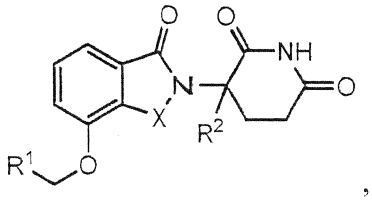
CLAIMS

What is claimed is:

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt, solvate or stereoisomer thereof, wherein:

X is C=O or CH_2;

R^1 is -Y-R^3;

R^2 is H or (C_1-C_6)alkyl;

Y is: 6 to 10 membered aryl, heteroaryl or heterocycle, each of which may be optionally substituted with one or more halogen; or a bond;

R^3 is: -$(CH_2)_n$-aryl, -O-$(CH_2)_n$-aryl or -$(CH_2)_n$-O-aryl, wherein the aryl is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano; hydroxyl; halogen; deuterium; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or halogen; -$CONH_2$; or -COO-(C_1-C_6)alkyl, wherein the alkyl may be optionally substituted with one or more halogen;

-$(CH_2)_n$-heterocycle, -O-$(CH_2)_n$-heterocycle or -$(CH_2)_n$-O-heterocycle, wherein the heterocycle is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano; hydroxyl; halogen; deuterium; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or halogen; -$CONH_2$; or -COO-(C_1-C_6)alkyl, wherein the alkyl may be optionally substituted with one or more halogen; or

-$(CH_2)_n$-heteroaryl, -O-$(CH_2)_n$-heteroaryl or -$(CH_2)_n$-O-heteroaryl, wherein the heteroaryl is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano;

hydroxyl; halogen; deuterium; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or halogen; -$CONH_2$; or -COO-(C_1-C_6)alkyl, wherein the alkyl may be optionally substituted with one or more halogen; and

n is 0, 1, 2 or 3.

2. The compound of claim 1, wherein X is CH_2.

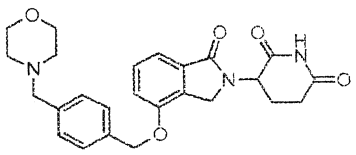
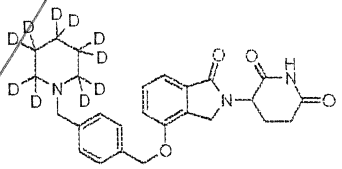
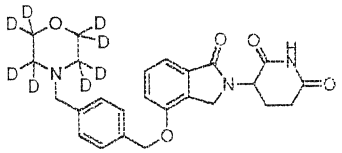
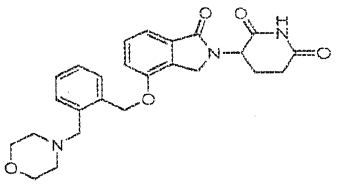
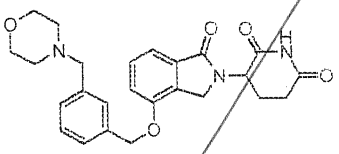
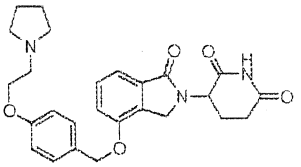
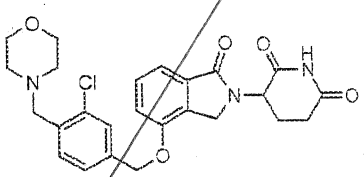
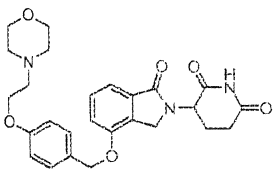
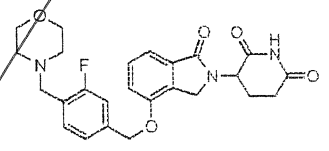
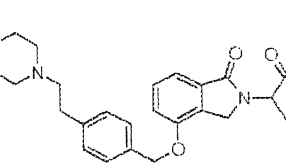
3. The compound of claim 1, wherein Y is phenyl, and R^3 is -$(CH_2)_n$-heterocycle.

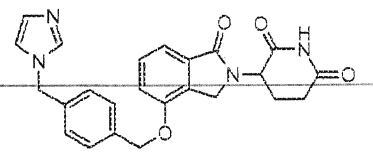
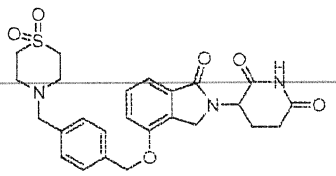
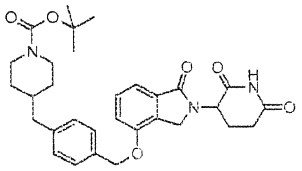
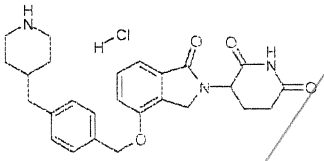
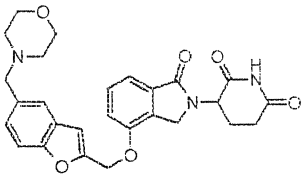
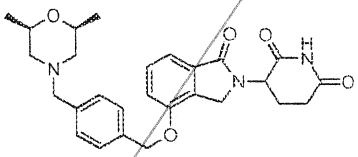
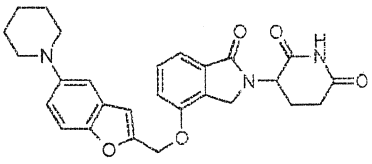
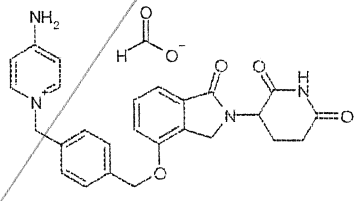
4. The compound of claim 1, wherein Y is heteroaryl, and R^3 is -$(CH_2)_n$-heterocycle.

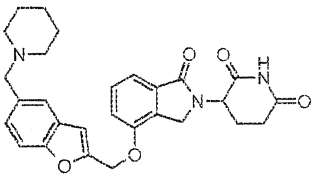
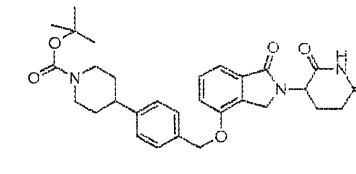
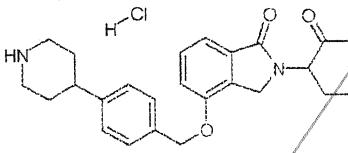
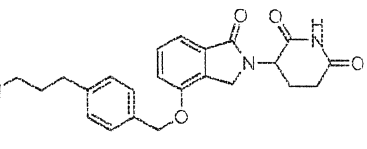
5. The compound of claim 1, wherein Y is a bond.

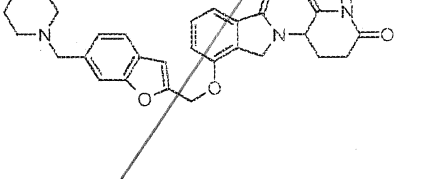
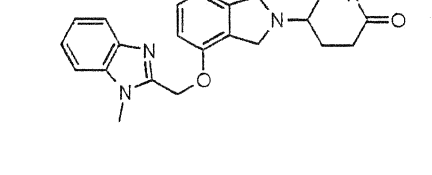
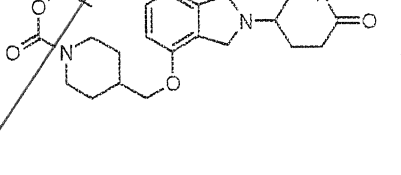
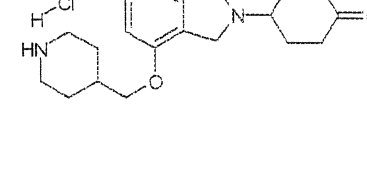
6. The compound of claim 1, wherein Y is a bond, and R^3 is -$(CH_2)_n$-heterocycle or -$(CH_2)_n$-heteroaryl.

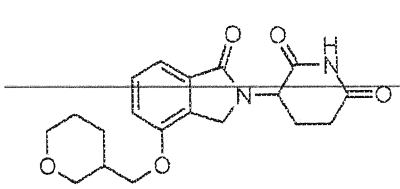
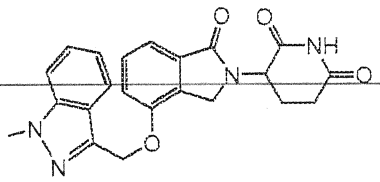
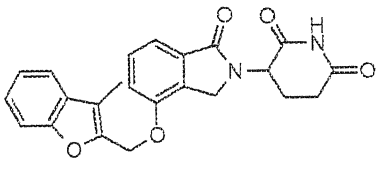
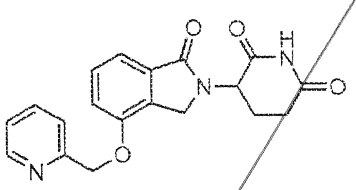
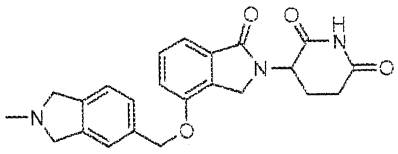
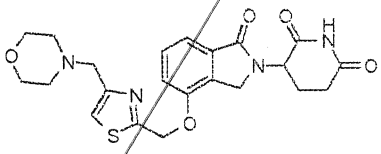
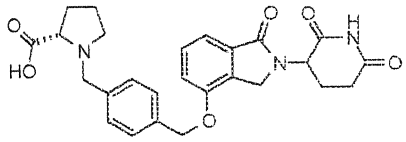
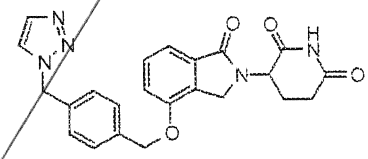
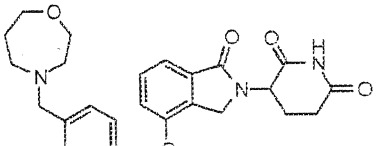
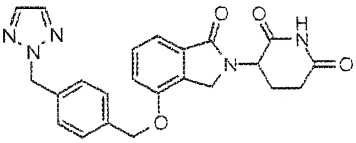
7. The compound of claim 1, which is:

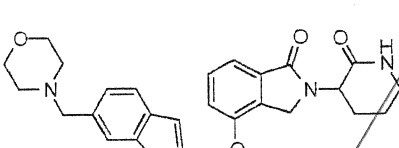
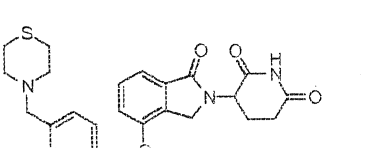











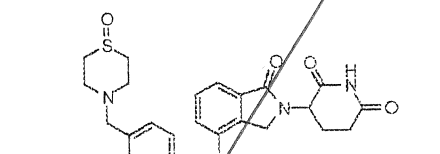
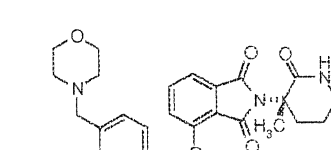









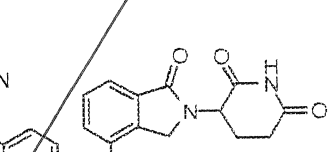
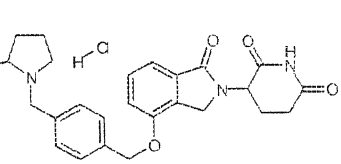





