CLAIMS

1. A compound represented by Formula (1):

GBM-DT

(1)

or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof;

wherein:

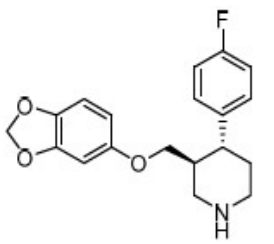
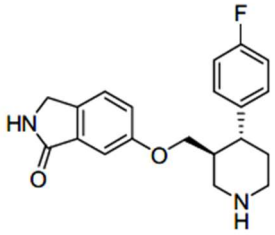
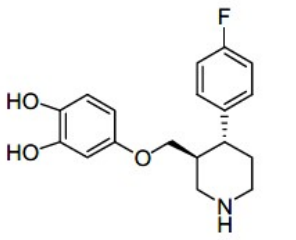
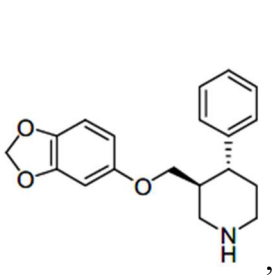
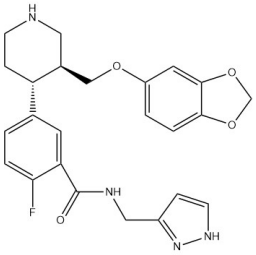
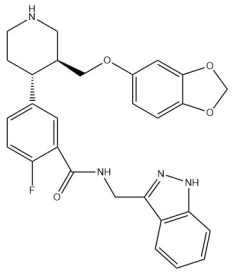
GBM is a GRK2 binding moiety; and

DT is a degradation tag having E3 ligase binding capacity,

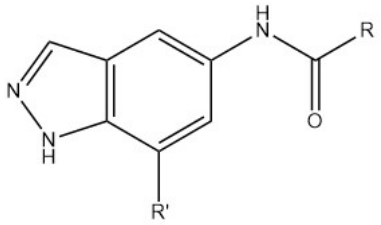
wherein the GBM is:

(a) a moiety derived from polyanionic and polycationic compounds;

(b) a moiety derived from balanol, or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof;

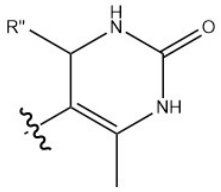
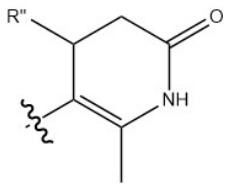
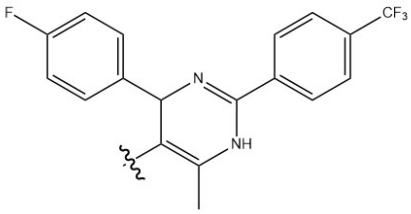
(c) a moiety derived from paroxetine series selected from , , , ,  and , or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof;

(d) a moiety derived from indazole or dihydropyrimidine series represented by Formula (2), or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof

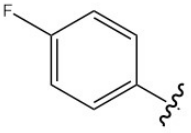
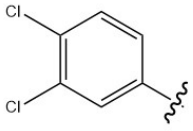
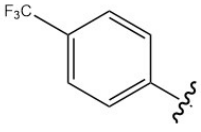
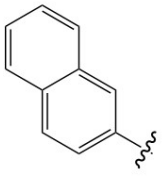


(2)

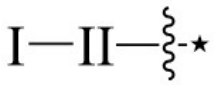
wherein

R is selected from ,  and ;

R' is selected from H and halogen; and

R'' is selected from , ,  and ; or

(e) is represented by Formula (3):



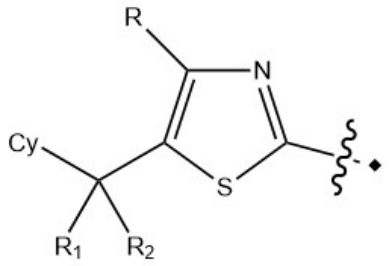
(3)

wherein ★denotes the point of attachment with the DT;

the Formula I is a moiety covalently linked to the Formula II, wherein the Formula I comprises a thiazole ring or triazole ring in its backbone and is capable of binding to GRK2 by itself or along with the Formula II; and

the Formula II is a moiety covalently linked to both the Formula I and the DT, wherein the Formula II comprises an acyclic or cyclic saturated or unsaturated carbon, ethylene glycol group, amide group, ester group, amino group, oxy group, thio group, ether group, urea group, carbamate group, aromatic group, heteroaromatic group, heterocyclic group, carbonyl group or the combination thereof,

wherein the Formula I is represented by Formula (4A):



(4A)

wherein:

◆ denotes the point of attachment with the Formula II;

each of R_1 and R_2 is independently selected from H, halogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, -NO_2, -OR_a, -SR_a, -NR_bR_c, -C(=O)R_a, -C(=O)OR_a, -OC(=O)R_a, -C(=O)NR_bR_c, -S(=O)R_a, -S(=O)$_2R_a$, -S(=O)$_2NR_bR_c$, optionally substituted C_{3-6} carbocyclyl and optionally substituted 3- to 6-membered heterocyclyl, or R_1 and R_2 may be taken together along with the atom to which they are attached to form an optionally substituted C_{3-12} carbocyclyl or optionally substituted 3- to 12-membered heterocyclyl;

R is selected from H, halogen, -CN, -N(=O), -NO_2, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -OR_a, -C(=O)R_a, -C(=S)R_a, -C(=O)OR_a, -OC(=O)R_a, -SR_a, -S(=O)R_a, -S(=O)$_2R_a$, -NR_bR_c, -C(=O)NR_bR_c, -S(=O)NR_bR_c, -S(=O)$_2NR_bR_c$, -NR_dC(=O)R_a, -NR_dC(=O)OR_a, -NR_dC(=O)NR_bR_c, -NR_dS(=O)R_a, -NR_dS(=O)$_2R_a$, -NR_dS(=O)NR_bR_c, -NR_dS(=O)$_2NR_bR_c$, -SN(=O), -NR_dN(=O), optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl,

optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

Cy is selected from aryl, C_{3-12} carbocyclyl, 5- to 12-membered heteroaryl and 3- to 12-membered heterocyclyl, each of which is optionally substituted by 1, 2, 3 or more R';

R' is selected from halogen, -CN, -N(=O), $-NO_2$, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-OR_a$, $-C(=O)R_a$, $-C(=S)R_a$, $-C(=O)OR_a$, $-OC(=O)R_a$, $-SR_a$, $-S(=O)R_a$, $-S(=O)_2R_a$, $-NR_bR_c$, $-C(=O)NR_bR_c$, $-S(=O)NR_bR_c$, $-S(=O)_2NR_bR_c$, $-NR_dC(=O)R_a$, $-NR_dC(=O)OR_a$, $-NR_dC(=O)NR_bR_c$, $-NR_dS(=O)R_a$, $-NR_dS(=O)_2R_a$, $-NR_dS(=O)NR_bR_c$, $-NR_dS(=O)_2NR_bR_c$, -SN(=O), $-NR_dN(=O)$, optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

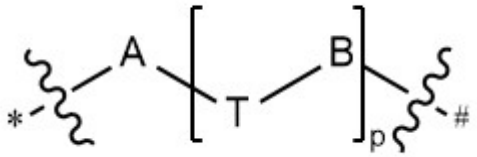
each R_a is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl;

each of R_b and R_c is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6}cycloalkyl; or an R_b and an R_c may be taken together along with the nitrogen atom to which they are attached to form an optionally substituted 3- to 12-membered heterocyclyl;

each R_d is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl; and

the term "optionally substituted" before a chemical group without specifying the substituents(s) thereof indicates that said chemical group is optionally substituted by 1, 2, 3 or more substituents selected from the group consisting of halogen, C_{1-6}alkyl, $-OR_a$, $-NR_bR_c$, $-C(=O)R_a$, $-C(=O)OR_a$, $-OC(=O)R_a$, $-NO_2$, =O, -CN and C_{3-6}cycloalkyl.

