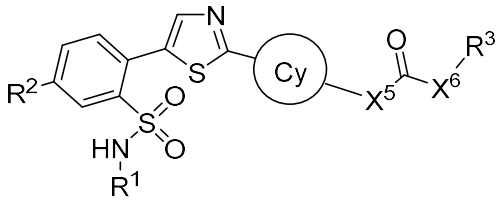
CLAIMS

1. A combination therapy comprising a compound represented by Formula (I):



Formula (I);

or a pharmaceutically acceptable salt thereof, wherein:

the thiazole ring is optionally substituted with –F or –Cl;

Cy is -(C_3–C_7)cycloalkyl, bridged (C_6–C_{12}) cycloalkyl, or a 4-12 membered heterocyclic ring, each of which is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, and (C_1-C_4)alkoxy;

when X^5 is connected with a nitrogen ring atom of Cy, X^5 is absent;

when X^5 is connected with a carbon ring atom of Cy, X^5 is NR^a or O;

X^6 is NR^a or O;

R^1 is (C_1–C_5)alkyl;

R^3 is (C_1–C_5)alkyl, -CH_2-phenyl, -(C_3–C_7)cycloalkyl, -CH_2-(C_3–C_7)cycloalkyl, -CH_2-monocyclic 3-7 membered heterocyclic ring, or monocyclic 3-7 membered heterocyclic ring, wherein the (C_1–C_5)alkyl, -(C_3–C_7)cycloalkyl, phenyl or monocyclic 3-7 membered heterocyclic ring represented by R^3 or in the group represented by R^3 is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, halomethyl, halomethoxy, -CN, and (C_1-C_4)alkoxy;

R^2 is -$NR^aC(O)O$(C_1-C_4)alkyl; -$NR^aC(O)NR^a$(C_1-C_4)alkyl; -$NR^aC(O)O$(C_2-C_4)alkenyl;
-$NR^aC(O)NR^a$(C_2-C_4)alkenyl; -$NR^aC(O)O$-(C_3-C_6)cycloalkyl; -$NR^aC(O)NR^a$-(C_3-C_7)cycloalkyl; -$NR^aC(O)O$-phenyl; -$NR^aC(O)NR^a$-phenyl; -$NR^aC(O)O$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)NR^a$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)O$-monocyclic 5-6 membered heteroaromatic ring; -$NR^aC(O)NR^a$-monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_1–C_4)alkyl and the (C_2-C_4)alkenyl in the group represented by R^2 are each optionally and independently substituted with one or more groups selected from the group consisting of halogen, N_3, –OR^a, -NR^aR^a, -(C_3–C_6)cycloalkyl, phenyl, a monocyclic 3-7 membered heterocyclic ring, and a monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_3–C_7)cycloalkyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, =O, -OR^a and -NR^aR^a;

wherein the phenyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, halomethyl, halomethoxy,
-CN, -OR^a, and -N_3;

wherein the heterocyclic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of =O, halogen, –OR^a, -CH_3, halomethyl, and halomethoxy;

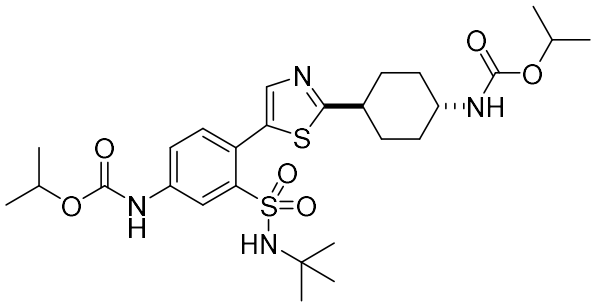
wherein the heteroaromatic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CN, -CH_3, halomethyl, halomethoxy, -OR^a and -NR^aR^a; and

each R^a is independently –H or -CH_3, and

a PARP inhibitor or a pharmaceutically acceptable salt thereof.