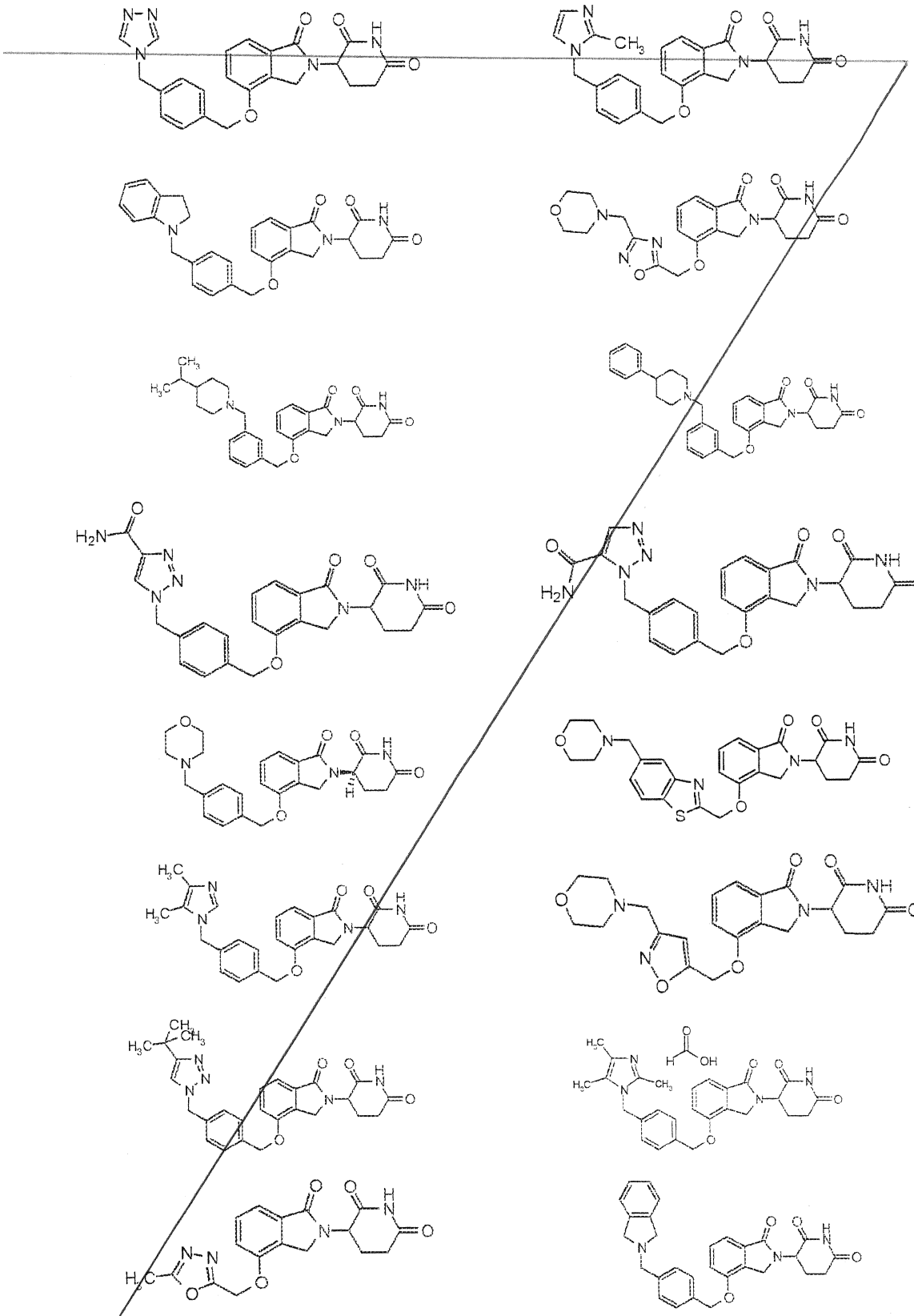











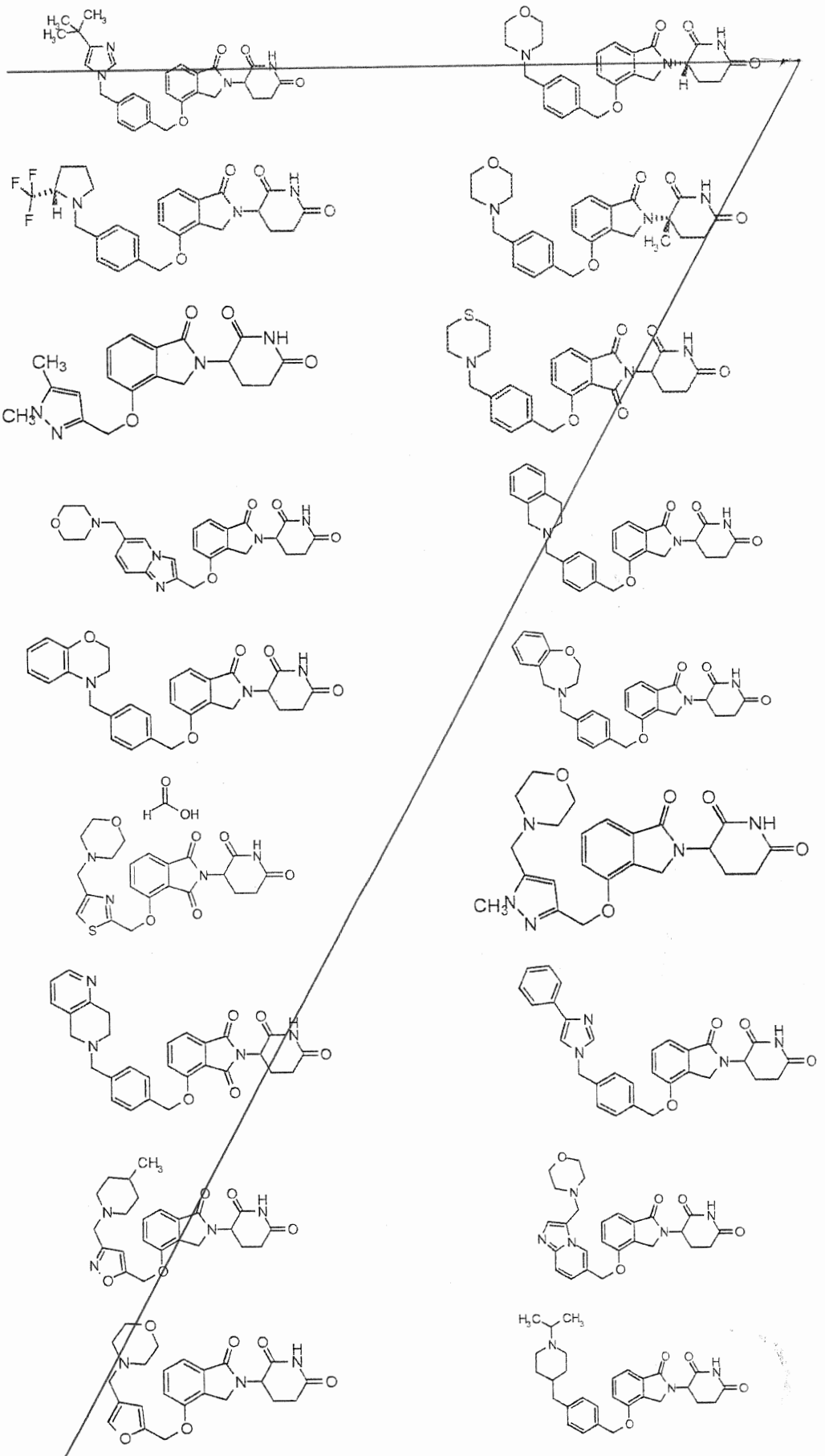



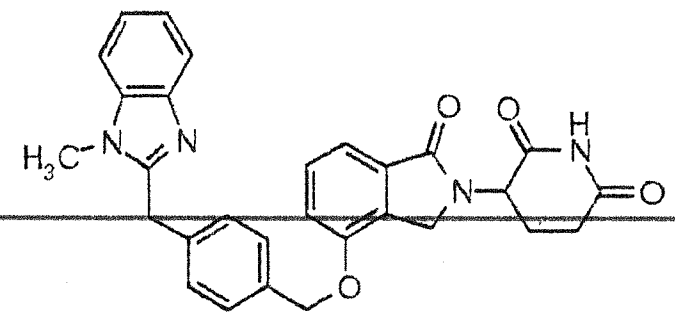



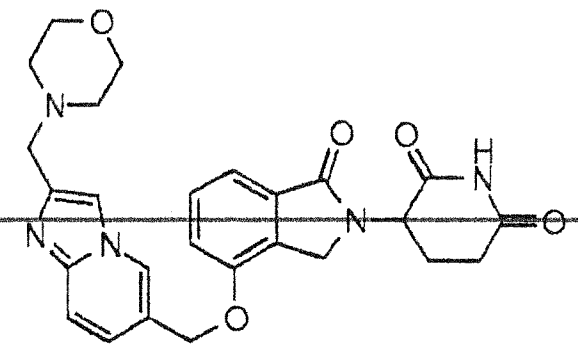



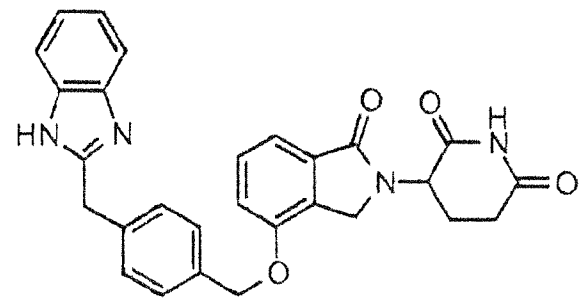


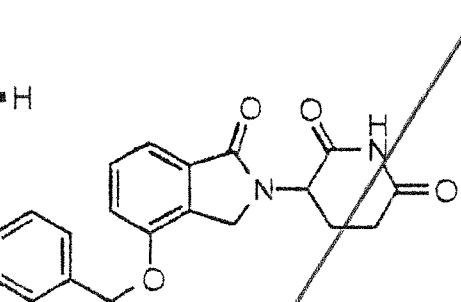


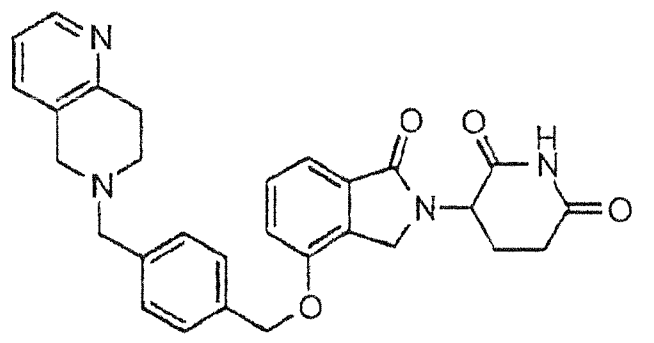


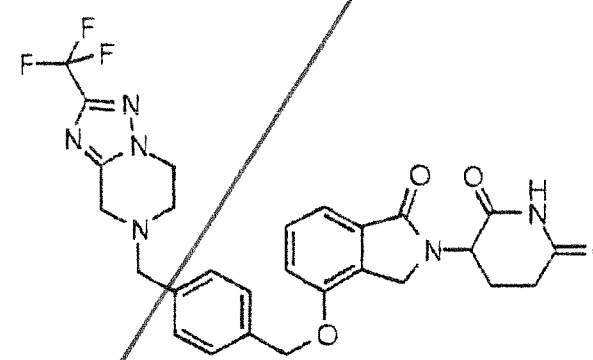


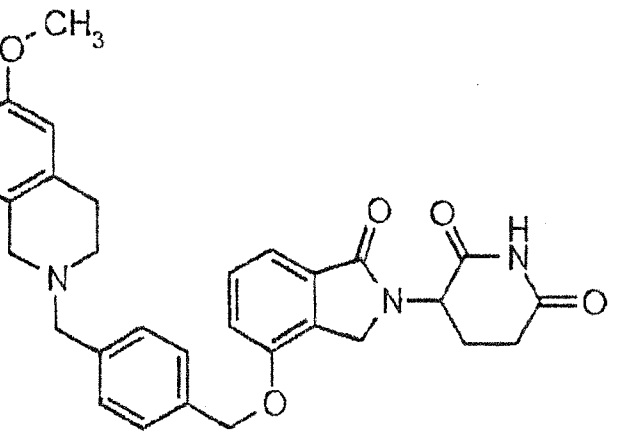


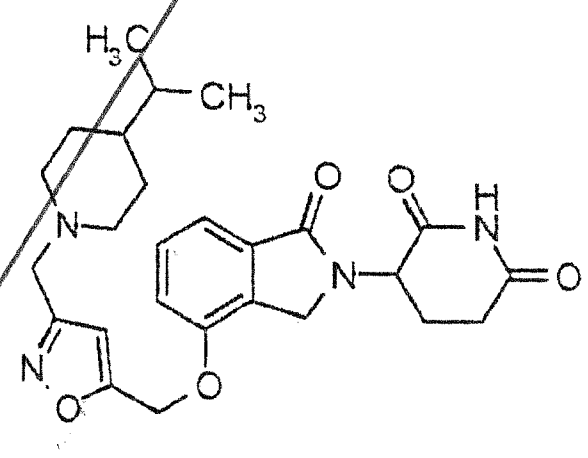


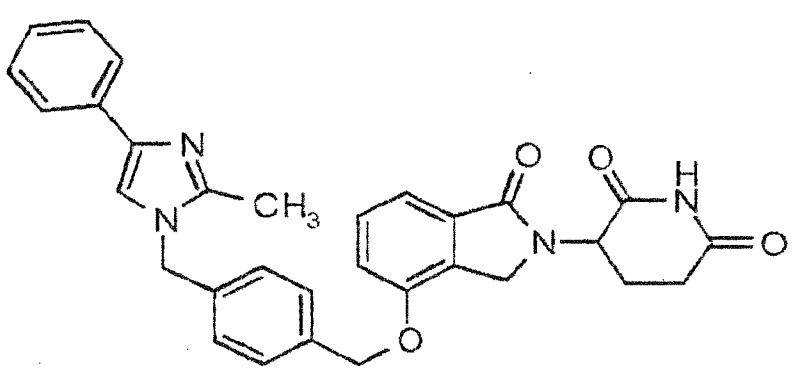


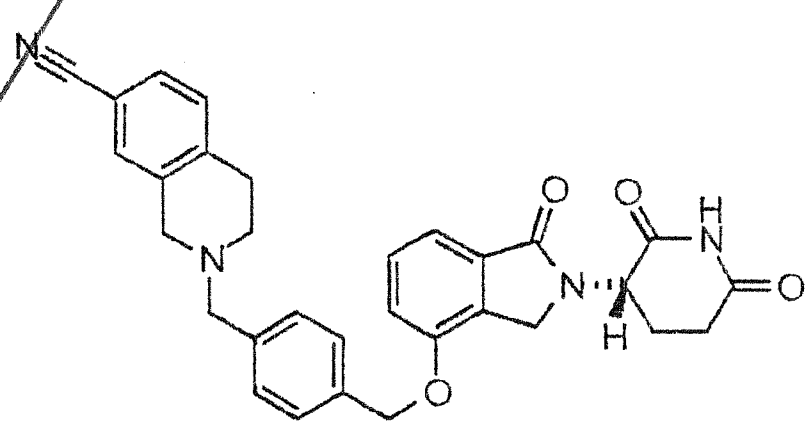


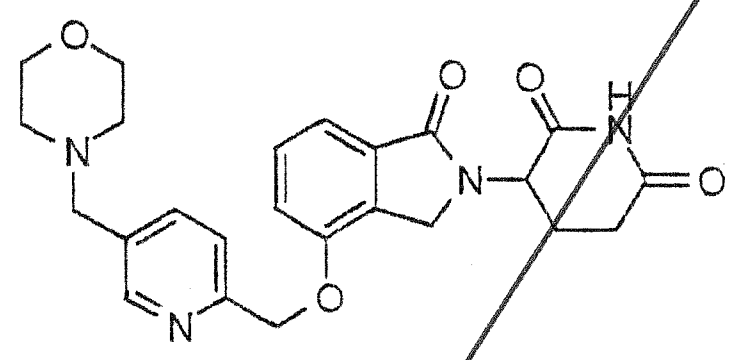


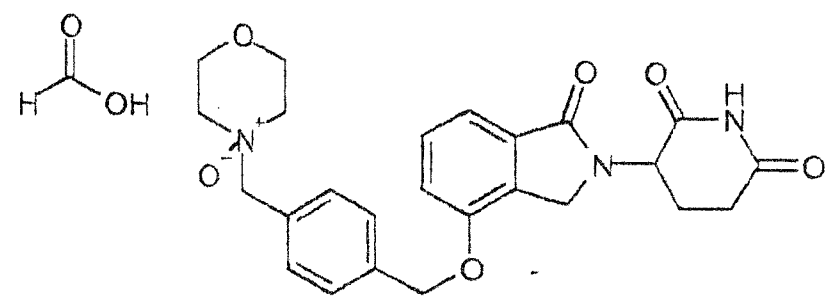


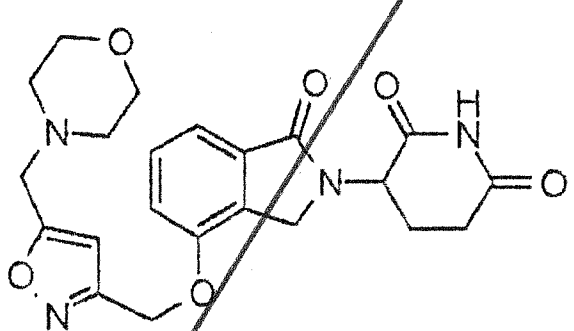


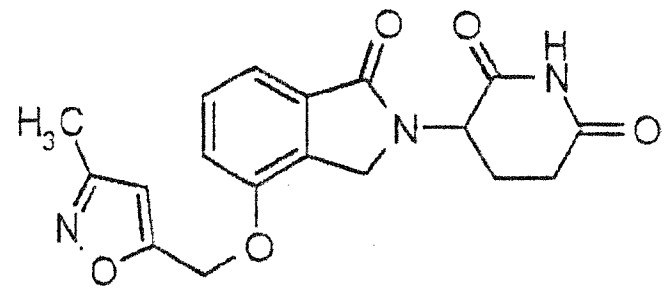


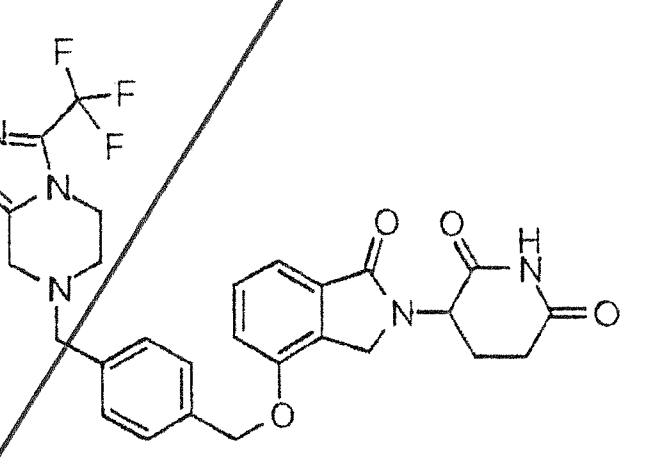


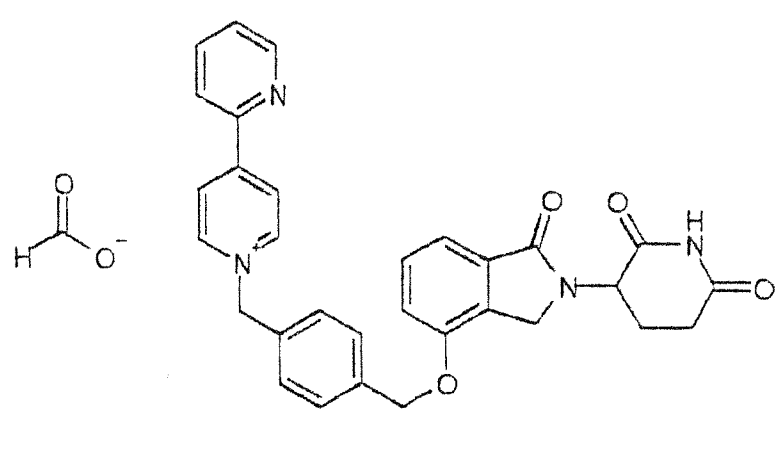


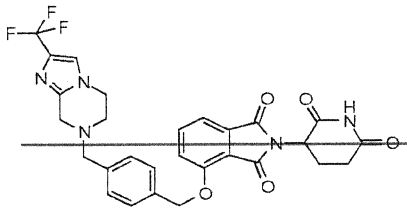
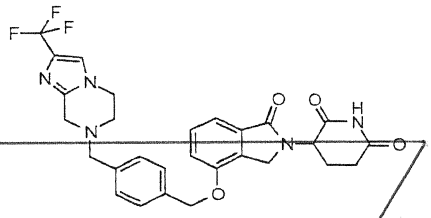
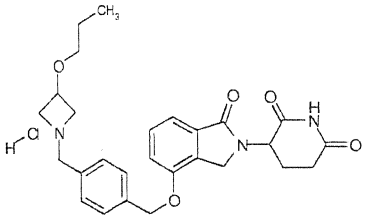
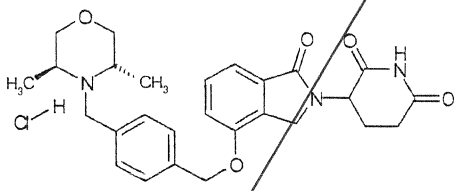
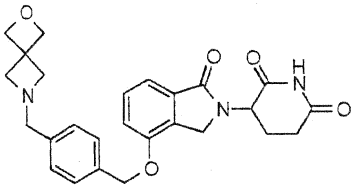
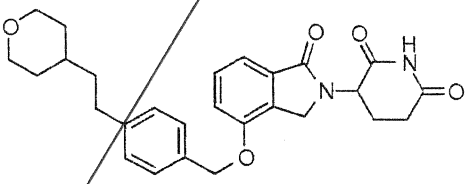
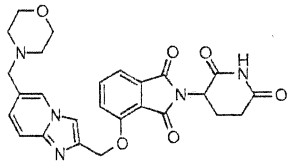
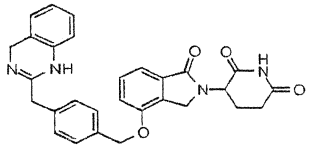