2. The compound according to claim 1, wherein the Formula II is represented by Formula (6):



(6)

wherein

* denotes the point of attachment with the Formula I;

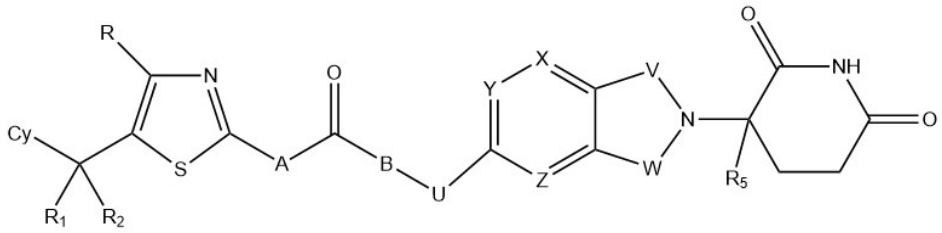
# denotes the point of attachment with the DT;

A, T, and B, at each occurrence, are independently selected from null, -C(=O)-, -C(=O)O-, -C(=O)NR^1-, -C(=S)NR^1-, -O-, -S-, -S(=O)-, -$S(=O)_2$-, -$S(=O)_2NR^1$-, -NR^1-, -NR^1C(=O)-, -NR^1C(=O)NR^2-, -NR^1C(=S)-, optionally substituted C_1-C_8 alkyl, optionally substituted C_1-C_8 alkoxy, optionally substituted C_1-C_8alkoxyC_1-C_8alkyl, optionally substituted C_1-C_8 haloalkyl, optionally substituted C_1-C_8 hydroxyalkyl, optionally substituted C_2-C_8 alkenyl, optionally substituted C_2-C_8 alkynyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_3-C_8 cycloalkoxy, optionally substituted 3-8 membered heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_3-C_{13} fused cycloalkyl, optionally substituted C_3-C_{13} fused heterocyclyl, optionally substituted C_3-C_{13} bridged cycloalkyl, optionally substituted C_3-C_{13} bridged heterocyclyl, optionally substituted C_3-C_{13} spiro cycloalkyl, and optionally substituted C_3-C_{13} spiro heterocyclyl, wherein

R^1 and R^2 are independently selected from hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_3-C_6 cycloalkyl, optionally substituted C_3-C_6 cycloalkoxy, optionally substituted 3-6 membered heterocyclyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_1-C_6 alkoxyalkyl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 hydroxyalkyl, optionally substituted C_1-C_6 alkylamino, and optionally substituted C_1-C_6alkylaminoC_1-C_6alkyl; and

p is 0 to 15.

3. The compound according to any one of claims 1-2, wherein the compound is represented by Formula (11)



(11)

wherein:

A is selected from C_{1-20}alkylene, -O-, -S-, -N(R_e)- and -N(R_e)-C_{1-20}alkylene-, and optionally wherein 1, 2, 3 or more methylene in the C_{1-20}alkylene group is independently replaced with a group selected from -O-, -S-, -N(R_e)-, -C(=O)- and -C(=S)-;

B is a bond or is selected from arylene, C_{3-12} carbocyclylene, 5- to 12-membered heteroarylene and 3- to 12-membered heterocyclylene, each of which is optionally substituted by 1, 2, 3 or more substituents selected from the group consisting of halogen, -CN, -NO_2, C_{1-6} alkyl optionally substituted by 1, 2 or 3 halogen, C_{1-6} heteroalkyl optionally substituted by 1, 2 or 3 halogen, C_{2-6} alkenyl optionally substituted by 1, 2 or 3 halogen, C_{2-6} alkynyl optionally substituted by 1, 2 or 3 halogen, -OR_a, -SR_a and -NR_bR_c;

U is independently selected from -CH_2-, -NH- and -O-;

each of V and W is independently selected from -C(=O)- and -CH_2-;

each of X, Y, and Z is independently selected from CR_6 and N;

each of R_1 and R_2 is independently selected from H, halogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, -NO_2, -OR_a, -SR_a, -NR_bR_c, -C(=O)R_a, -C(=O)OR_a, -OC(=O)R_a, -C(=O)NR_bR_c, -S(=O)R_a, -S(=O)$_2R_a$, -S(=O)$_2NR_bR_c$, optionally substituted C_{3-6} carbocyclyl and optionally substituted 3- to 6-membered heterocyclyl, or R_1 and R_2 may be taken together along with the atom to which they are attached to form an optionally substituted C_{3-12} carbocyclyl or optionally substituted 3- to 12-membered heterocyclyl;

R is selected from H, halogen, -CN, -N(=O), -NO_2, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -OR_a, -C(=O)R_a, -C(=S)R_a, -C(=O)OR_a, -OC(=O)R_a, -SR_a, -S(=O)R_a, -S(=O)$_2R_a$, -NR_bR_c, -C(=O)NR_bR_c, -S(=O)NR_bR_c, -S(=O)$_2NR_bR_c$, -NR_dC(=O)R_a, -NR_dC(=O)OR_a, -NR_dC(=O)NR_bR_c, -NR_dS(=O)R_a, -NR_dS(=O)$_2R_a$, -NR_dS(=O)NR_bR_c, -NR_dS(=O)$_2NR_bR_c$, -

SN(=O), -NR_dN(=O), optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

Cy is selected from aryl, C_{3-12} carbocyclyl, 5- to 12-membered heteroaryl and 3- to 12-membered heterocyclyl, each of which is optionally substituted by 1, 2, 3 or more R';

R' is selected from halogen, -CN, -N(=O), -NO_2, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -OR_a, -$C(=O)R_a$, -$C(=S)R_a$, -$C(=O)OR_a$, -$OC(=O)R_a$, -SR_a, -$S(=O)R_a$, -$S(=O)_2R_a$, -NR_bR_c, -$C(=O)NR_bR_c$, -$S(=O)NR_bR_c$, -$S(=O)_2NR_bR_c$, -$NR_dC(=O)R_a$, -$NR_dC(=O)OR_a$, -$NR_dC(=O)NR_bR_c$, -$NR_dS(=O)R_a$, -$NR_dS(=O)_2R_a$, -$NR_dS(=O)NR_bR_c$, -$NR_dS(=O)_2NR_bR_c$, -SN(=O), -NR_dN(=O), optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

R_5 is selected from H, halogen and optionally substituted C_1-C_6 alkyl;

R_6 is selected from H, halogen and optionally substituted C_1-C_6 alkyl;

each R_a is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl;

each of R_b and R_c is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6}cycloalkyl; or an R_b and an R_c may be taken together along with the nitrogen atom to which they are attached to form an optionally substituted 3- to 12-membered heterocyclyl;

each R_d is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl;

R_e is selected from H and optionally substituted C_{1-6} alkyl; and

the term "optionally substituted" before a chemical group without specifying the substituents(s) thereof indicates that said chemical group is optionally substituted by 1, 2, 3 or more substituents selected from the group consisting of halogen, C_{1-6}alkyl, -OR_a, -NR_bR_c, -$C(=O)R_a$, -$C(=O)OR_a$, -$OC(=O)R_a$, -NO_2, =O, -CN and C_{3-6}cycloalkyl.

4. A compound represented by Formula (1*):

GBM-DT

(1*)

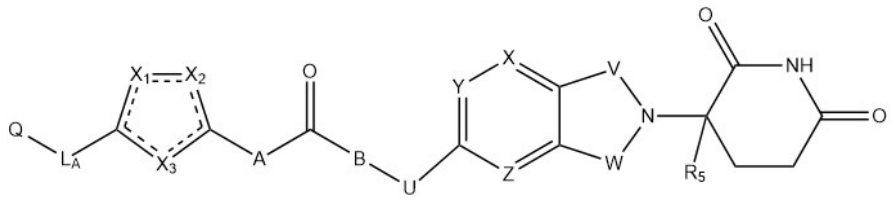
or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof;

wherein:

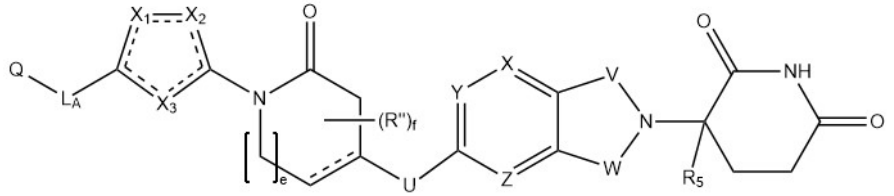
GBM is a GRK2 binding moiety; and

DT is a degradation tag having E3 ligase binding capacity;

wherein the compound is represented by Formula (16A) or (16B)



(16A)



(16B)

wherein:

each of ---- is independently a single bond or a double bond;

Q is selected from optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-OR_a$, $-SR_a$, $-NR_bR_c$, $-C(=O)R_a$, $-C(=O)OR_a$, $-OC(=O)R_a$, $-C(=O)NR_bR_c$, $-S(=O)R_a$, $-S(=O)_2R_a$, $-S(=O)_2NR_bR_c$ and Cy;

Cy is selected from aryl, C_{3-12} carbocyclyl, 5- to 12-membered heteroaryl and 3- to 12-membered heterocyclyl, each of which is optionally substituted by 1, 2, 3 or more R';

L_A is selected from a bond, $-(CH_2)_aC(R_1)(R_2)(CH_2)_b-$, $-N(R_1)-$, -O-, -S-, -C(=O)-, -C(=S)-, -S(=O)- and $-S(=O)_2-$;

X_1, X_2 and X_3 are each independently selected from CR, S or N;

with the proviso that at least one of X_1, X_2 and X_3 is N and one of X_1, X_2 and X_3 is S;

