $C_{1–6}$ alkyl, $C_{1–3}$ fluoroalkyl, C_{1-2} bromoalkyl, C_{1-2} cyanoalkyl, C_{1-2} hydroxyalkyl, $–CH_2NR_aR_a$, $–(CH_2)_{1–2}O(C_{1–2}$ alkyl), $–(CH_2)_{1–2}NR_xC(O)O(C_{1-2}$ alkyl), $C_{1–4}$ alkoxy, $–O(C_{1–4}$ hydroxyalkyl), $–O(CR_xR_x)_{1–2}O(C_{1–2}$ alkyl), $C_{1–3}$ fluoroalkoxy, $C_{1–3}$ cyanoalkoxy, $–O(CH_2)_{1–2}NR_cR_c$, $–OCH_2CH=CH_2$, $–OCH_2C≡CH$, $–C(O)(C_{1–4}$ alkyl), –C(O)OH, $–C(O)O(C_{1–4}$ alkyl), $–NR_cR_c$, $–NR_aS(O)_2(C_{1–3}$ alkyl), $–NR_aC(O)(C_{1–3}$ alkyl), $–NR_aC(O)O(C_{1–4}$ alkyl), $–P(O)(C_{1–2}$ alkyl)$_2$, $–S(O)_2(C_{1–3}$ alkyl), $–(CH_2)_{1–2}(C_{3–4}$ cycloalkyl), $–CR_xR_x$(morpholinyl), $–CR_xR_x$(difluoromorpholinyl), $–CR_xR_x$(dimethylmorpholinyl), $–CR_xR_x$(oxaazabicyclo[2.2.1]heptanyl), $–CR_xR_x$(oxaazaspiro[3.3]heptanyl), $–CR_xR_x$(methylpiperazinonyl), $–CR_xR_x$(acetylpiperazinyl), $–CR_xR_x$(piperidinyl), $–CR_xR_x$(difluoropiperidinyl), $–CR_xR_x$(methoxypiperidinyl), $–CR_xR_x$(hydroxypiperidinyl), $–O(CH_2)_{0–2}(C_{3–4}$ cycloalkyl),

$-O(CH_2)_{0-2}$(methylcyclopropyl), $-O(CH_2)_{0-2}$((ethoxycarbonyl)cyclopropyl), $-O(CH_2)_{0-2}$(oxetanyl), $-O(CH_2)_{0-2}$(methylazetidinyl), $-O(CH_2)_{1-2}$(morpholinyl), $-O(CH_2)_{0-2}$(tetrahydropyranyl), $-O(CH_2)_{0-2}$(thiazolyl), cyclopropyl, cyanocyclopropyl, methylazetidinyl, acetylazetidinyl, (*tert*-butoxycarbonyl)azetidinyl, dioxolanyl, pyrrolidinonyl, triazolyl, tetrahydropyranyl, morpholinyl, thiophenyl, methylpiperidinyl, and R_d; or

(iii) C_{1-3} alkyl substituted with one cyclic group selected from C_{3-6} cycloalkyl, 4- to 10-membered heterocyclyl, mono- or bicyclic aryl, or 5-to 10-membered heteroaryl, said cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, $-OH$, $-CN$, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} alkoxy, C_{1-2} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, $-NR_aS(O)_2(C_{1-3}$ alkyl), $-NR_aC(O)(C_{1-3}$ alkyl), $-NR_aC(O)O(C_{1-4}$ alkyl), and C_{3-4} cycloalkyl;

or R_{4a} and R_{4b} together with the carbon atom to which they are attached, form a C_{3-6} cycloalkyl or a 3- to 6-membered heterocyclyl, each substituted with zero to 3 R_f;

each R_f is independently F, Cl, Br, $-OH$, $-CN$, C_{1-4} alkyl, C_{1-2} fluoroalkyl, C_{1-3} alkoxy, C_{1-2} fluoroalkoxy, $-OCH_2CH=CH_2$, $-OCH_2C\equiv CH$, $-NR_cR_c$, or a cyclic group selected from C_{3-6} cycloalkyl, 3- to 6-membered heterocyclyl, phenyl, monocyclic heteroaryl, and bicyclic heteroaryl, each cyclic group substituted with zero to 3 substituents independently selected from F, Cl, Br, $-OH$, $-CN$, C_{1-4} alkyl, C_{1-2} fluoroalkyl, C_{1-3} alkoxy, C_{1-2} fluoroalkoxy, and $-NR_cR_c$;