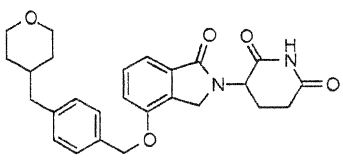
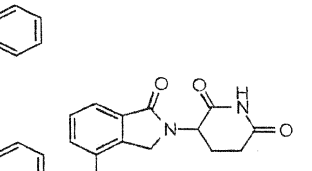
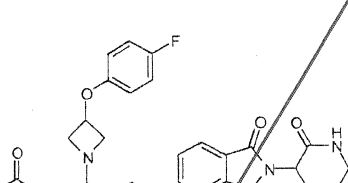


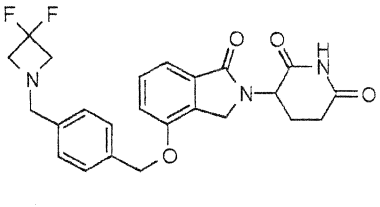
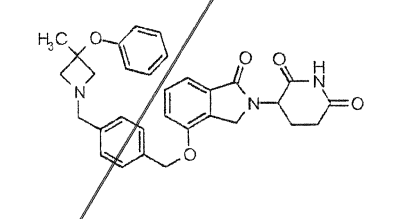
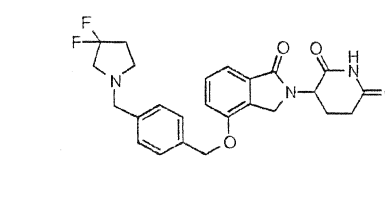
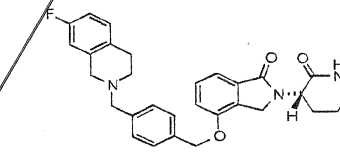
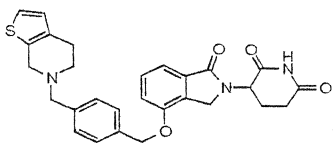


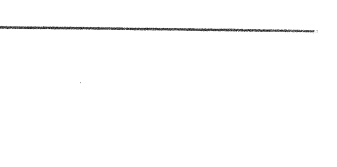


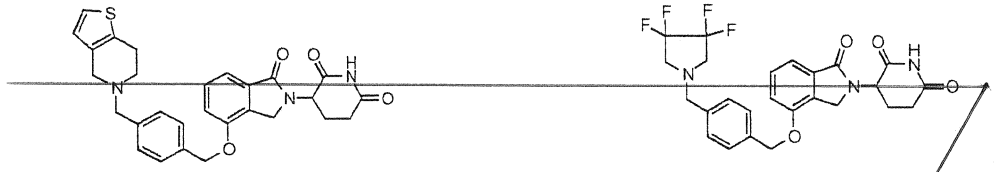


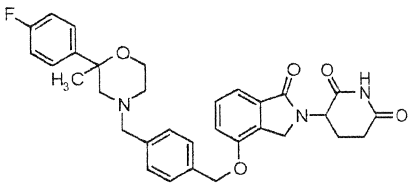
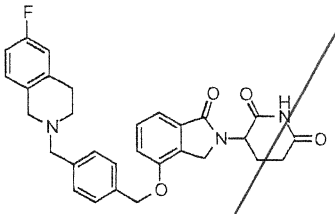
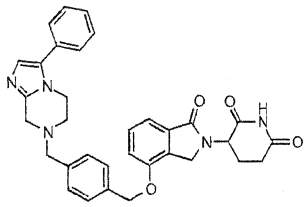
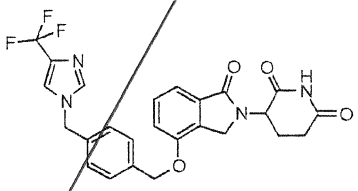
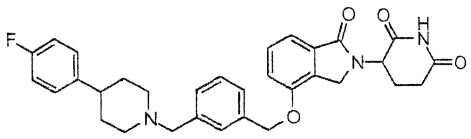
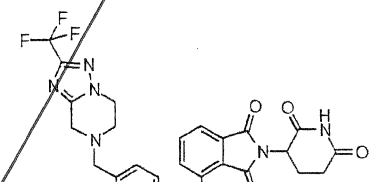


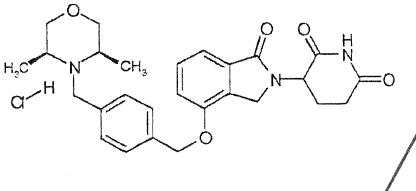
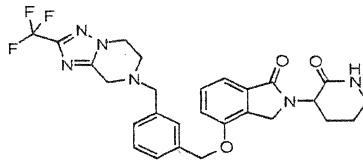












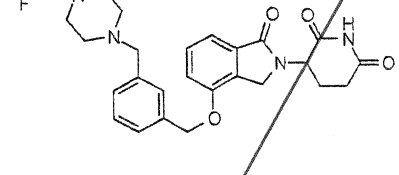






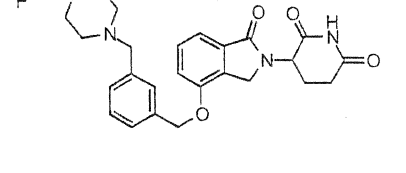
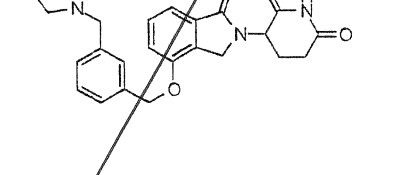
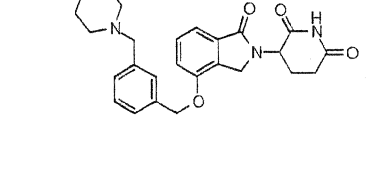


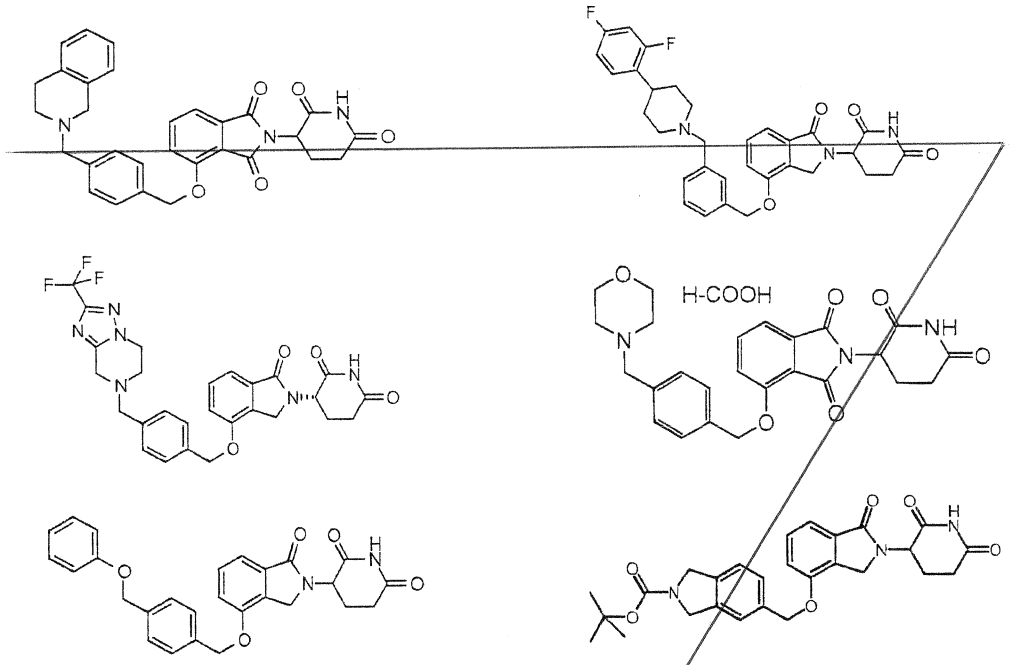


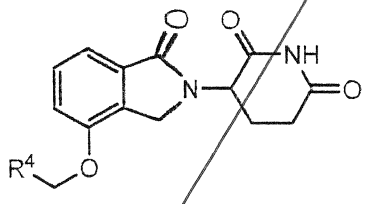


or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

8. A compound of formula (II):



(II)