A is selected from C_{1-20}alkylene, -O-, -S-, -N(R_e)- and -N(R_e)-C_{1-20}alkylene-, and optionally wherein 1, 2, 3 or more methylene in the C_{1-20}alkylene group is independently replaced with a group selected from -O-, -S-, -N(R_e)-, -C(=O)- and -C(=S)-;

B is a bond or is selected from arylene, C_{3-12} carbocyclylene, 5- to 12-membered heteroarylene and 3- to 12-membered heterocyclylene, each of which is optionally substituted by 1, 2, 3 or more substituents selected from the group consisting of halogen, -CN, -NO_2, C_{1-6} alkyl optionally substituted by 1, 2 or 3 halogen, C_{1-6} heteroalkyl optionally substituted by 1, 2 or 3 halogen, C_{2-6} alkenyl optionally substituted by 1, 2 or 3 halogen, C_{2-6} alkynyl optionally substituted by 1, 2 or 3 halogen, -OR_a, -SR_a and -NR_bR_c;

U is independently selected from a bond, -CH_2-, -NH- and -O-;

each of V and W is independently selected from -C(=O)- and -CH_2-;

each of X, Y, and Z is independently selected from CR_6 and N;

each of R_1 and R_2 is independently selected from H, halogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, -NO_2, -OR_a, -SR_a, -NR_bR_c, -C(=O)R_a, -C(=O)OR_a, -OC(=O)R_a, -C(=O)NR_bR_c, -S(=O)R_a, -S(=O)$_2R_a$, -S(=O)$_2NR_bR_c$, optionally substituted C_{3-6} carbocyclyl and optionally substituted 3- to 6-membered heterocyclyl, or R_1 and R_2 may be taken together along with the atom to which they are attached to form an optionally substituted C_{3-12} carbocyclyl or optionally substituted 3- to 12-membered heterocyclyl;

R is selected from H, halogen, -CN, -N(=O), -NO_2, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -OR_a, -C(=O)R_a, -C(=S)R_a, -C(=O)OR_a, -OC(=O)R_a, -SR_a, -S(=O)R_a, -S(=O)$_2R_a$, -NR_bR_c, -C(=O)NR_bR_c, -S(=O)NR_bR_c, -S(=O)$_2NR_bR_c$, -NR_dC(=O)R_a, -NR_dC(=O)OR_a, -NR_dC(=O)NR_bR_c, -NR_dS(=O)R_a, -NR_dS(=O)$_2R_a$, -NR_dS(=O)NR_bR_c, -NR_dS(=O)$_2NR_bR_c$, -SN(=O), -NR_dN(=O), optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

R' is selected from halogen, -CN, -N(=O), -NO_2, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -OR_a, -C(=O)R_a, -C(=S)R_a, -C(=O)OR_a, -OC(=O)R_a, -SR_a, -S(=O)R_a, -S(=O)$_2R_a$, -NR_bR_c, -C(=O)NR_bR_c, -S(=O)NR_bR_c, -S(=O)$_2NR_bR_c$, -NR_dC(=O)R_a, -

$NR_dC(=O)OR_a$, $-NR_dC(=O)NR_bR_c$, $-NR_dS(=O)R_a$, $-NR_dS(=O)_2R_a$, $-NR_dS(=O)NR_bR_c$, $-NR_dS(=O)_2NR_bR_c$, -SN(=O), $-NR_dN(=O)$, optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

R'' is selected from halogen, -CN, -N(=O), $-NO_2$, -ON(=O), optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-OR_a$, $-C(=O)R_a$, $-C(=S)R_a$, $-C(=O)OR_a$, $-OC(=O)R_a$, $-SR_a$, $-S(=O)R_a$, $-S(=O)_2R_a$, $-NR_bR_c$, $-C(=O)NR_bR_c$, $-S(=O)NR_bR_c$, $-S(=O)_2NR_bR_c$, $-NR_dC(=O)R_a$, $-NR_dC(=O)OR_a$, $-NR_dC(=O)NR_bR_c$, $-NR_dS(=O)R_a$, $-NR_dS(=O)_2R_a$, $-NR_dS(=O)NR_bR_c$, $-NR_dS(=O)_2NR_bR_c$, -SN(=O), $-NR_dN(=O)$, optionally substituted aryl, optionally substituted C_{3-12} carbocyclyl, optionally substituted 5- to 12-membered heteroaryl and optionally substituted 3- to 12-membered heterocyclyl;

R_5 is selected from H, halogen and optionally substituted C_1-C_6 alkyl;

R_6 is selected from H, halogen and optionally substituted C_1-C_6 alkyl;

each R_a is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl;

each of R_b and R_c is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6}cycloalkyl; or an R_b and an R_c may be taken together along with the nitrogen atom to which they are attached to form an optionally substituted 3- to 12-membered heterocyclyl;

each R_d is independently selected from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl and C_{3-6} cycloalkyl;

R_e is selected from H and optionally substituted C_{1-6} alkyl;

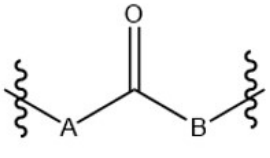
a is selected from 0, 1, 2, 3, 4 and 5, b is selected from 0, 1, 2, 3, 4 and 5, with the proviso that $a + b \leqslant 5$;

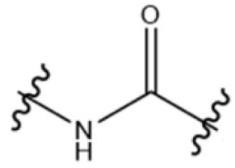
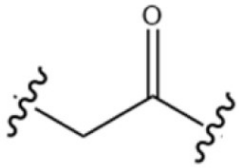
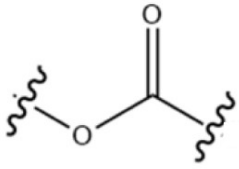
e is 0 or 1;

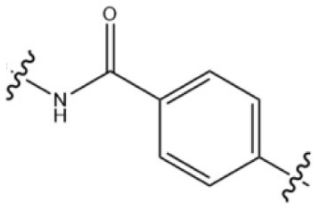
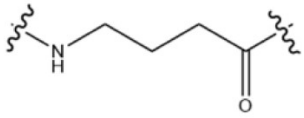
f is selected from 0, 1, 2 and 3; and

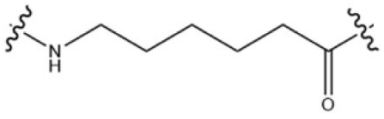
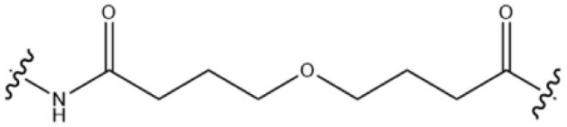
the term "optionally substituted" before a chemical group without specifying the substituents(s) thereof indicates that said chemical group is optionally substituted by 1, 2, 3 or more substituents selected from the group consisting of halogen, C_{1-6}alkyl, $-OR_a$, $-NR_bR_c$, $-C(=O)R_a$, $-C(=O)OR_a$, $-OC(=O)R_a$, $-NO_2$, =O, -CN and C_{3-6}cycloalkyl.

5. The compound according to any one of claims 1-4, wherein A is selected from -CH_2-, -O- and -NH-.

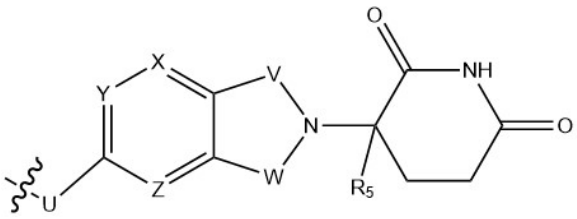
6. The compound according to any one of claims 1-5, wherein  is a moiety selected from:

, , ,

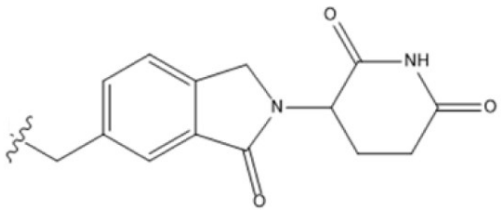
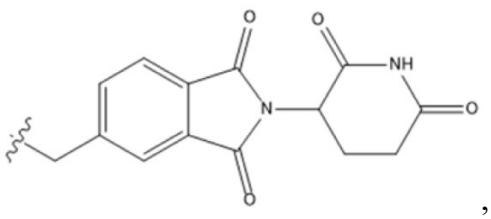
, ,

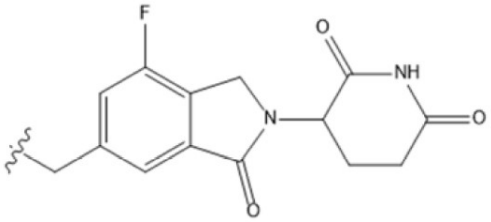
 and .