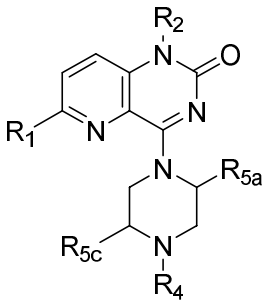
R_{4c} is C_{1-4} alkyl or C_{3-6} cycloalkyl, each substituted with zero to 4 substituents independently selected from F, Cl, $-OH$, C_{1-2} alkoxy, C_{1-2} fluoroalkoxy, and $-CN$;

each R_5 is independently $-CN$, C_{1-5} alkyl substituted with zero to 4 R_g, C_{2-3} alkenyl substituted with zero to 4 R_g, C_{2-3} alkynyl substituted with zero to 4 R_g, C_{3-4} cycloalkyl substituted with zero to 4 R_g, phenyl substituted with zero to 3 R_g, oxadiazolyl substituted with zero to 3 R_g, pyridinyl substituted with zero to 3 R_g, $-(CH_2)_{1-2}$(4- to 10-membered heterocyclyl substituted with zero to 4 R_g), $-(CH_2)_{1-2}NR_cC(O)(C_{1-4}$ alkyl), $-(CH_2)_{1-2}NR_cC(O)O(C_{1-4}$ alkyl), $-(CH_2)_{1-2}NR_cS(O)_2(C_{1-4}$ alkyl), $-C(O)(C_{1-4}$ alkyl), $-C(O)OH$, $-C(O)O(C_{1-4}$ alkyl), $-C(O)O(C_{3-4}$ cycloalkyl), $-C(O)NR_aR_a$, or $-C(O)NR_a(C_{3-4}$ cycloalkyl);

each R_x is independently H or $-CH_3$; and

m is 1, 2, or 3.

7. The inhibitor for use or the use of claim 6, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) or a pharmaceutically acceptable salt thereof having the structure:



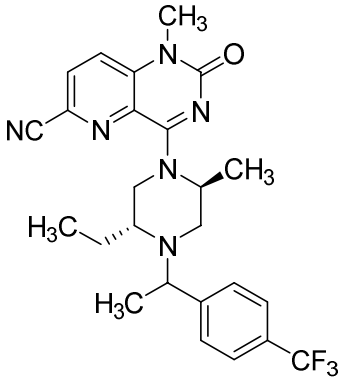
R_1 is –CN;

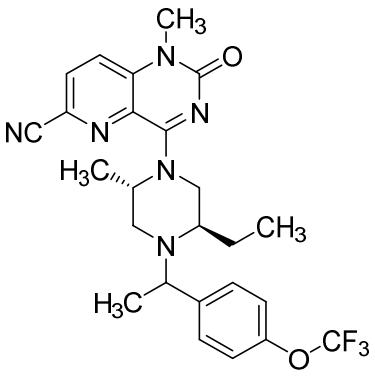
R_2 is $–CH_3$;