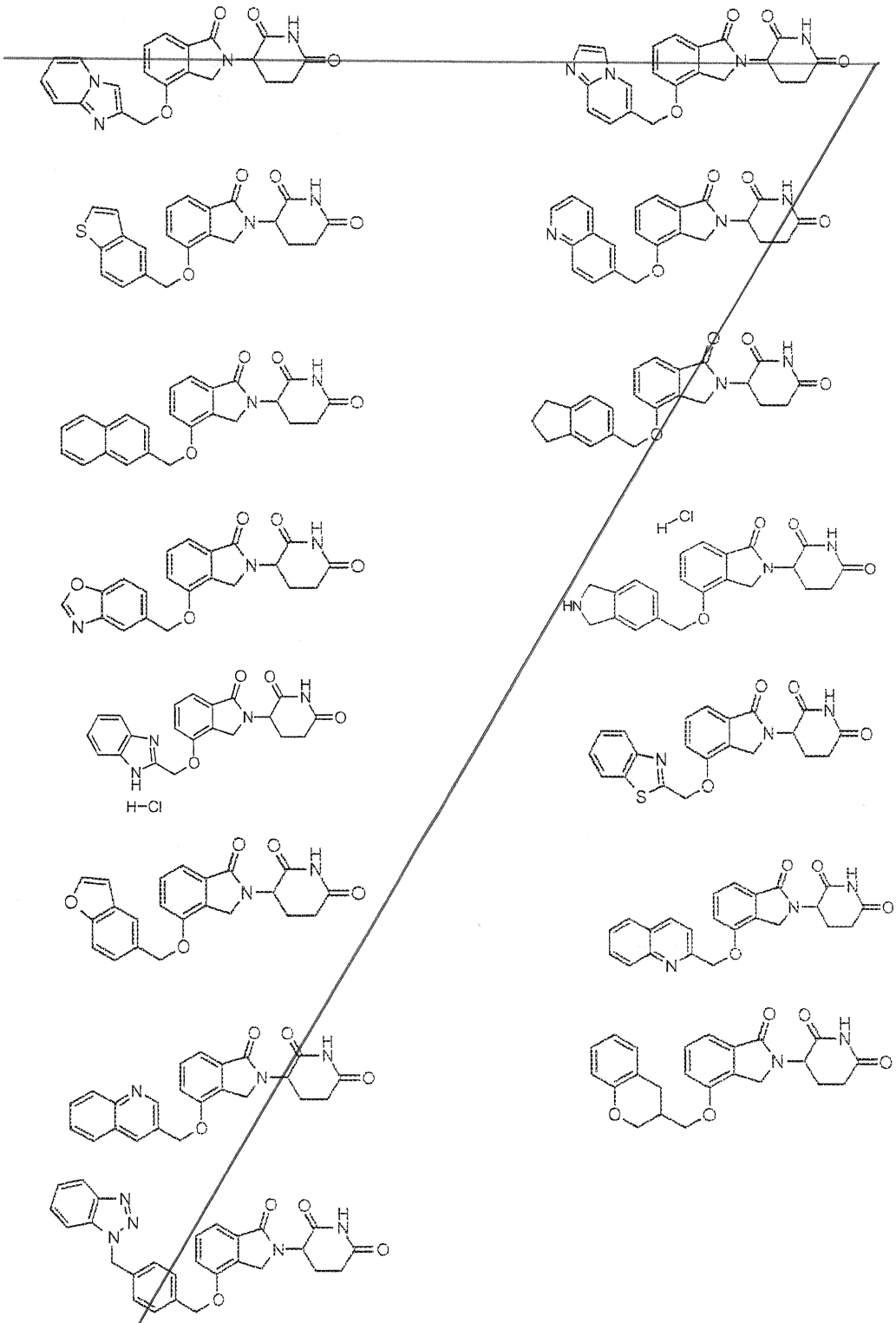
or a pharmaceutically acceptable salt, solvate or stereoisomer thereof, wherein:

R^4 is unsubstituted 9 to 10 membered bicyclic ring is benzothiazole, quinoline, isoquinoline, naphthalene, 2,3-dihydro-1H-indene, benzo[d][1,2,3]triazole, imidazo[1,2-a]pyridine, benzofuran, 2,3-dihydrobenzofuran, benzothiophene, benzo[d]oxazole isoindoline or chroman;

with the proviso that if the bicyclic ring is benzofuran or benzothiophene, then the ring is not connected to the isoindole ring through the 2-position.

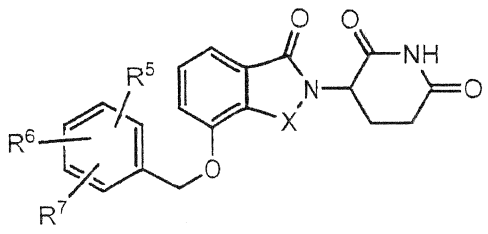
9. The compound of claim 8, which is:





or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

10. A compound of formula (III):



(III)

or a pharmaceutically acceptable salt, solvate or stereoisomer thereof, wherein:

X is CH_2 or C=O;

R^5, R^6 and R^7 are each independently hydrogen, halogen, nitro, carbamoyl, amino, $-SO_2R^8$, $-CONR^9R^{10}$, $-(C_1-C_6)$alkyl or $-(C_1-C_6)$alkoxy, said alkyl or alkoxy may be optionally substituted with one or more halogen, amino, hydroxyl, or NR^9R^{10};

R^8 is: (C_1-C_6)alkyl, optionally substituted with (C_1-C_6)alkyl or (C_6-C_{10})aryl; amino, optionally substituted with (C_1-C_6)alkyl or (C_6-C_{10})aryl; or 6 to 10 membered heterocycle, optionally substituted with (C_1-C_6)alkyl or (C_6-C_{10})aryl;

R^9 and R^{10} are each independently hydrogen, 6 to 10 membered aryl, $-COO-(C_1-C_6)$alkyl, $-(C_0-C_6)$alkyl-CHO, $-(C_0-C_6)$alkyl-COOH, $-(C_0-C_6)$alkyl-$NR^{9'}R^{10'}$, $-(C_0-C_6)$alkyl-(5 to 10 membered heterocycle), $-(C_1-C_6)$alkyl-OH, $-(C_1-C_6)$alkyl-O-(C_1-C_6)alkyl, (C_1-C_6)alkyl, or (C_3-C_6)cycloalkyl; or

R^9 and R^{10} together may form an optionally substituted 5 to 6 membered ring containing one or more heteroatoms; and

$R^{9'}$ and $R^{10'}$ are each independently hydrogen or (C_1-C_6)alkyl;

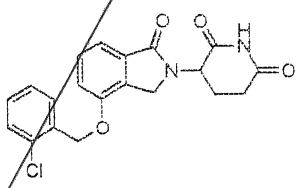
with the proviso that all of R^5-R^7 cannot be hydrogen; and

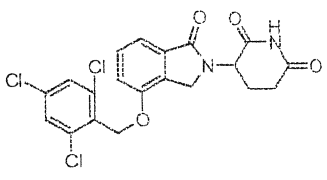
with the proviso that if one of R^5-R^7 is hydrogen and the remaining two of R^5-R^7 are both chloride, then the two chloride atoms cannot be on 3 and 4 position of the phenyl ring.

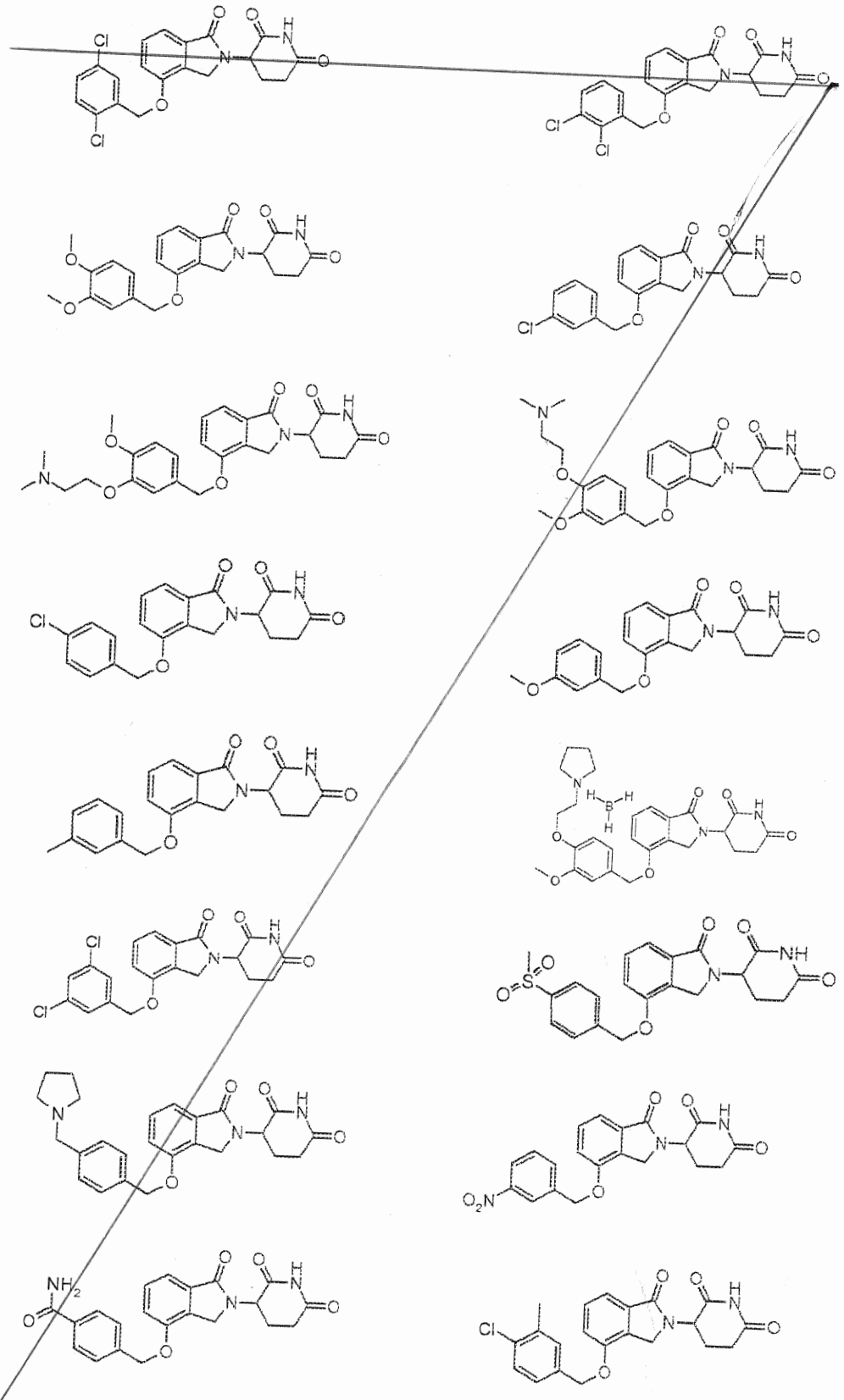
11. The compound of claim 10, wherein one of R^5-R^7 is hydrogen, and the remaining two of R^5-R^7 are each independently halogen, (C_1-C_6)alkoxy or (C_1-C_6)alkyl.

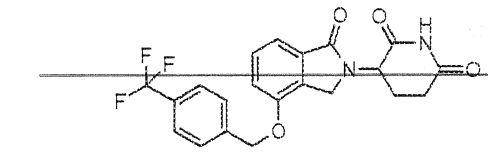
12. The compound of claim 10, wherein two of R^5-R^7 are hydrogen and the remaining one of R^5-R^7 is halogen, (C_1-C_6)alkoxy or (C_1-C_6)alkyl.

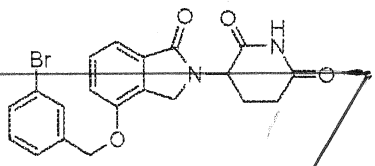
13. The compound of claim 10, which is:

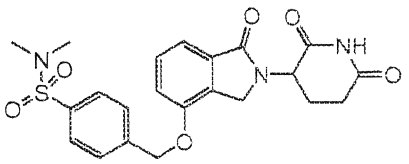


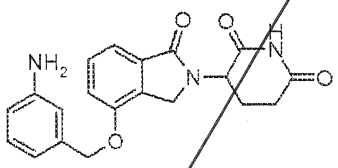


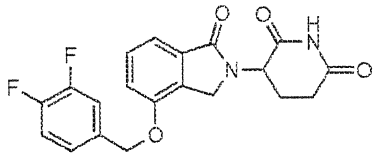


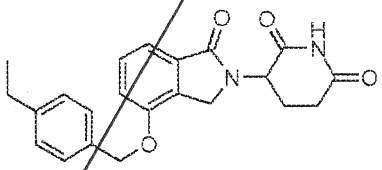


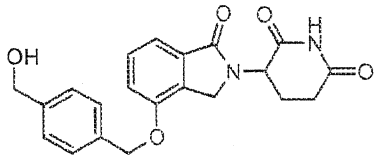


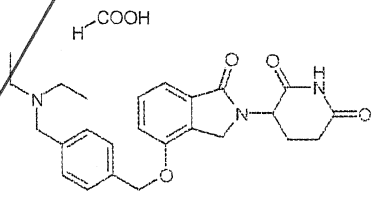


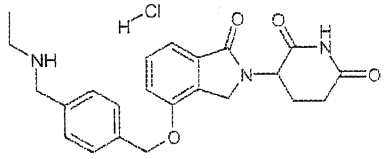


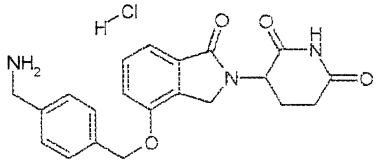


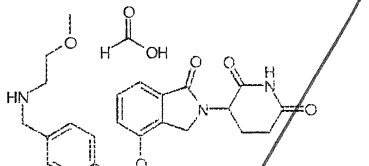


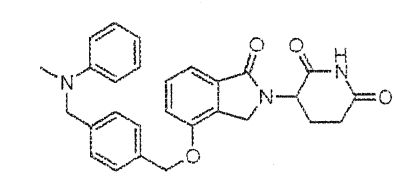


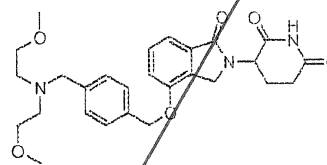


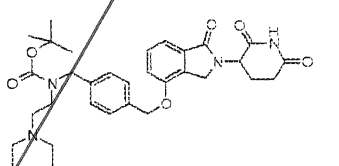


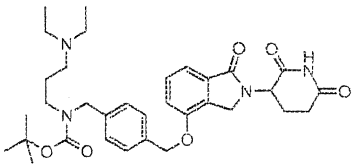


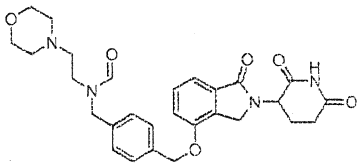


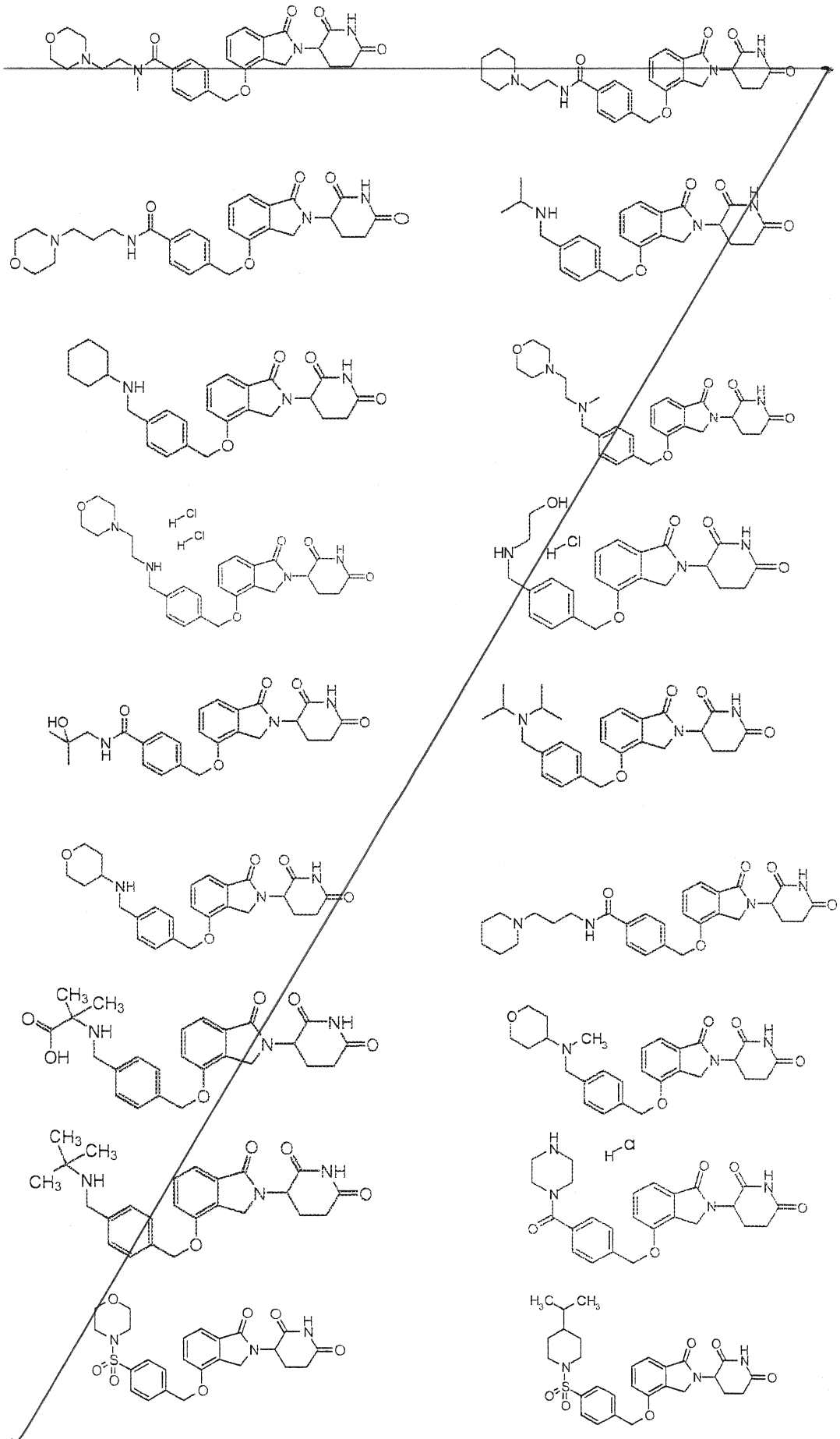


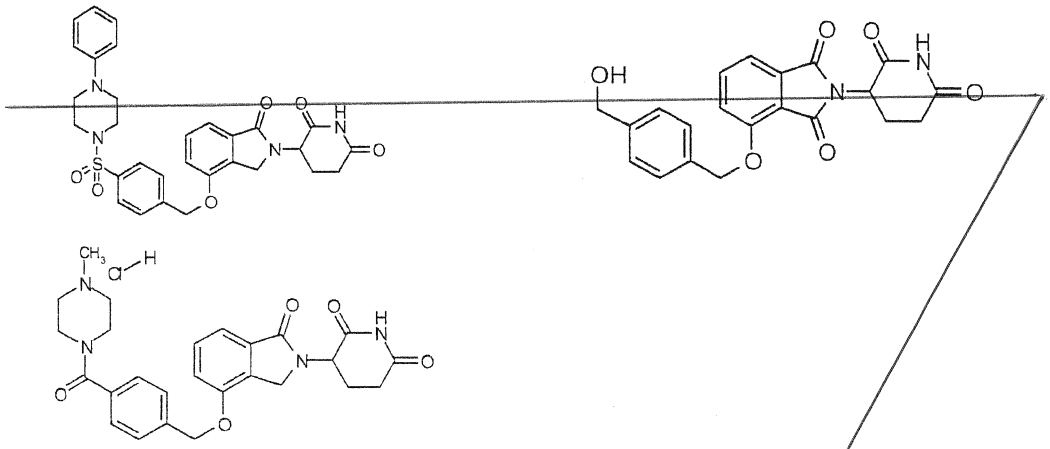






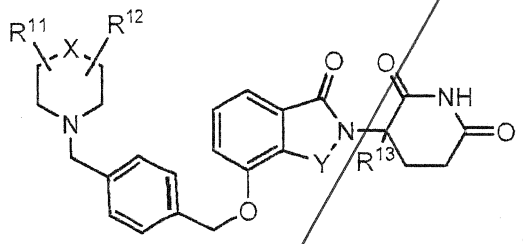






or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

14. A compound of formula (IV):



(IV)

or a pharmaceutically acceptable salt, solvate or stereoisomer thereof, wherein:

X is N or C;

Y is CH_2 or C=O;

R^{11} and R^{12} are each independently hydrogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkyl-(C_3-C_6)cycloalkyl, -(C_1-C_6)alkoxy, -(C_6-C_{10})aryl, -CO(C_1-C_6)alkyl, -CO(C_3-C_6)cycloalkyl, -CO(C_6-C_{10})aryl, -COO(C_1-C_6)alkyl, halogen, hydroxyl, oxo, 3 to 10 membered heterocycle, 6 to 10 membered heteroaryl, -NHCO(C_1-C_6)alkyl, -(CH_2)$_n$-phenyl, -SO_2(C_1-C_6)alkyl, -SO_2(C_3-C_6)cycloalkyl, -SO_2(C_6-C_{10})aryl or -$NR^{14}R^{15}$, wherein the alkyl, aryl or heteroaryl portion of each of the groups may be optionally substituted with one or more halogen, hydroxyl or -(C_1-C_6)alkoxy;

R^{13} is hydrogen or -(C_1-C_6)alkyl;

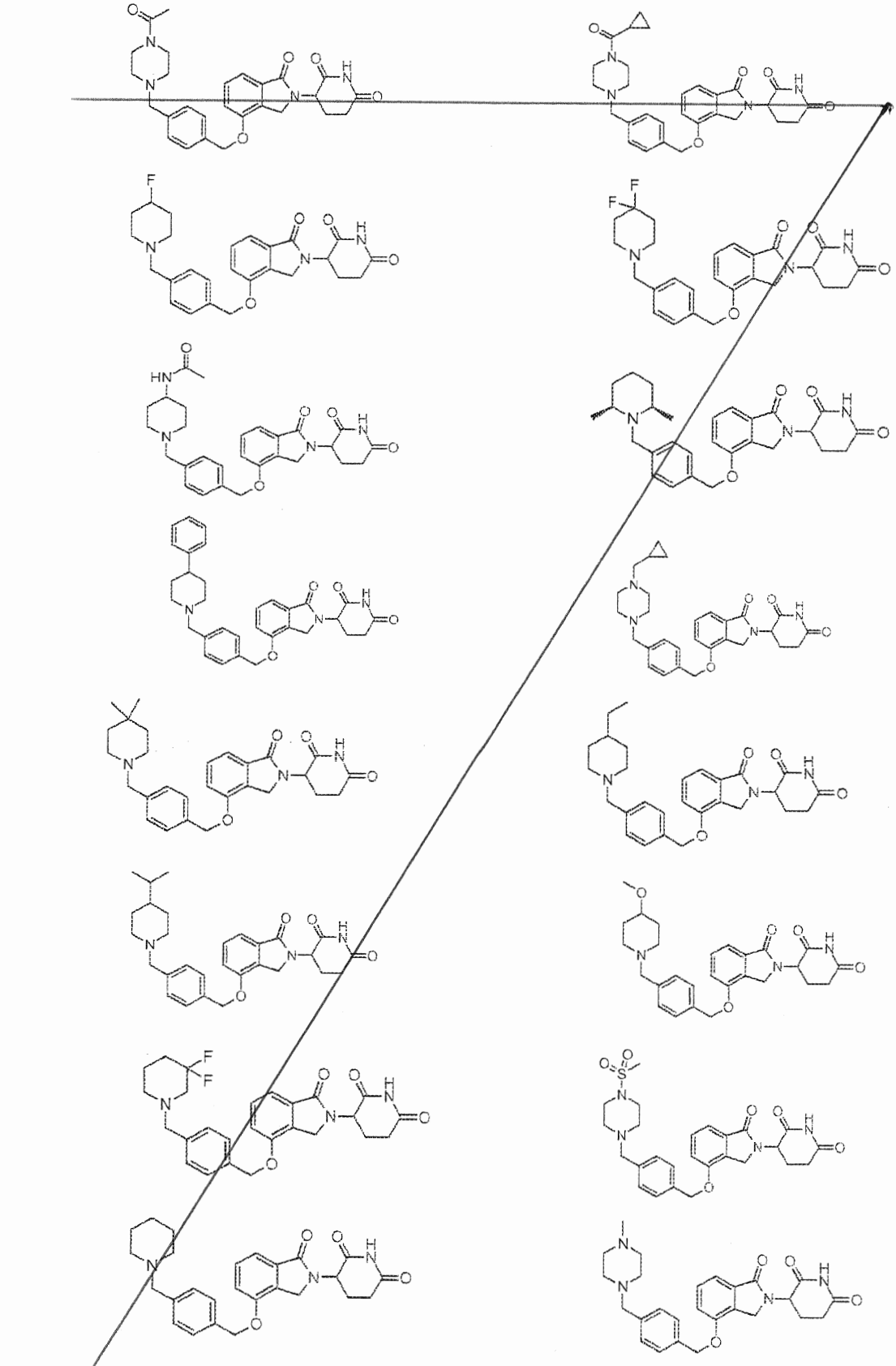
R^{14} and R^{15} are each independently hydrogen or -(C_1-C_6)alkyl; and

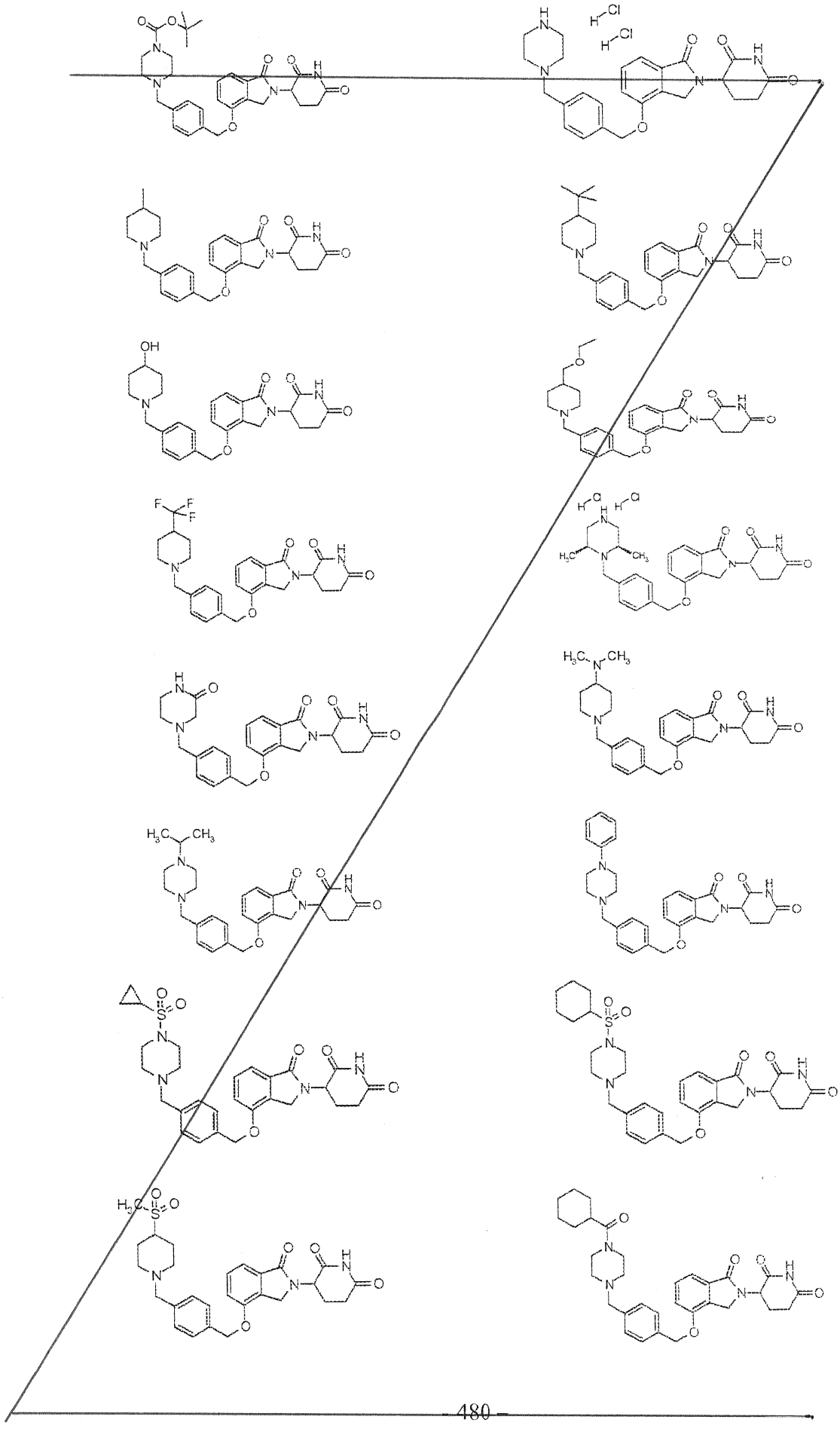
n is 0, 1, 2 or 3.