7. The compound according to any one of claims 1-6, wherein



is a moiety selected from:

, ,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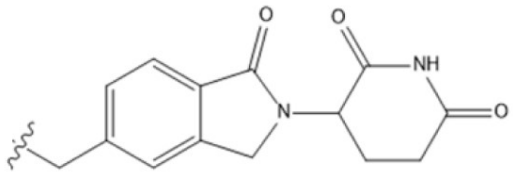
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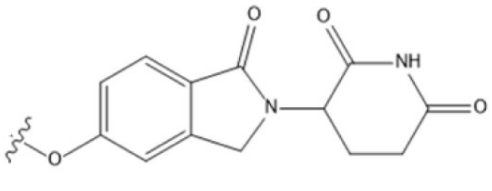
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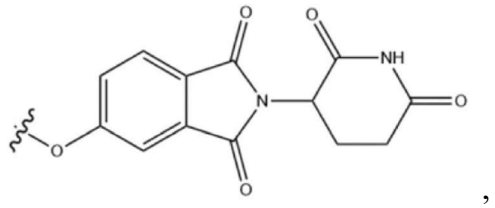
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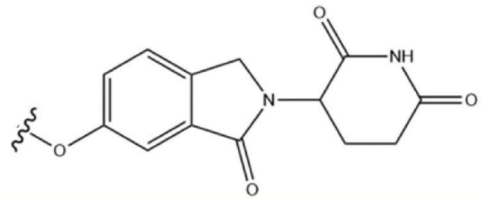
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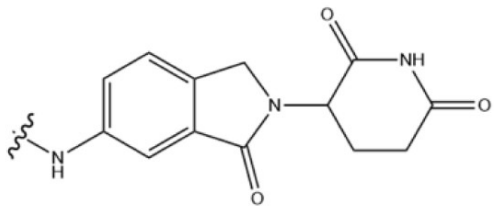
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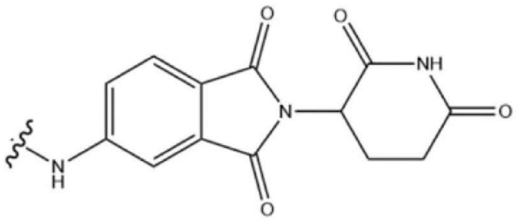
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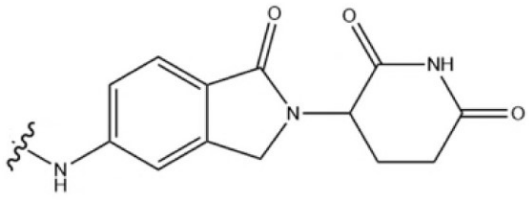
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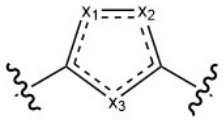
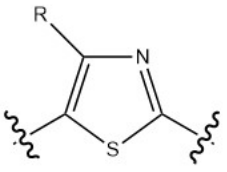
8. The compound according to claim 4, wherein  is selected from: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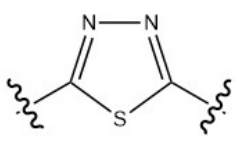
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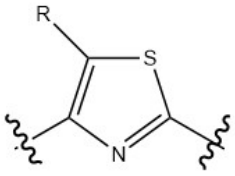
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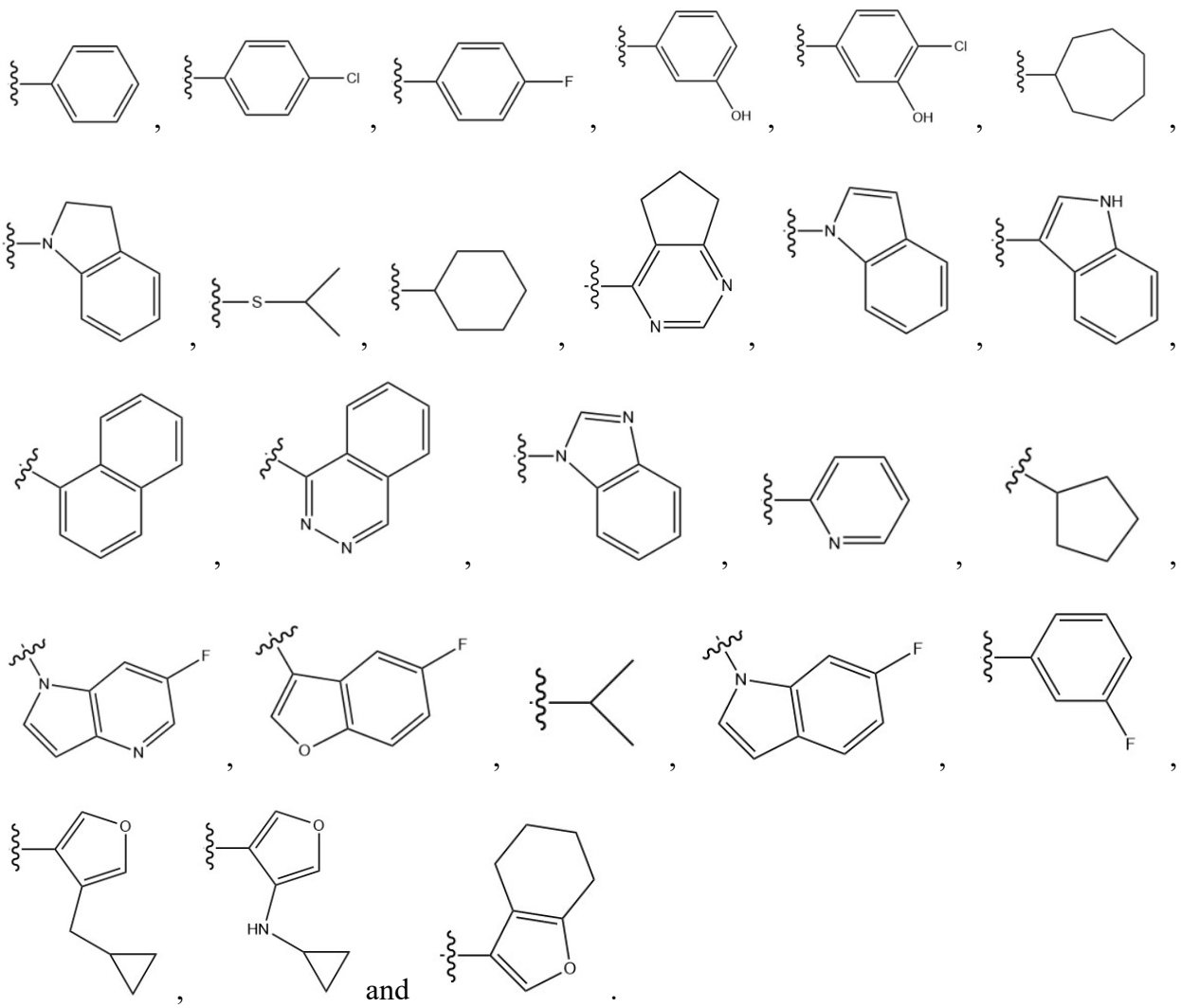
9. The compound according to any one of claims 1-8, wherein Cy is phenyl which is optionally substituted by 1, 2, 3 or more R'.

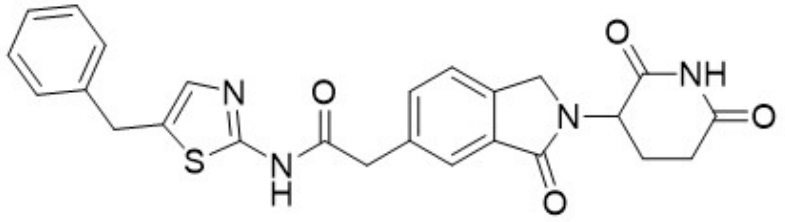
10. The compound according to any one of claims 1-8, wherein Q is selected from:



11. The compound according to any one of claims 1-10, wherein V is -C(=O)- and W is $-CH_2-$, V is $-CH_2-$ and W is -C(=O)-, or V and W are both -C(=O)-, and each of X, Y, and Z is independently selected from CR_6.

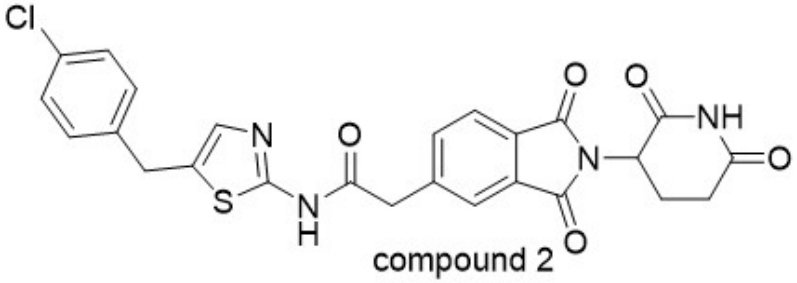
12. The compound according to any one of claims 1-11, wherein each of R_1 and R_2 is independently selected from H, F, Cl, Br, methyl, ethyl and propyl, R is selected from H, F, Cl, Br, methyl, ethyl, propyl, -OH, $-O(CH_3)$ and $-NH_2$.