2. The combination therapy of claim 1, wherein the PARP inhibitor is olaparib.

3. The combination therapy of claim 1, wherein the compound of Formula (I) has the following structure:



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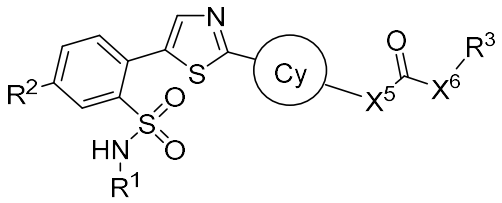
4. A pharmaceutical composition comprising a compound represented by Formula (I):



Formula (I);

or a pharmaceutically acceptable salt thereof, wherein:

the thiazole ring is optionally substituted with –F or –Cl;

Cy is -(C_3–C_7)cycloalkyl, bridged (C_6–C_{12}) cycloalkyl, or a 4-12 membered heterocyclic ring, each of which is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, and (C_1-C_4)alkoxy;

when X^5 is connected with a nitrogen ring atom of Cy, X^5 is absent;

when X^5 is connected with a carbon ring atom of Cy, X^5 is NR^a or O;

X^6 is NR^a or O;

R^1 is (C_1–C_5)alkyl;

R^3 is (C_1–C_5)alkyl, -CH_2-phenyl, -(C_3–C_7)cycloalkyl, -CH_2-(C_3–C_7)cycloalkyl, -CH_2-monocyclic 3-7 membered heterocyclic ring, or monocyclic 3-7 membered heterocyclic ring, wherein the (C_1–C_5)alkyl, -(C_3–C_7)cycloalkyl, phenyl or monocyclic 3-7 membered heterocyclic ring represented by R^3 or in the group represented by R^3 is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, halomethyl, halomethoxy, -CN, and (C_1-C_4)alkoxy;

R^2 is -$NR^aC(O)O$(C_1-C_4)alkyl; -$NR^aC(O)NR^a$(C_1-C_4)alkyl; -$NR^aC(O)O$(C_2-C_4)alkenyl;
-$NR^aC(O)NR^a$(C_2-C_4)alkenyl; -$NR^aC(O)O$-(C_3-C_6)cycloalkyl; -$NR^aC(O)NR^a$-(C_3-C_7)cycloalkyl; -$NR^aC(O)O$-phenyl; -$NR^aC(O)NR^a$-phenyl; -$NR^aC(O)O$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)NR^a$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)O$-monocyclic 5-6 membered heteroaromatic ring; -$NR^aC(O)NR^a$-monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_1–C_4)alkyl and the (C_2-C_4)alkenyl in the group represented by R^2 are each optionally and independently substituted with one or more groups selected from the group consisting of halogen, N_3, –OR^a, -NR^aR^a, -(C_3–C_6)cycloalkyl, phenyl, a monocyclic 3-7 membered heterocyclic ring, and a monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_3–C_7)cycloalkyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, =O, -OR^a and -NR^aR^a;

wherein the phenyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, halomethyl, halomethoxy,
-CN, -OR^a, and -N_3;

wherein the heterocyclic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of =O, halogen, $–OR^a$, $-CH_3$, halomethyl, and halomethoxy;

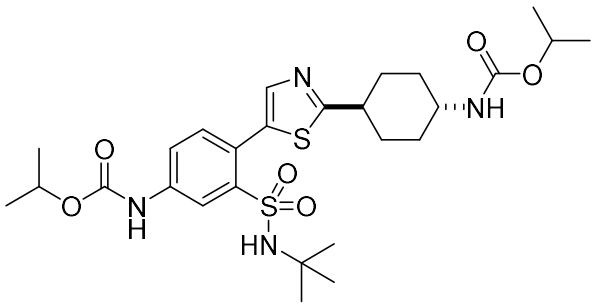
wherein the heteroaromatic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CN, $-CH_3$, halomethyl, halomethoxy, $-OR^a$ and $-NR^aR^a$; and

each R^a is independently –H or $-CH_3$, and

a PARP inhibitor or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition of claim 4, wherein the PARP inhibitor is olaparib.

6. The pharmaceutical composition of claim 4, wherein the compound of Formula (I) has the following structure:



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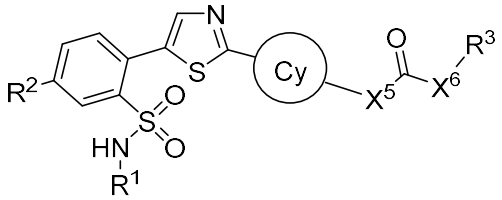
7. A kit comprising a compound represented by Formula (I):



Formula (I);

or a pharmaceutically acceptable salt thereof, wherein:

the thiazole ring is optionally substituted with –F or –Cl;

Cy is $-(C_3–C_7)$cycloalkyl, bridged $(C_6–C_{12})$ cycloalkyl, or a 4-12 membered heterocyclic ring, each of which is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, $(C_1$-$C_4)$alkyl, and $(C_1$-$C_4)$alkoxy;

when X^5 is connected with a nitrogen ring atom of Cy, X^5 is absent;

when X^5 is connected with a carbon ring atom of Cy, X^5 is NR^a or O;