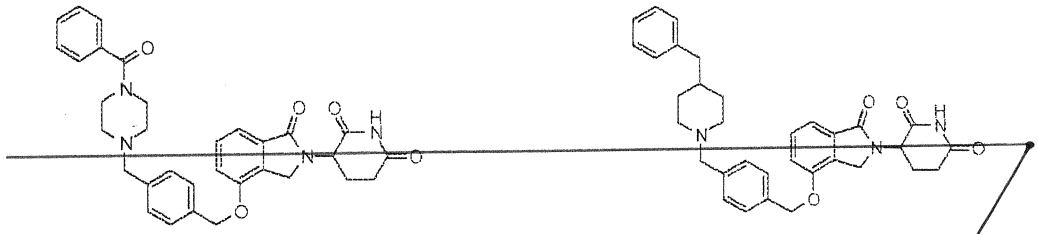
15. The compound of claim 14, wherein X is N.

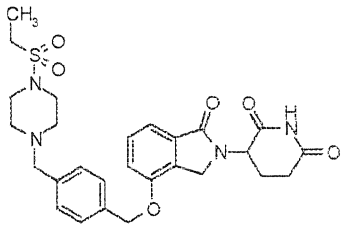
16. The compound of claim 14, wherein Y is CH_2.

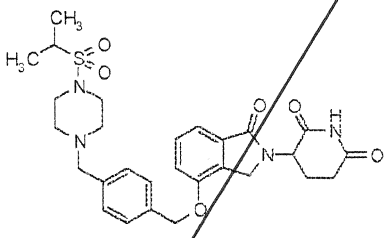
17. The compound of claim 14, which is:

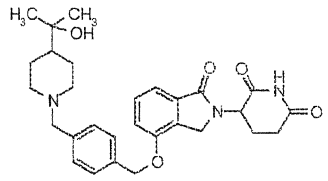


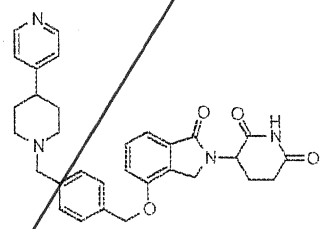


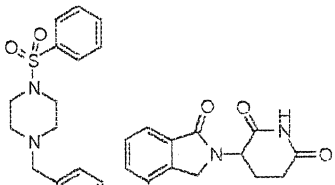


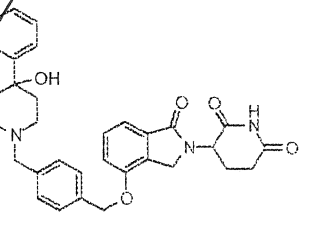


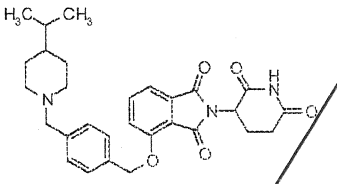


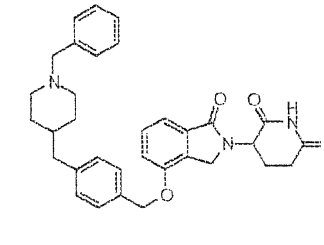


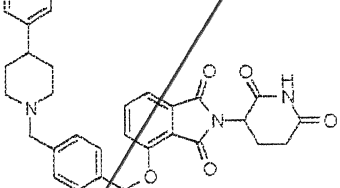


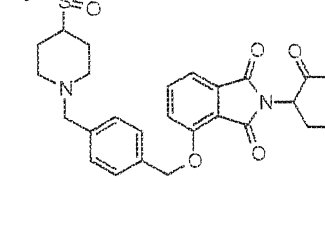




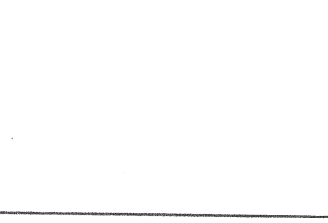


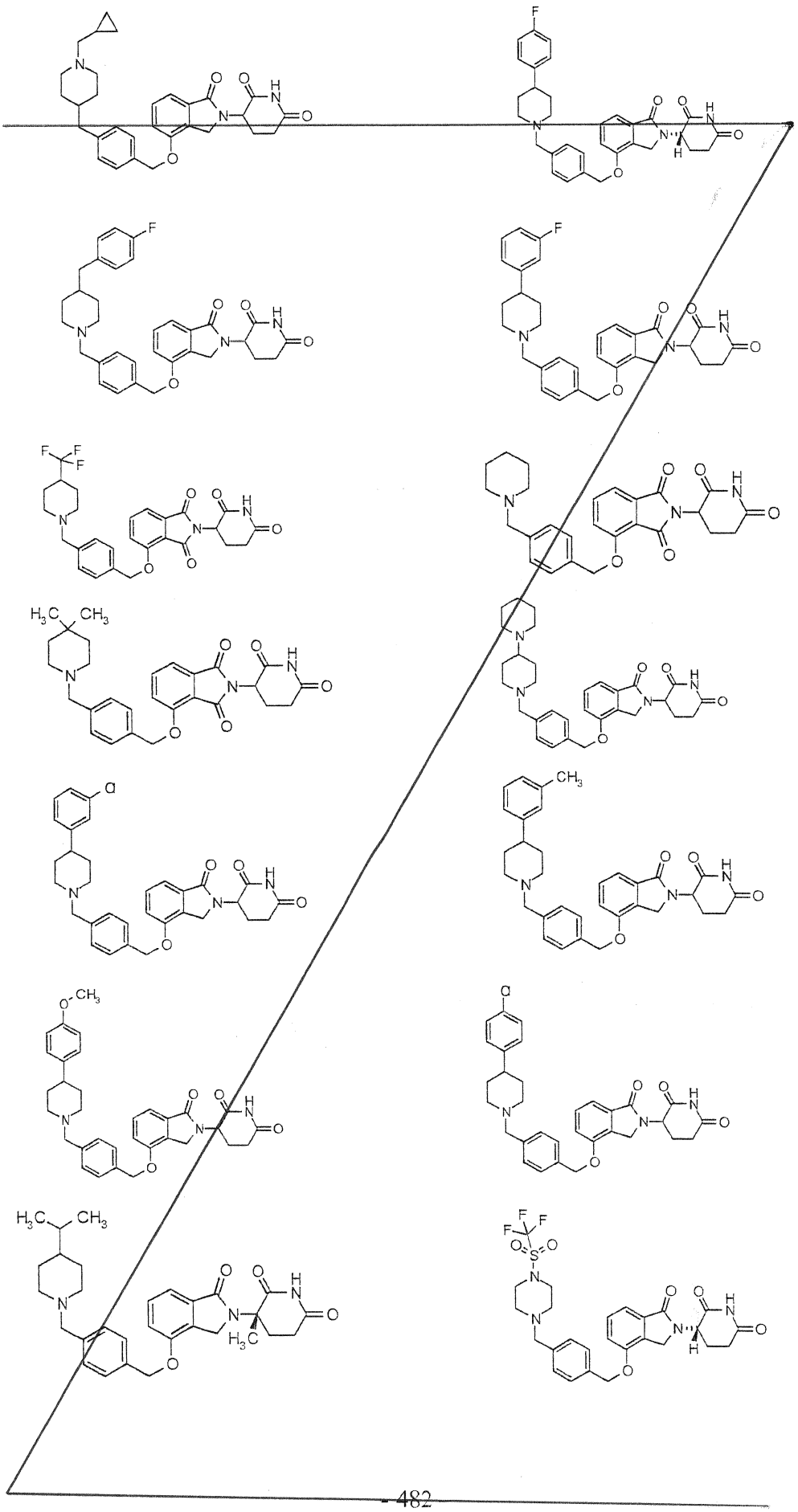


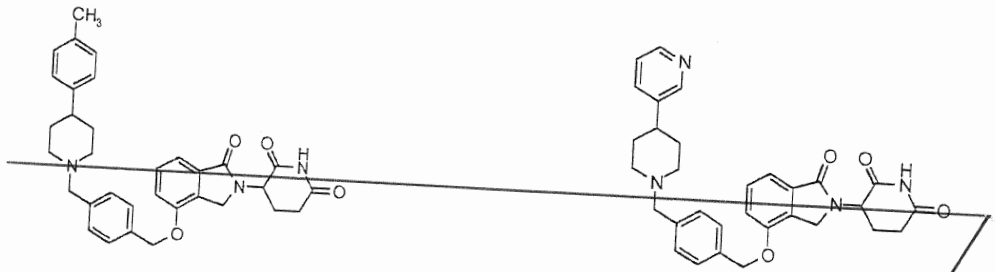


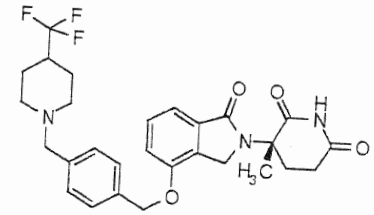


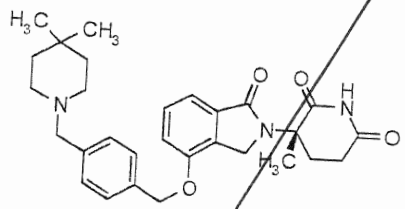


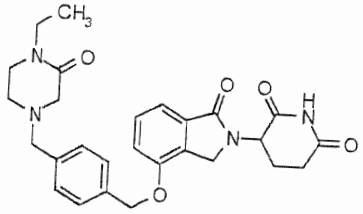


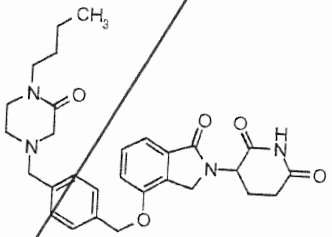


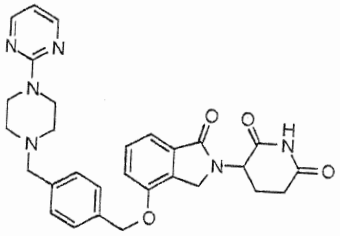


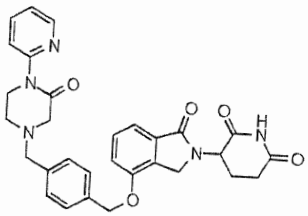


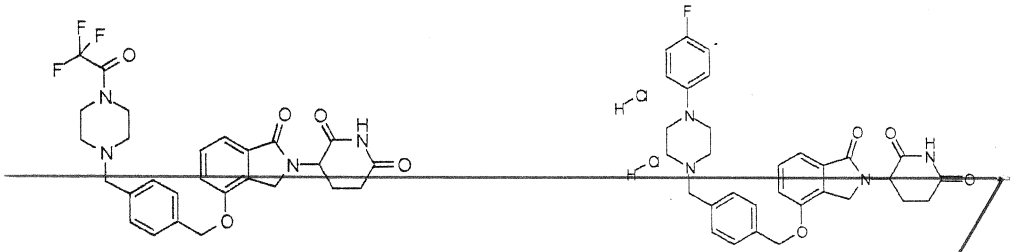


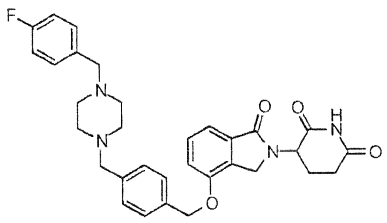
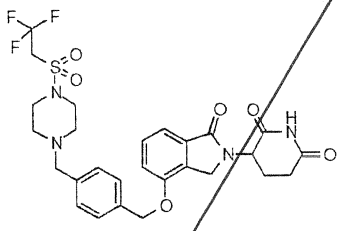
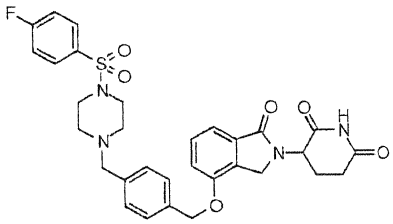
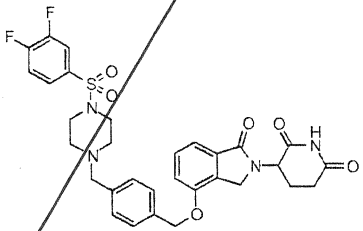
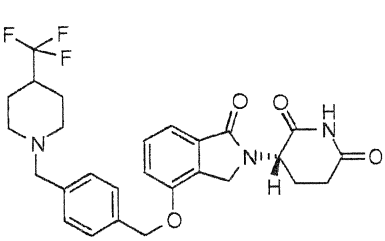
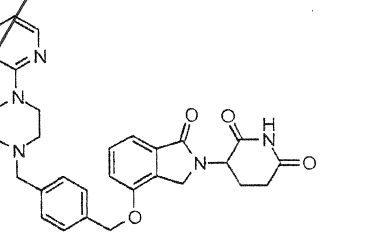
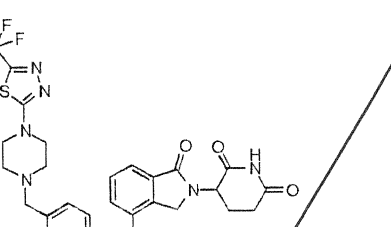
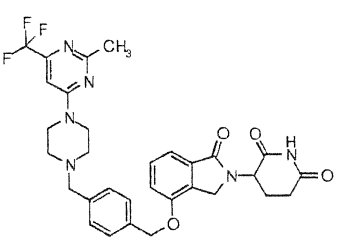
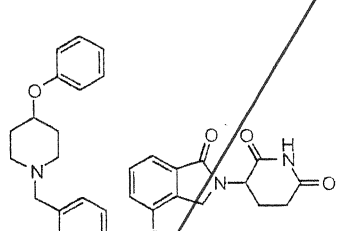
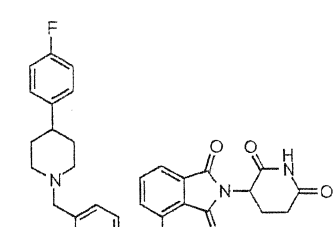
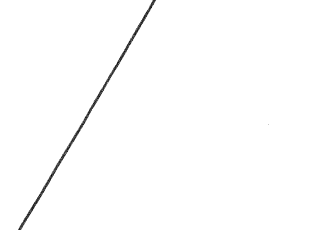