13. A compound according to claim 1 or 4 selected from the group consisting of



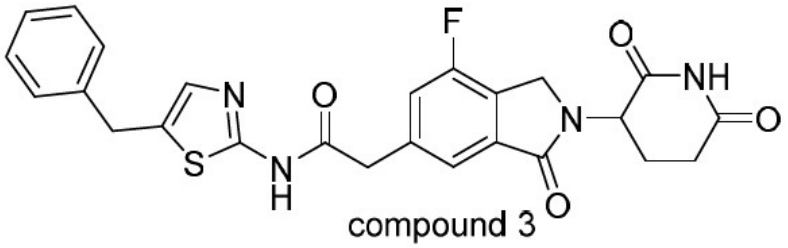
compound 1

,



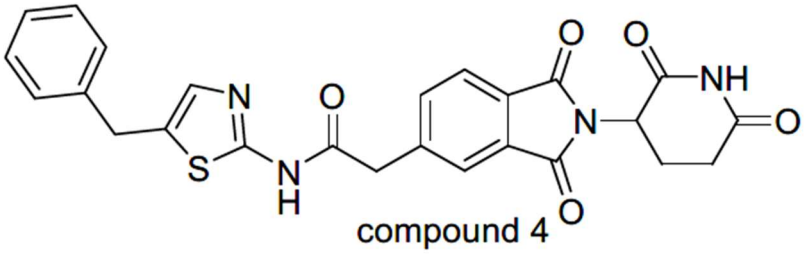
compound 2

,



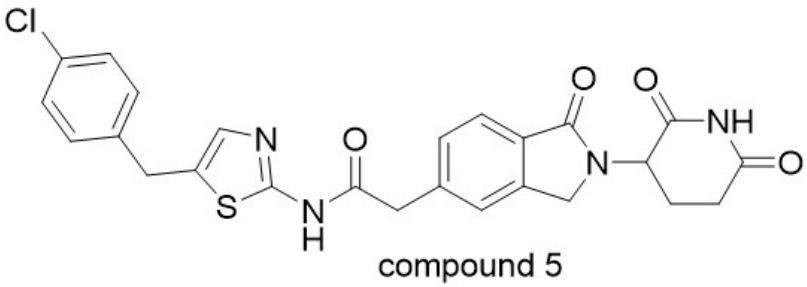
compound 3

,



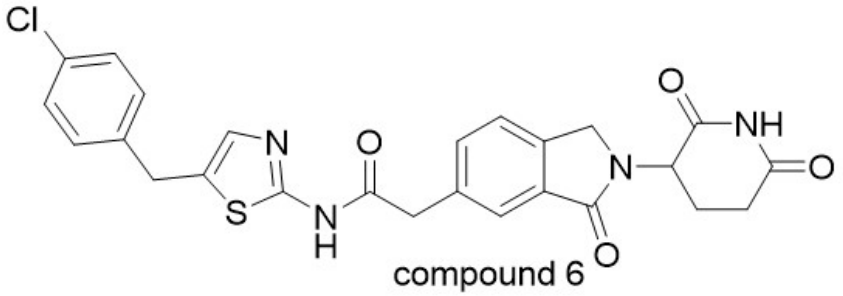
compound 4

,

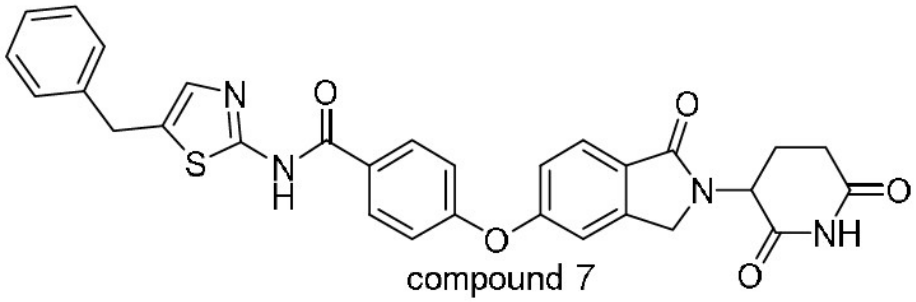


compound 5

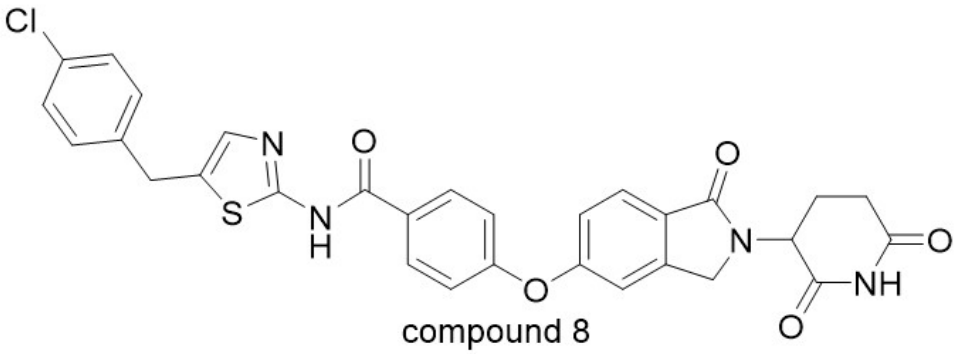
,



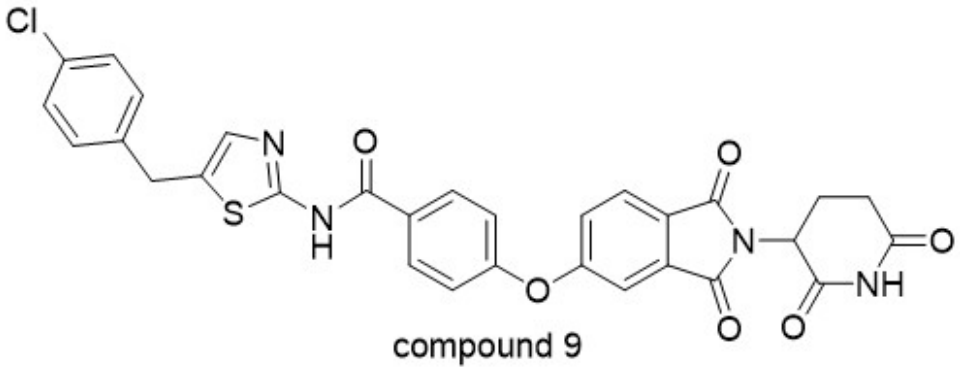
compound 6 ,



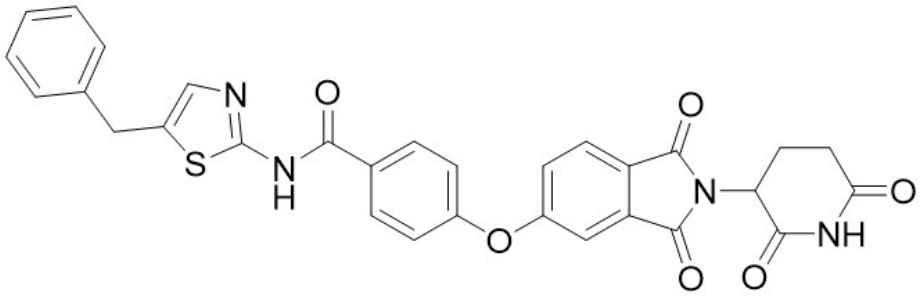
compound 7 ,



compound 8 ,



compound 9 ,



compound 10

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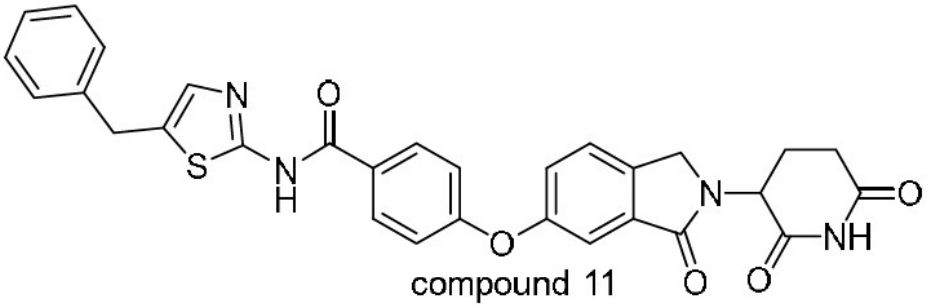