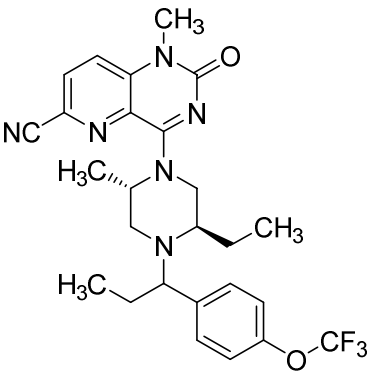
R_{5a} is $–CH_3$ or $–CH_2CH_3$; and

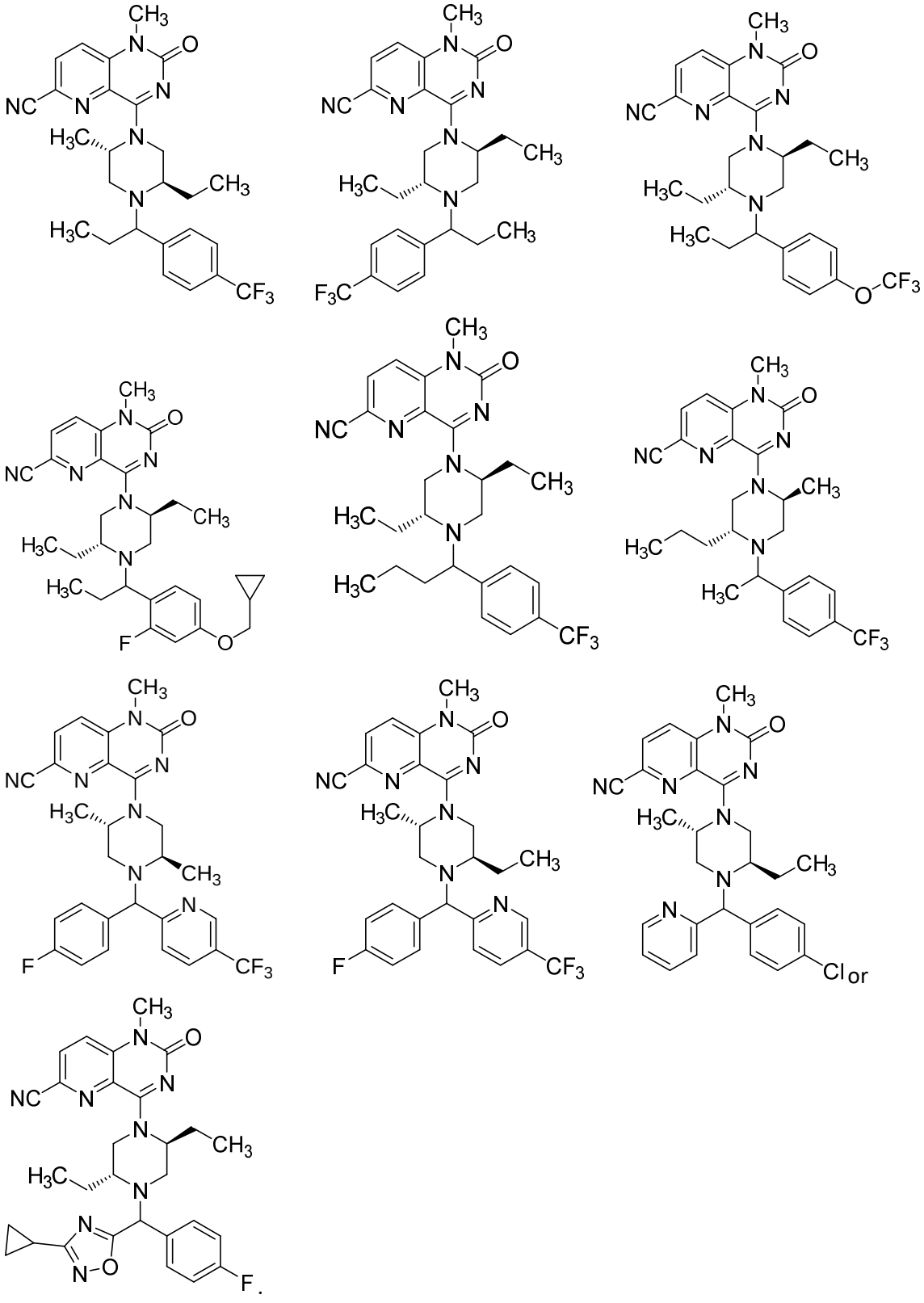
R_{5c} is $–CH_3$, $–CH_2CH_3$, or $–CH_2CH_2CH_3$.

8. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) or a pharmaceutically acceptable salt thereof having the structure:



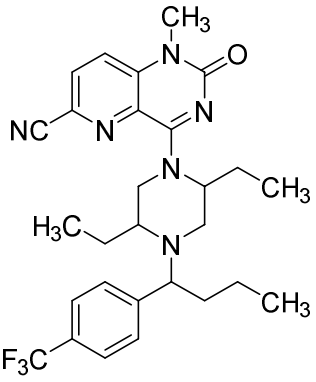






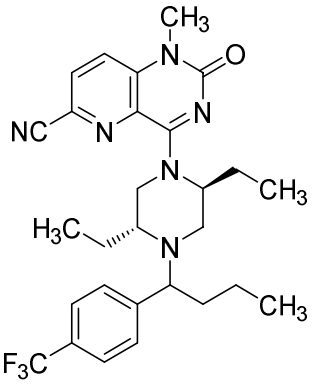
9. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of

claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



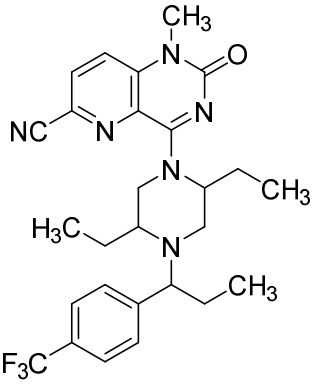
or a pharmaceutically acceptable salt thereof.

10. The inhibitor for use or the use of claim 9, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



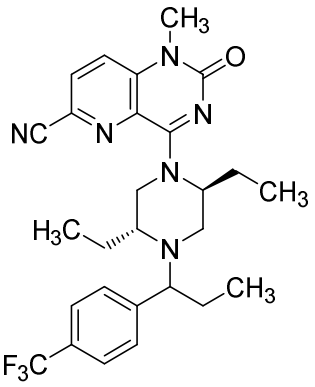
or a pharmaceutically acceptable salt thereof.

11. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



or a pharmaceutically acceptable salt thereof.

12. The inhibitor for use or the use of claim 11, wherein the inhibitor of DGKα and/or DGKζ is a compound having the structure:



or a pharmaceutically acceptable salt thereof.

13. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein said inhibitor is a compound of Formula (II) selected from:

4-((2S,5R)-2,5-diethyl-4-((S)-1-(4-(trifluoromethyl)phenyl)propyl)piperazin-1-yl)-1-methyl-2-oxo-1,2-dihydropyrido[3,2-d]pyrimidine-6-carbonitrile;

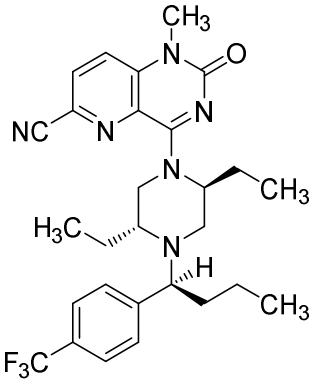
4-((2S,5R)-2,5-diethyl-4-((R)-1-(4-(trifluoromethyl)phenyl)propyl)piperazin-1-yl)-1-methyl-2-oxo-1,2-dihydropyrido[3,2-d]pyrimidine-6-carbonitrile;

4-((2S,5R)-2,5-diethyl-4-((S)-1-(4-(trifluoromethyl)phenyl)butyl)piperazin-1-yl)-1-methyl-2-oxo-1,2-dihydropyrido[3,2-d]pyrimidine-6-carbonitrile;

4-((2S,5R)-2,5-diethyl-4-((R)-1-(4-(trifluoromethyl)phenyl)butyl)piperazin-1-yl)-1-methyl-2-oxo-1,2-dihydropyrido[3,2-d]pyrimidine-6-carbonitrile;

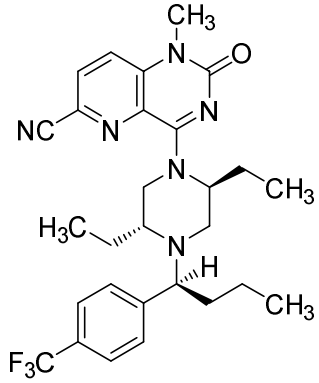
or a pharmaceutically acceptable salt thereof.

14. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



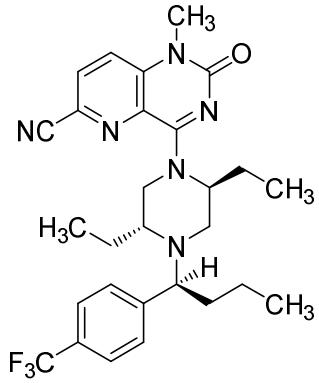
or a pharmaceutically acceptable salt thereof.

15. The inhibitor for use or the use of claim 14, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



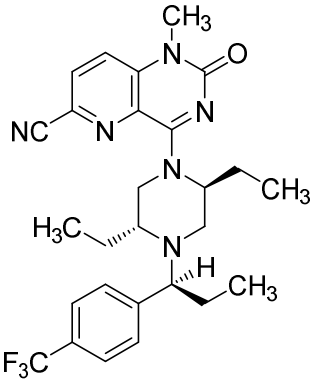
.

16. The inhibitor for use or the use of claim 14, wherein the inhibitor of DGKα and/or DGKζ is a pharmaceutically acceptable salt of a compound of Formula (II) having the structure:



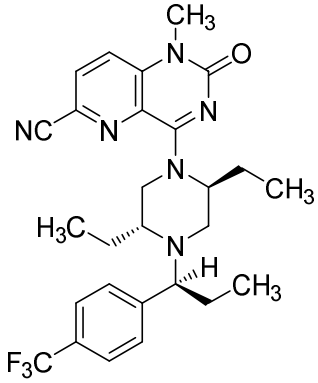
.

17. The inhibitor for use of any one of claims 1 and 3-5 or the use of any one of claims 2-5, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



or a pharmaceutically acceptable salt thereof.

18. The inhibitor for use or the use of claim 17, wherein the inhibitor of DGKα and/or DGKζ is a compound of Formula (II) having the structure:



.

19. The inhibitor for use of any one of claims 1 and 3-18 or the use of any one of claims 2-18, wherein the cancer is a solid tumor or a hematological (liquid) tumor.

20. The inhibitor for use of any one of claims 1 and 3-19 or the use of any one of claims 2-19, wherein the one or more other cancer treatments is to be administered to the subject, wherein the one or more other cancer treatments includes radiation, surgery, chemotherapy, and/or administration of a biologic drug.

21. The inhibitor for use or the use of claim 20, wherein the one or more other cancer treatments is the administration of a biologic drug and the biologic drug is a drug that stimulates the immune system.

22. The inhibitor for use of any one of claims 1 and 3-21 or the use of any one of claims 2-21, wherein the another cancer treatment is not to be administred during the treatment with an inhibitor of DGKα and/or DGKζ, an antagonist of the PD1/PD-L1 axis and/or an antagonist of CTLA4.

23. The inhibitor for use of any one of claims 1 and 3-22 or the use of any one of claims 2-22, wherein the subject has not been treated with an antagonist of the PD1/PD-L1 axis or an antagonist of CTLA4 prior to the administration of an inhibitor of DGKα and/or DGKζ, an antagonist of the PD1/PD-L1 axis and/or an antagonist of CTLA4.

24. The inhibitor for use of any one of claims 1 and 3-23 or the use of any one of claims 2-23, wherein the subject is resistant or refractory to treatment with an antagonist of a checkpoint inhibitor.

25. The inhibitor for use of any one of claims 1 and 3-24 or the use of any one of claims 2-24, wherein the inhibitor of DGKα and/or DGKζ is an inhibitor of DGKα and DGKζ.