X^6 is NR^a or O;

R^1 is $(C_1–C_5)$alkyl;

R^3 is $(C_1–C_5)$alkyl, -CH_2-phenyl, -$(C_3–C_7)$cycloalkyl, -CH_2-$(C_3–C_7)$cycloalkyl, -CH_2-monocyclic 3-7 membered heterocyclic ring, or monocyclic 3-7 membered heterocyclic ring, wherein the $(C_1–C_5)$alkyl, -$(C_3–C_7)$cycloalkyl, phenyl or monocyclic 3-7 membered heterocyclic ring represented by R^3 or in the group represented by R^3 is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, $(C_1$-$C_4)$alkyl, halomethyl, halomethoxy, -CN, and $(C_1$-$C_4)$alkoxy;

R^2 is -$NR^aC(O)O(C_1$-$C_4)$alkyl; -$NR^aC(O)NR^a(C_1$-$C_4)$alkyl; -$NR^aC(O)O(C_2$-$C_4)$alkenyl;
-$NR^aC(O)NR^a(C_2$-$C_4)$alkenyl; -$NR^aC(O)O$-$(C_3$-$C_6)$cycloalkyl; -$NR^aC(O)NR^a$-$(C_3$-$C_7)$cycloalkyl; -$NR^aC(O)O$-phenyl; -$NR^aC(O)NR^a$-phenyl; -$NR^aC(O)O$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)NR^a$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)O$-monocyclic 5-6 membered heteroaromatic ring; -$NR^aC(O)NR^a$-monocyclic 5-6 membered heteroaromatic ring;

wherein the $(C_1–C_4)$alkyl and the $(C_2$-$C_4)$alkenyl in the group represented by R^2 are each optionally and independently substituted with one or more groups selected from the group consisting of halogen, N_3, –OR^a, -NR^aR^a, -$(C_3–C_6)$cycloalkyl, phenyl, a monocyclic 3-7 membered heterocyclic ring, and a monocyclic 5-6 membered heteroaromatic ring;

wherein the $(C_3–C_7)$cycloalkyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, =O, -OR^a and -NR^aR^a;

wherein the phenyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, halomethyl, halomethoxy,
-CN, -OR^a, and -N_3;

wherein the heterocyclic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of =O, halogen, –OR^a, -CH_3, halomethyl, and halomethoxy;

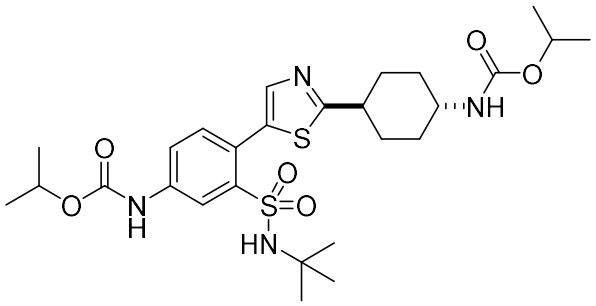
wherein the heteroaromatic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CN, -CH_3, halomethyl, halomethoxy, -OR^a and -NR^aR^a; and

each R^a is independently –H or -CH_3, and

a PARP inhibitor or a pharmaceutically acceptable salt thereof.

8. The kit of claim 7, wherein the PARP inhibitor is olaparib.

9. The kit of claim 7, wherein the compound of Formula (I) has the following structure:



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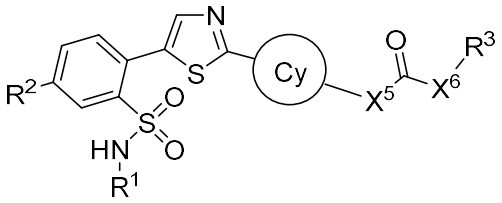
10. Use of the combination therapy of any one of claims 1-3 or the pharmaceutical composition of any one of claims 4-6 in the manufacture of a medicament for treatment of cancer, an autoimmune disease, an immune deficiency, or a neurodegenerative disease.