compound 11

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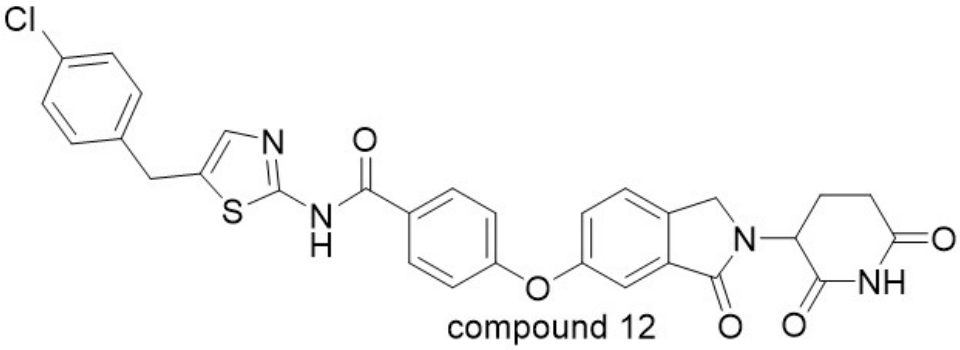

compound 12

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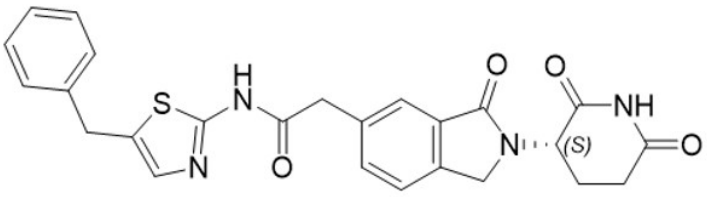
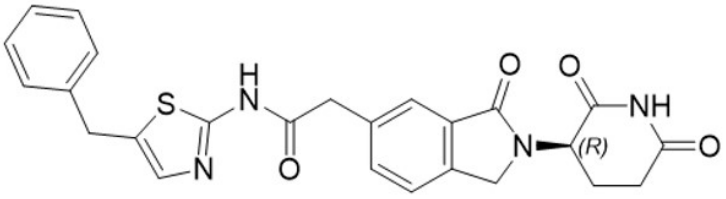


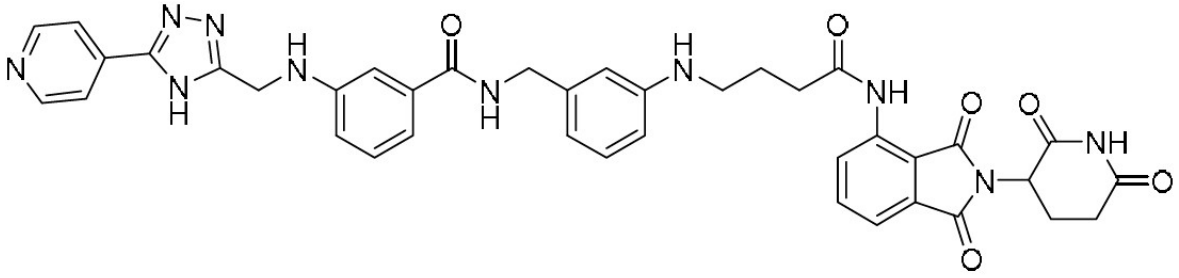
compound 1-P1

,



compound 1-P2

,



compound 13

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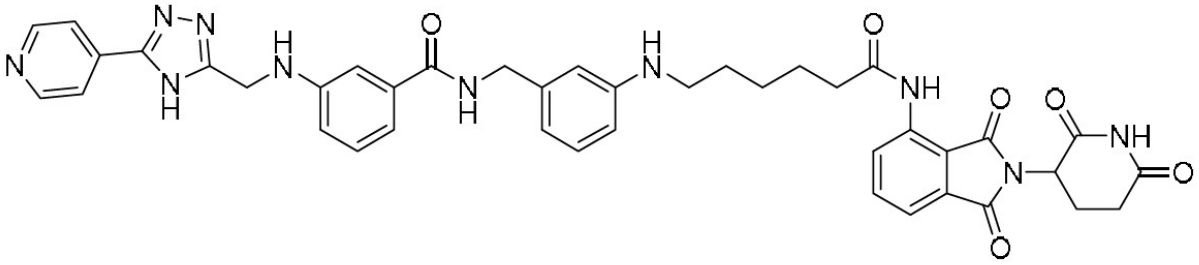

compound 14

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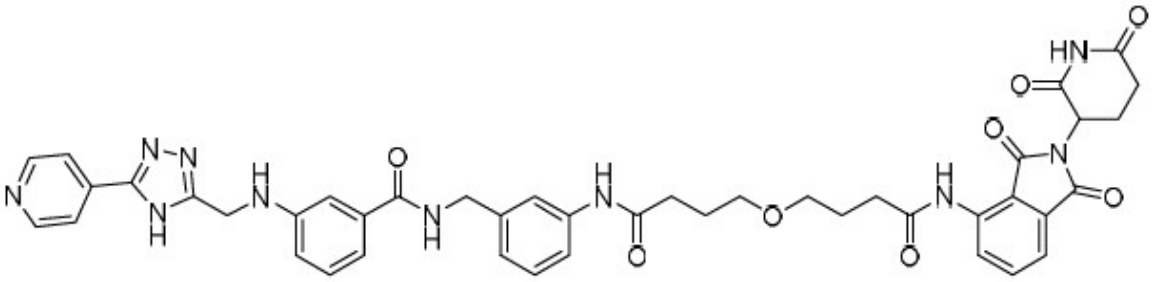

compound 15

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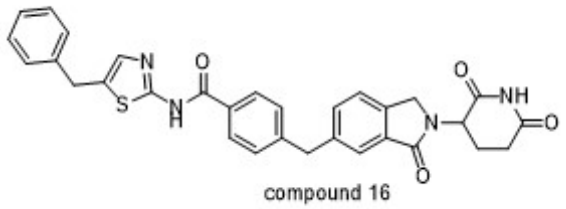

compound 16

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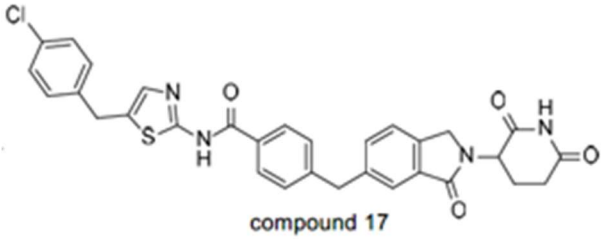

compound 17

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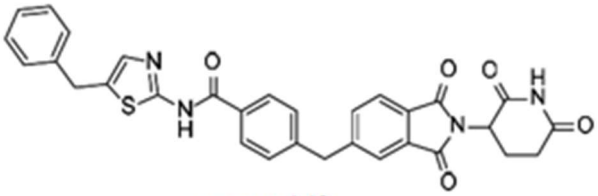
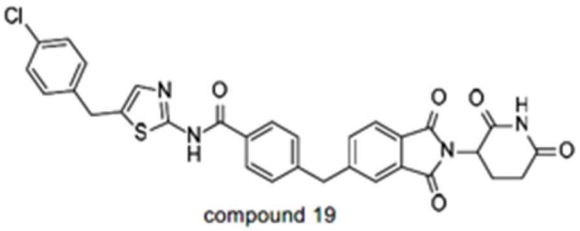


compound 18



compound 19

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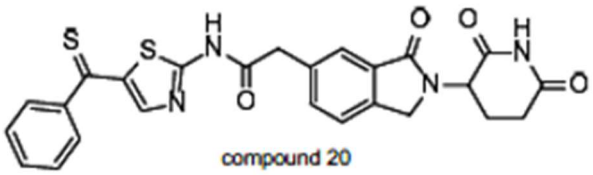

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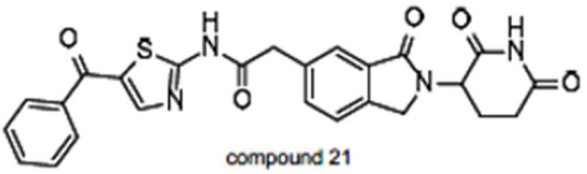

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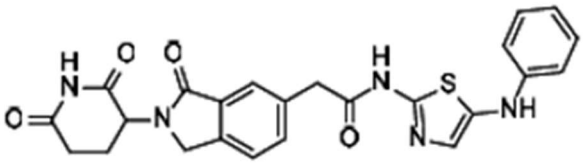

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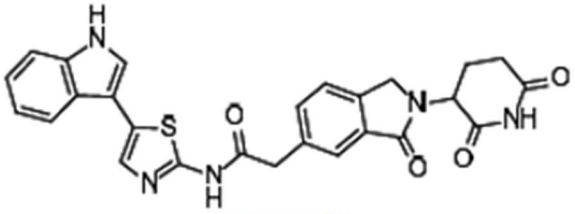