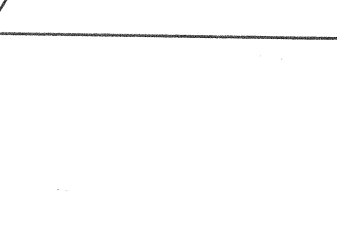


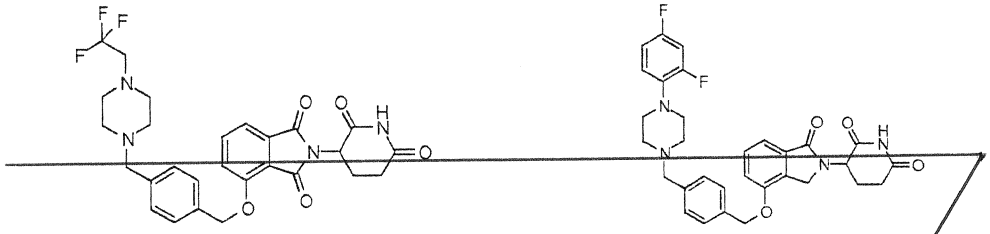
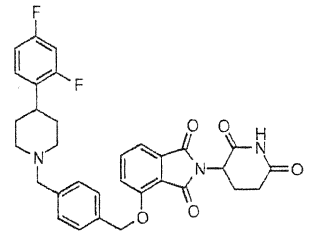
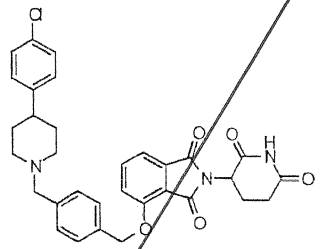
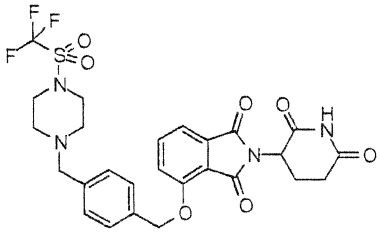
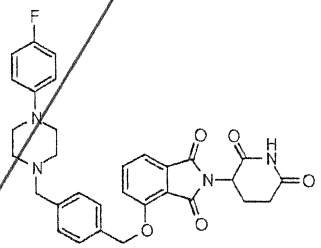






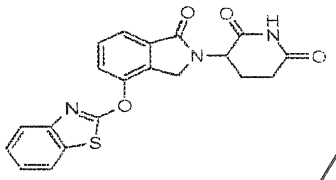
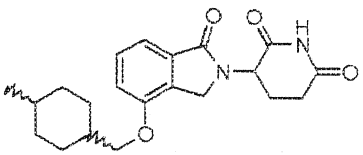
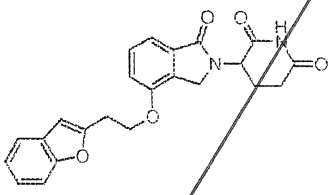
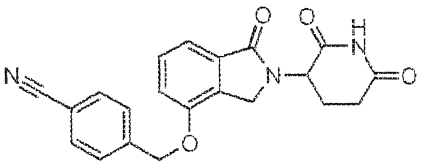
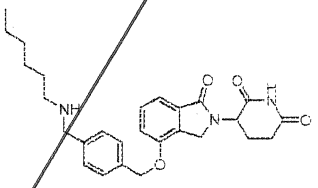
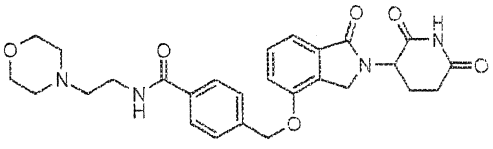
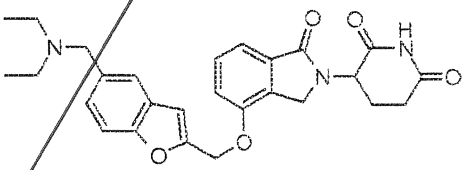
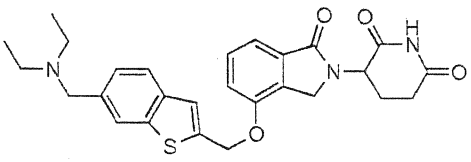












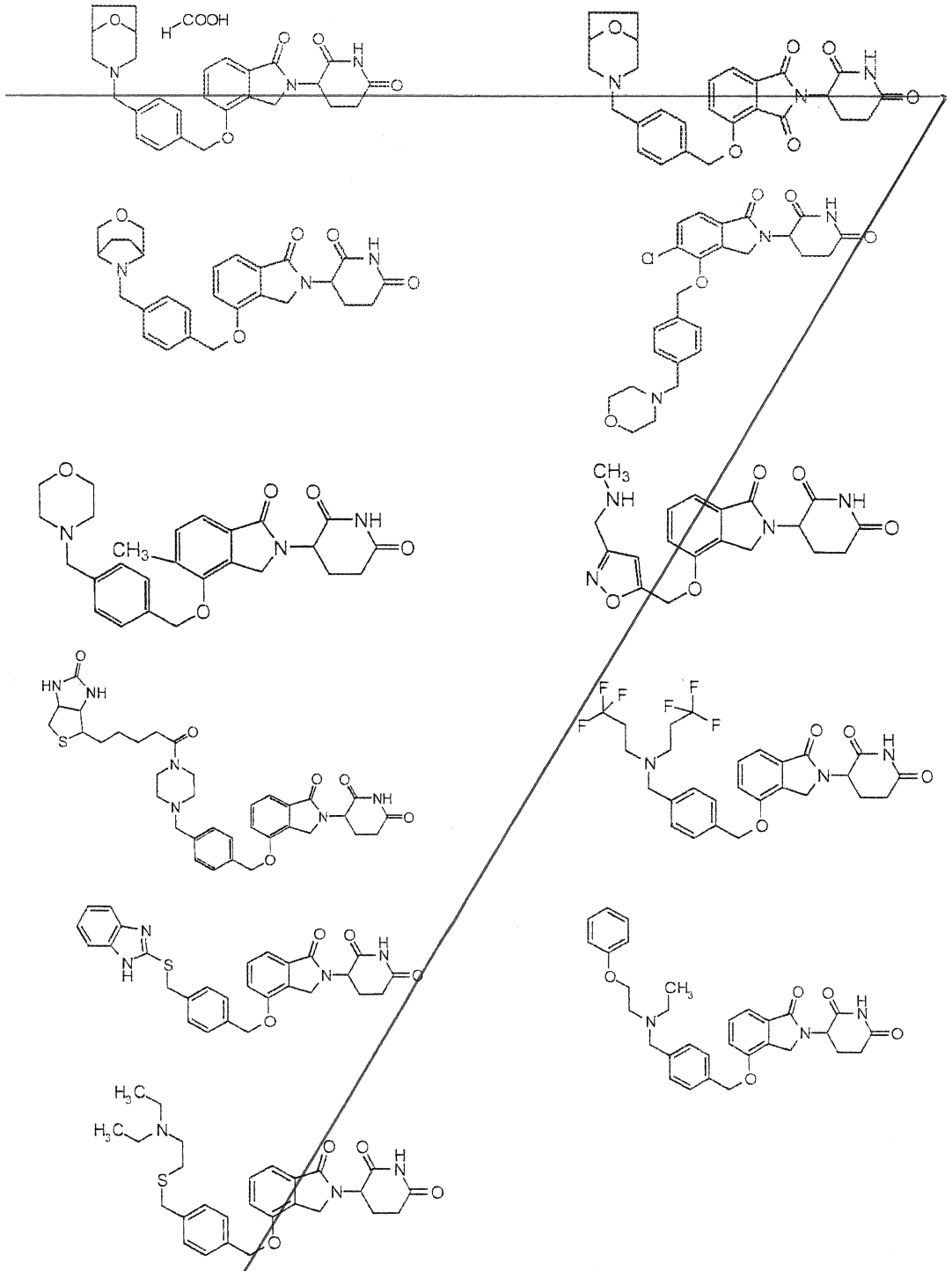


or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

18. A compound, which is:



or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

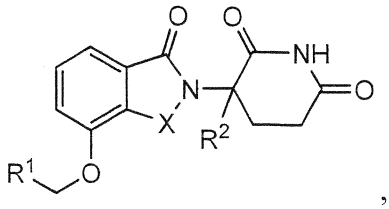
19. A pharmaceutical composition comprising a compound of any one of claims 1-18, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

20. A method of treating, managing or preventing a disease or disorder comprising administering to a patient a compound of any one of claims 1-18, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein the disease or disorder is cancer, a disorder associated with angiogenesis, pain, macular degeneration or a

related syndrome, a skin disease, a pulmonary disorder, an asbestos-related disorder, a parasitic disease, an immunodeficiency disorder, a CNS disorder, CNS injury, atherosclerosis or a related disorder, dysfunctional sleep or a related disorder, an infectious disease, hemoglobinopathy or a related disorder, or a TNFα related disorder.

What is claimed is:

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt or stereoisomer thereof, for use in treating, managing, or preventing a disease or disorder, wherein the disease or disorder is cancer, a disorder associated with angiogenesis, pain, macular degeneration or a related syndrome, a skin disease, a pulmonary disorder, an asbestos-related disorder, a parasitic disease, an immunodeficiency disorder, a CNS disorder, CNS injury, atherosclerosis or a related disorder, dysfunctional sleep or a related disorder, an infectious disease, hemoglobinopathy or a related disorder, or a TNFα related disorder.

wherein:

X is C=O or CH_2;

R^1 is -Y-R^3;

R^2 is H or (C_1-C_6)alkyl;

Y is: 6 to 10 membered aryl optionally substituted with one or more halogen;

R^3 is: -$(CH_2)_n$-aryl, -O-$(CH_2)_n$-aryl or -$(CH_2)_n$-O-aryl, wherein the aryl is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano; hydroxyl; halogen; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or halogen; -$CONH_2$; or -COO-(C_1-C_6)alkyl, wherein the alkyl may be optionally substituted with one or more halogen; -$(CH_2)_n$-heterocycle, -O-$(CH_2)_n$-heterocycle or -$(CH_2)_n$-O-heterocycle, wherein the heterocycle is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano; hydroxyl; halogen; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or

halogen; $-CONH_2$; or $-COO-(C_1-C_6)$alkyl, wherein the alkyl may be optionally substituted with one or more halogen; or

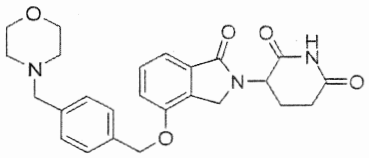
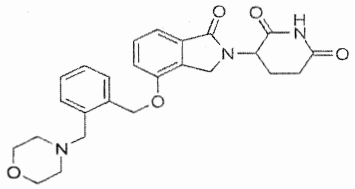
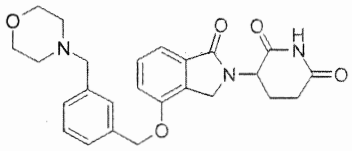
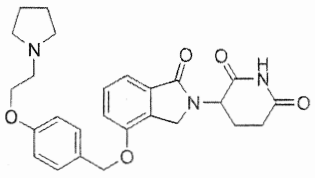
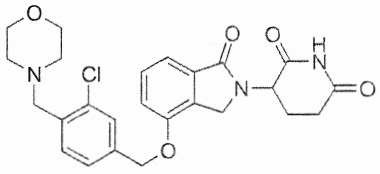
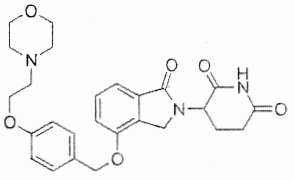
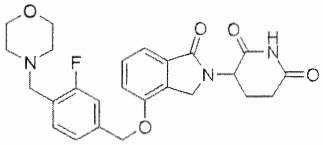
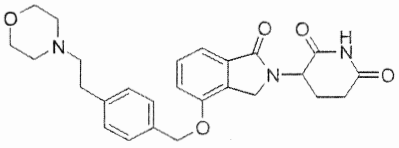
$-(CH_2)_n$-heteroaryl, $-O-(CH_2)_n$-heteroaryl or $-(CH_2)_n-O$-heteroaryl, wherein the heteroaryl is optionally substituted with one or more: (C_1-C_6)alkyl, itself optionally substituted with one or more halogen; (C_1-C_6)alkoxy, itself substituted with one or more halogen; oxo; amino; carboxyl; cyano; hydroxyl; halogen; 6 to 10 membered aryl or heteroaryl, optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy or halogen; $-CONH_2$; or $-COO-(C_1-C_6)$alkyl, wherein the alkyl may be optionally substituted with one or more halogen; and

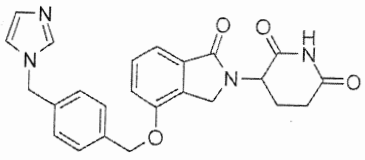
n is 0, 1, 2 or 3.

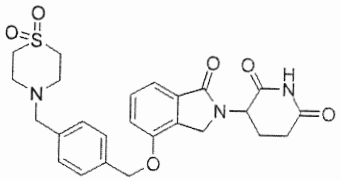
2. The use of claim 1, wherein X is CH_2.

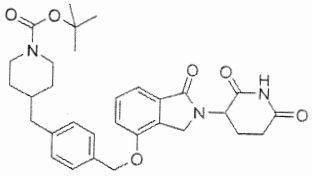
3. The use of claim 1, wherein Y is phenyl, and R^3 is $-(CH_2)_n$-heterocycle.