11. Use of a compound represented by Formula (I):



Formula (I);

or a pharmaceutically acceptable salt thereof, wherein:

the thiazole ring is optionally substituted with –F or –Cl;

Cy is -(C_3–C_7)cycloalkyl, bridged (C_6–C_{12}) cycloalkyl, or a 4-12 membered heterocyclic ring, each of which is optionally substituted with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, and (C_1-C_4)alkoxy;

when X^5 is connected with a nitrogen ring atom of Cy, X^5 is absent;

when X^5 is connected with a carbon ring atom of Cy, X^5 is NR^a or O;

X^6 is NR^a or O;

R^1 is (C_1–C_5)alkyl;

R^3 is (C_1–C_5)alkyl, -CH_2-phenyl, -(C_3–C_7)cycloalkyl, -CH_2-(C_3–C_7)cycloalkyl, -CH_2-monocyclic 3-7 membered heterocyclic ring, or monocyclic 3-7 membered heterocyclic ring, wherein the (C_1–C_5)alkyl, -(C_3–C_7)cycloalkyl, phenyl or monocyclic 3-7 membered heterocyclic ring represented by R^3 or in the group represented by R^3 is optionally substituted

with one or more groups selected from the group consisting of halogen, -OH, (C_1-C_4)alkyl, halomethyl, halomethoxy, -CN, and (C_1-C_4)alkoxy;

R^2 is -$NR^aC(O)O(C_1$-$C_4)$alkyl; -$NR^aC(O)NR^a(C_1$-$C_4)$alkyl; -$NR^aC(O)O(C_2$-$C_4)$alkenyl;
-$NR^aC(O)NR^a(C_2$-$C_4)$alkenyl; -$NR^aC(O)O$-$(C_3$-$C_6)$cycloalkyl; -$NR^aC(O)NR^a$-$(C_3$-$C_7)$cycloalkyl; -$NR^aC(O)O$-phenyl; -$NR^aC(O)NR^a$-phenyl; -$NR^aC(O)O$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)NR^a$-monocyclic 3-7 membered heterocyclic ring; -$NR^aC(O)O$-monocyclic 5-6 membered heteroaromatic ring; -$NR^aC(O)NR^a$-monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_1–C_4)alkyl and the (C_2-C_4)alkenyl in the group represented by R^2 are each optionally and independently substituted with one or more groups selected from the group consisting of halogen, N_3, –OR^a, -NR^aR^a, -(C_3–C_6)cycloalkyl, phenyl, a monocyclic 3-7 membered heterocyclic ring, and a monocyclic 5-6 membered heteroaromatic ring;

wherein the (C_3–C_7)cycloalkyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, =O, -OR^a and -NR^aR^a;

wherein the phenyl in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CH_3, halomethyl, halomethoxy,
-CN, -OR^a, and -N_3;

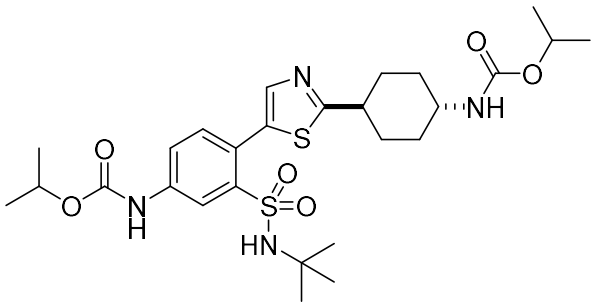
wherein the heterocyclic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of =O, halogen, –OR^a, -CH_3, halomethyl, and halomethoxy;

wherein the heteroaromatic ring in the group represented by R^2 is optionally substituted with one or more groups selected from the group consisting of halogen, -CN, -CH_3, halomethyl, halomethoxy, -OR^a and -NR^aR^a; and

each R^a is independently –H or -CH_3,
in combination with a PARP inhibitor or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer, an autoimmune disease, an immune deficiency, or a neurodegenerative disease.

12. The use of claim 11, wherein the PARP inhibitor is olaparib.

13. The use of claim 11, wherein the compound of Formula (I) has the following structure:



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14. The use of any one of claims 10-13, wherein the cancer is a hematological cancer or a solid tumor.

15. The use of any one of claims 10-13, wherein the cancer is a hematological cancer selected from lymphoma, leukemia, and a plasma cell neoplasm.

16. The use of claim 15, wherein the lymphoma is a B-cell lymphoma.

17. The use of claim 16, wherein the B-cell lymphoma is diffuse large B-cell lymphoma.

18. The use of claim 15, wherein the lymphoma is mantle cell lymphoma.

19. The use of claim 15, wherein the lymphoma is Burkitt's Lymphoma.

20. The use of any one of claims 10-13, wherein the cancer is a solid tumor.

21. The use of claim 20, wherein the solid tumor is selected from breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, fallopian tube cancer, peritoneal cancer, and lung cancer.