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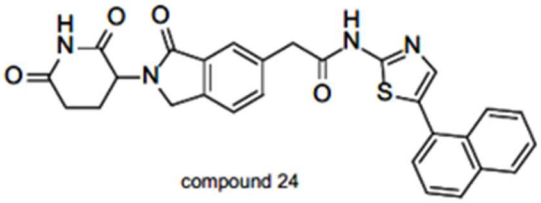

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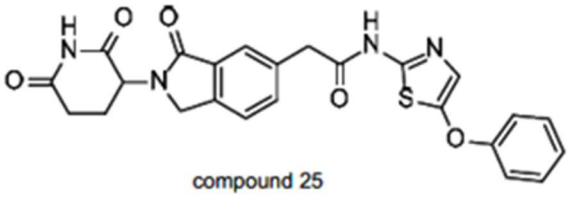

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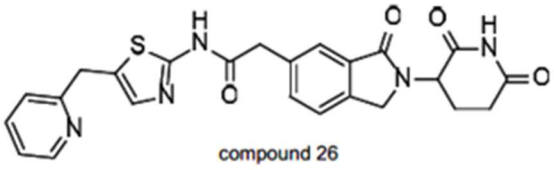

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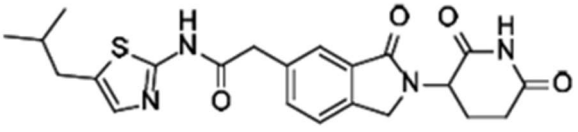

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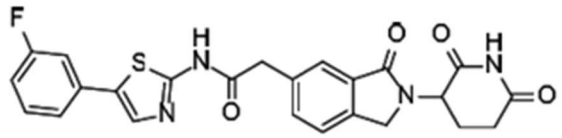

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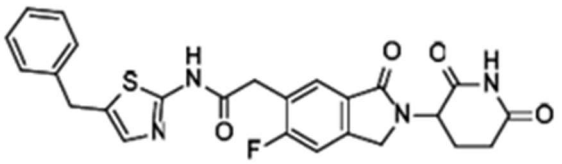

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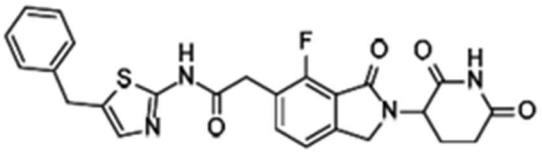

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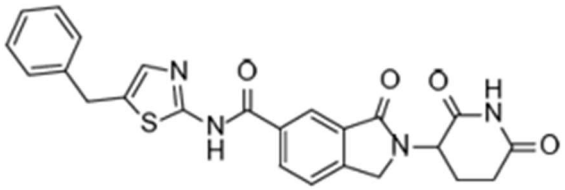

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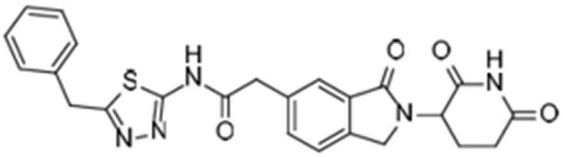

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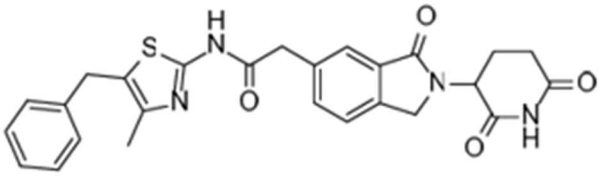

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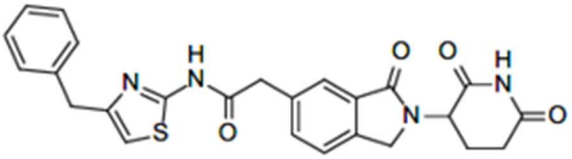

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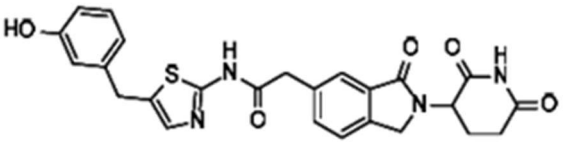

compound 35

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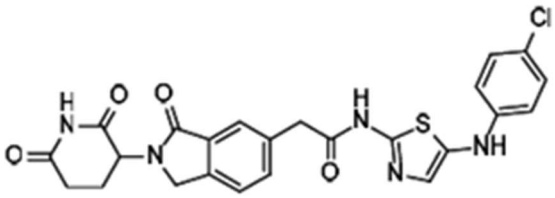

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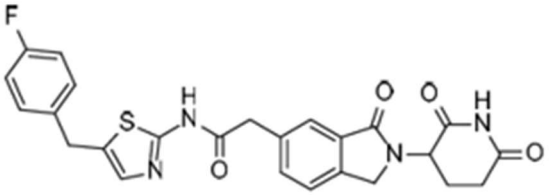

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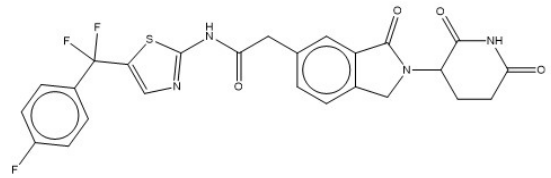

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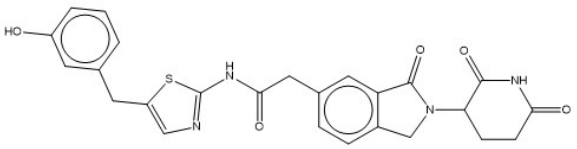

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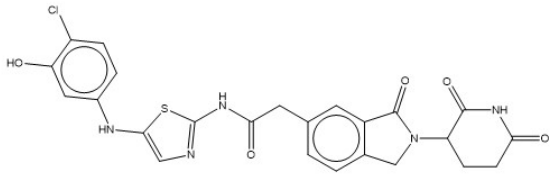

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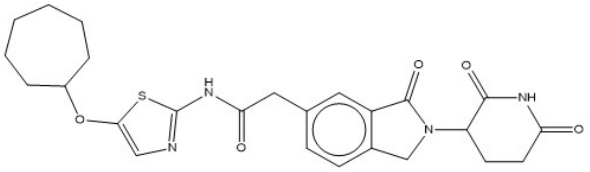

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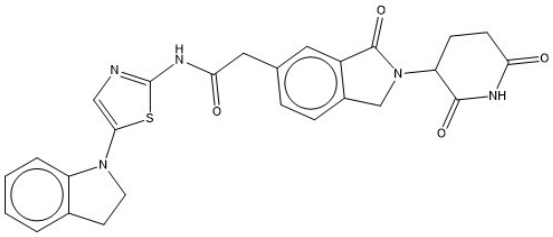

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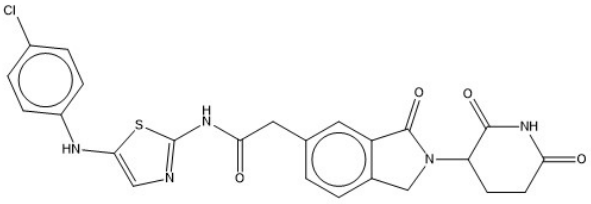

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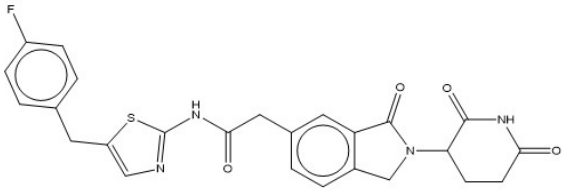

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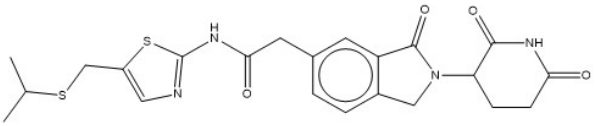

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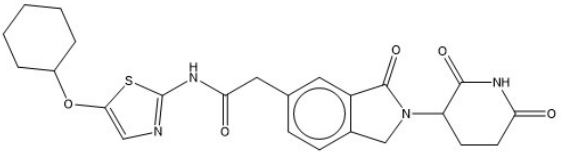

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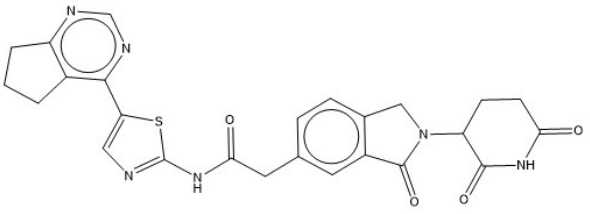

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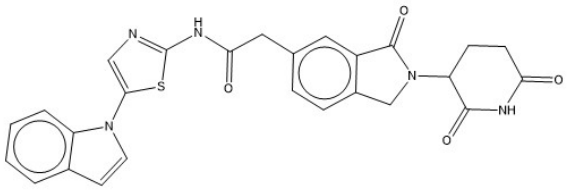

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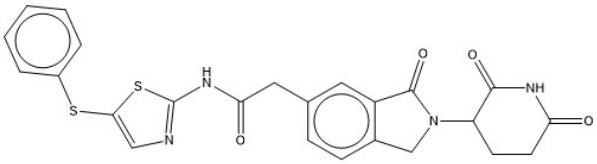

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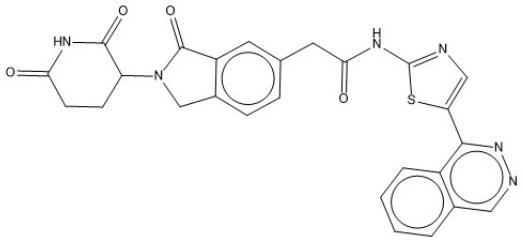

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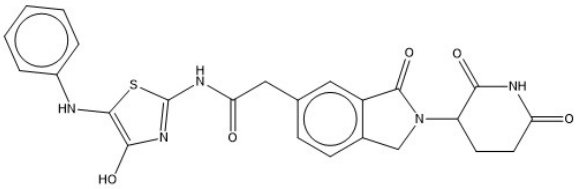

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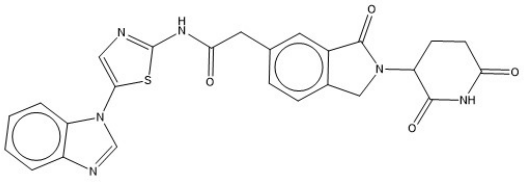

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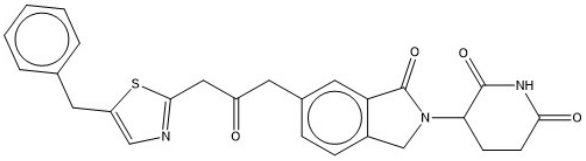

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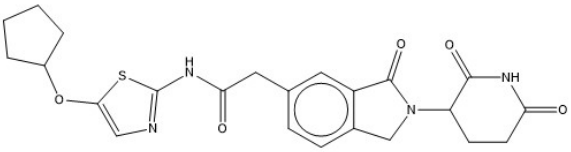

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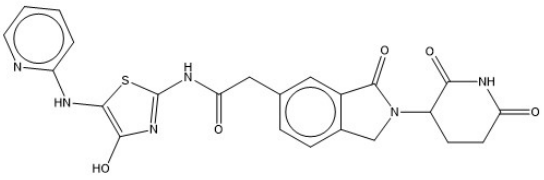

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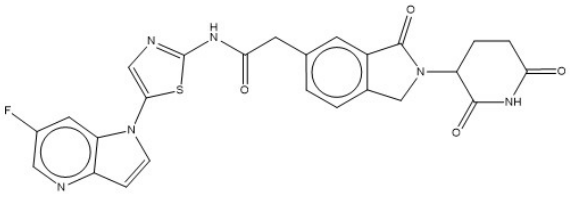

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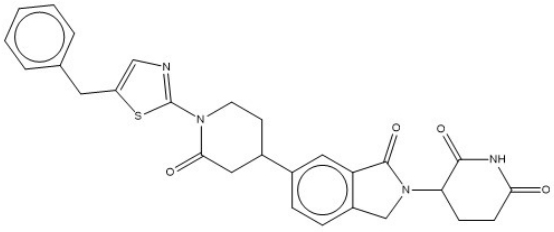

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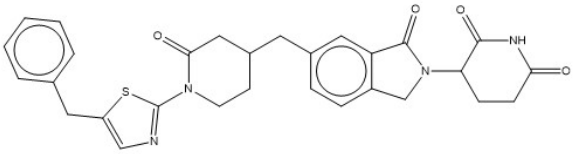

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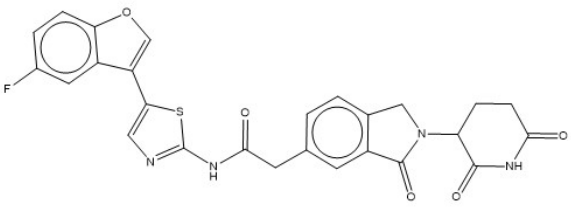

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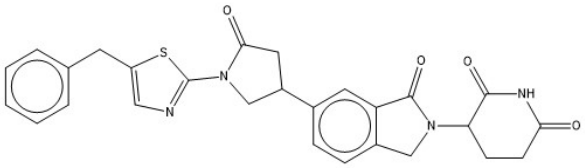

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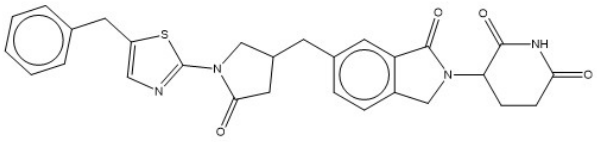

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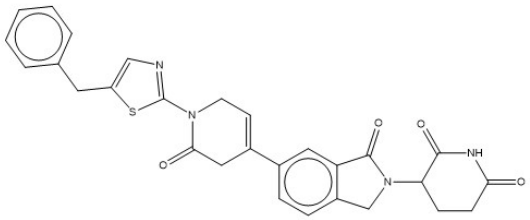

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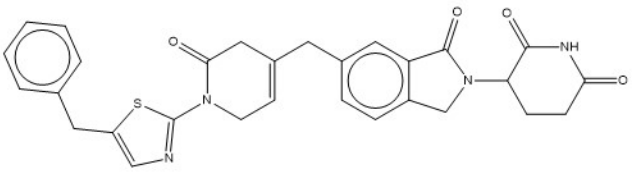

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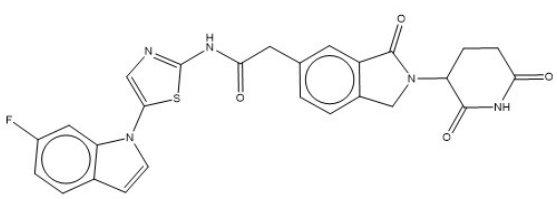

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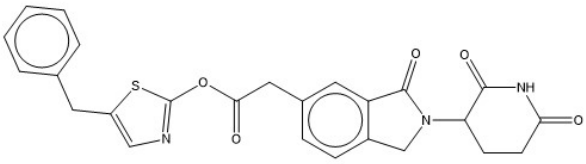

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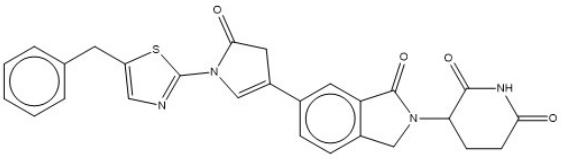

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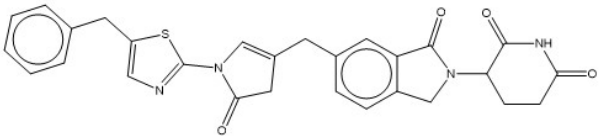

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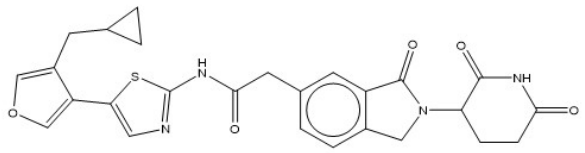

compound 68

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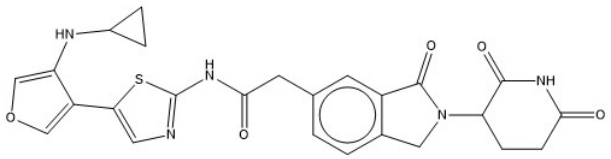

compound 69

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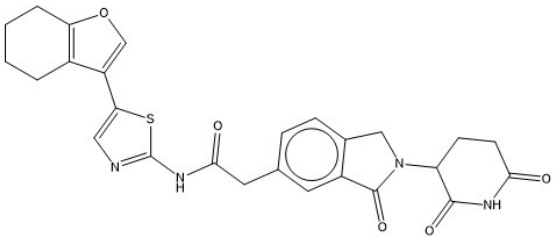

compound 70

and .

14. A pharmaceutical composition comprising the compound according to any one of claims 1-13 or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof and one or more pharmaceutically acceptable excipients.

15. Use of an effective amount of the compound according to any one of claims 1-13 or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof or the pharmaceutical composition according to claim 14 in the manufacture of a medicament for preventing or treating a disease or a condition for which the degradation of GRK2 is beneficial in a subject, wherein the disease or the condition is selected from a hyperproliferative disease, a cardiovascular disease, a hematological disease, an infective disease, an endocrinological disease, a metabolic disease, a gastroenterological disease, a respiratory disease, an inflammation, opioid addiction and a urological disease.

16. A compound according to any one of claims 1-13 or a pharmaceutically acceptable salt, an isomer, an isotope, a prodrug, a solvate, or a polymorph thereof or the pharmaceutical composition according to claim 14 for use as a medicament.