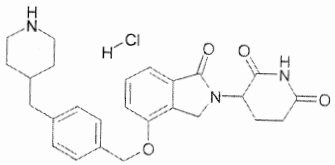
4. The use of claim 1, wherein the compound is:

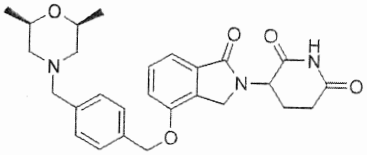









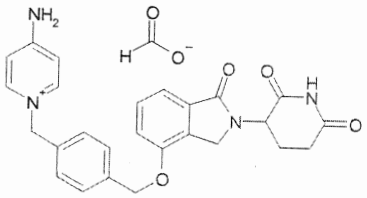


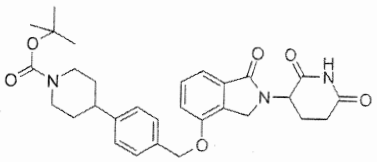


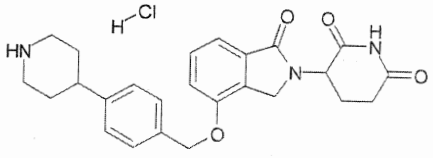


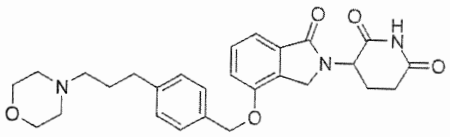


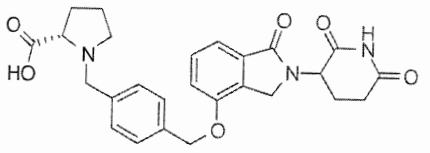


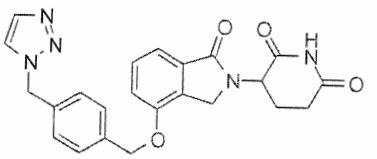


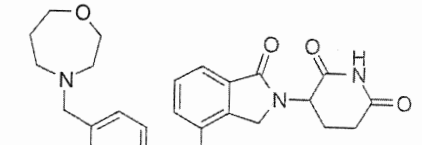


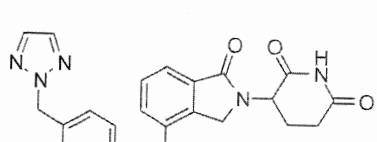


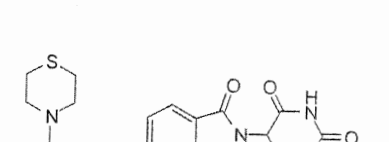


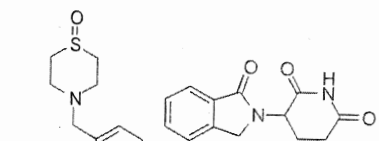


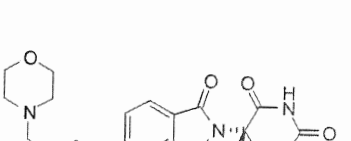




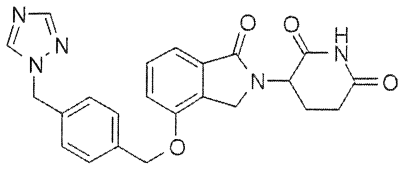


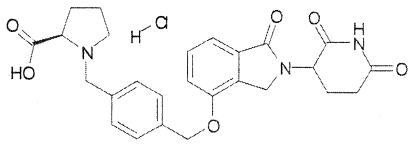


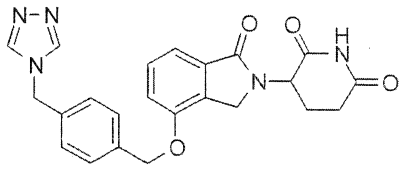


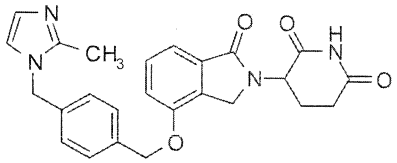


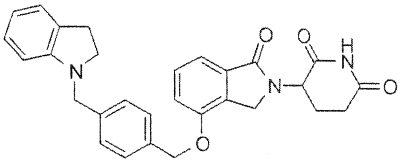


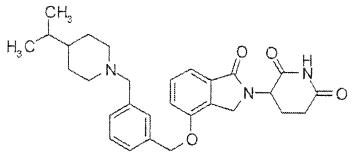


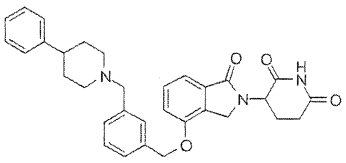


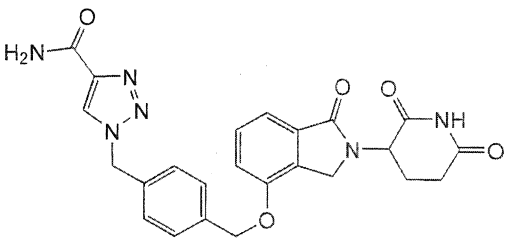


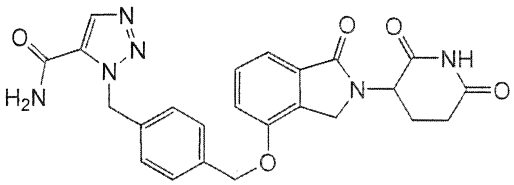


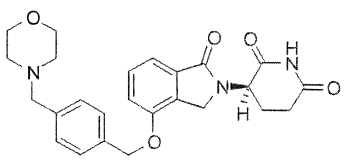


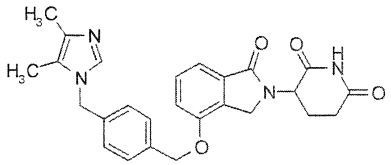


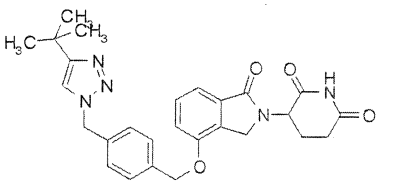


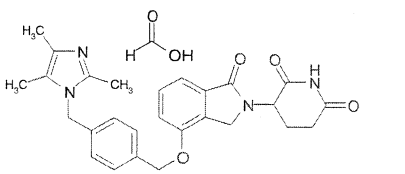


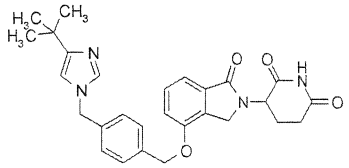


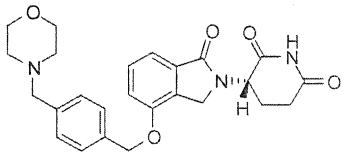


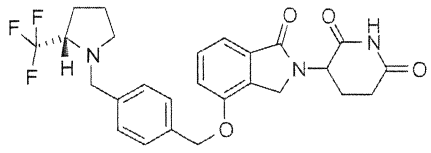


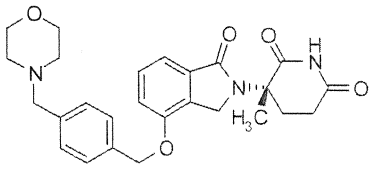


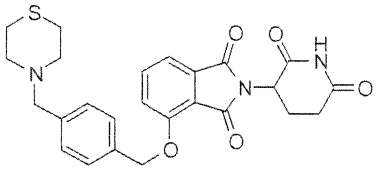


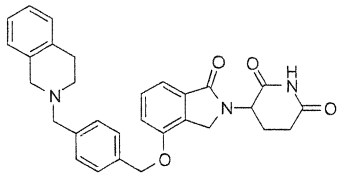


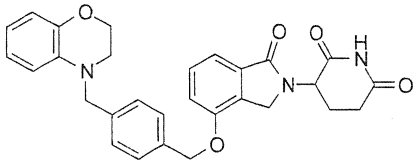


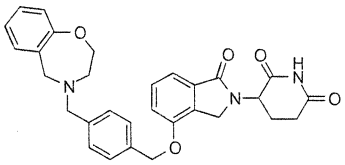


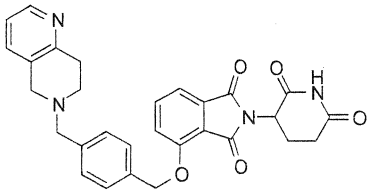


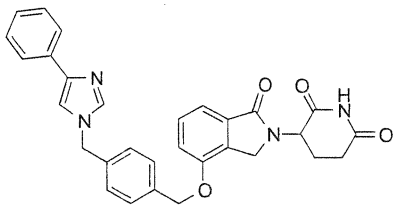


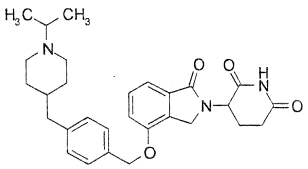


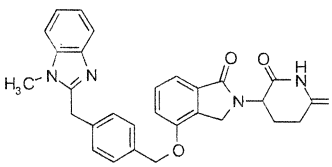


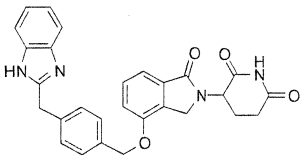


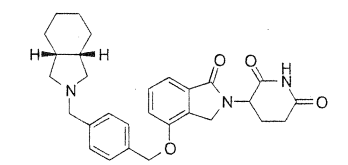


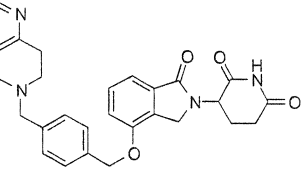


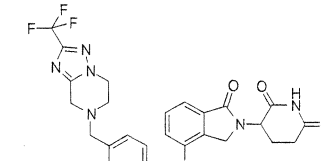




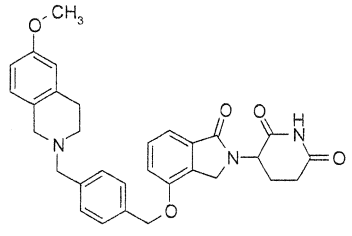


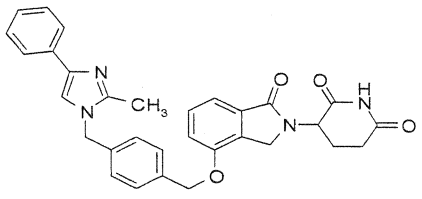


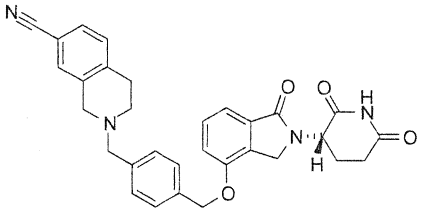


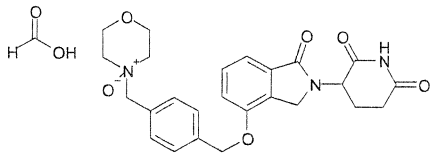


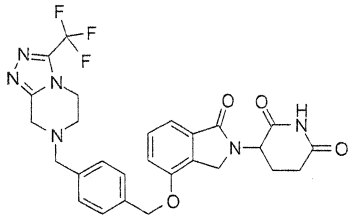


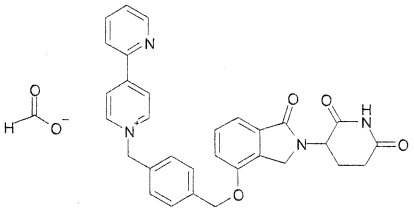


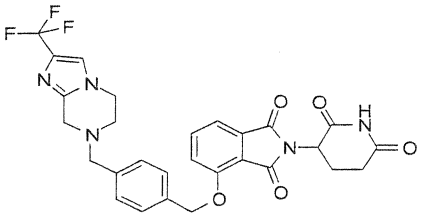


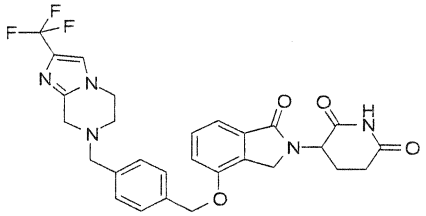


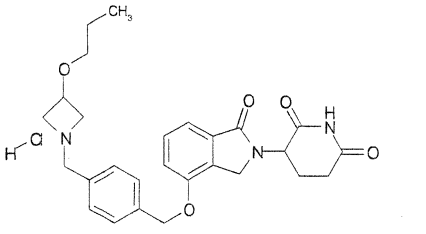


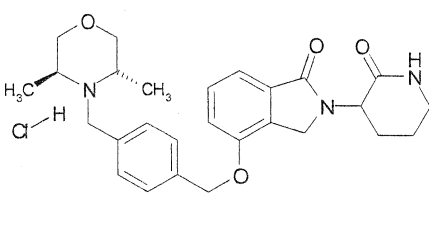


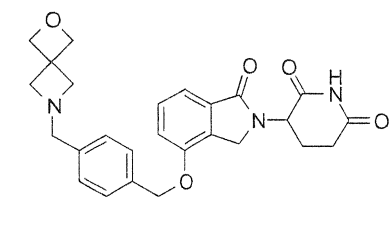


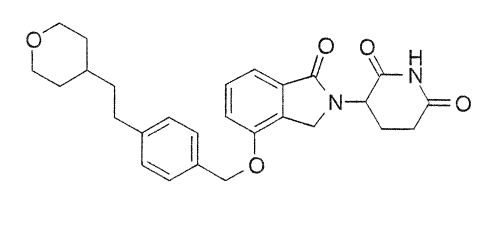


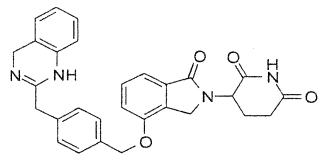


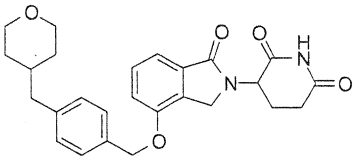


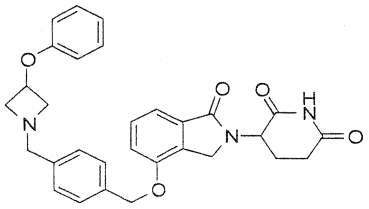


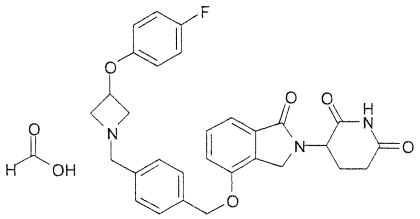


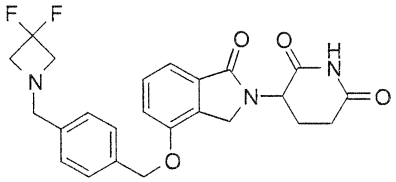


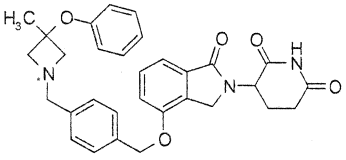


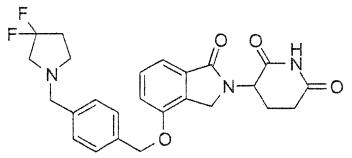


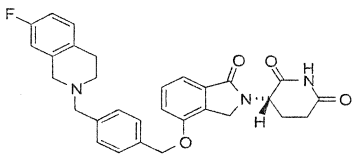


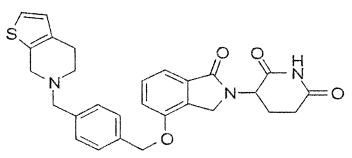


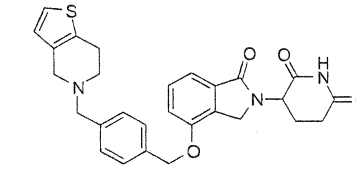


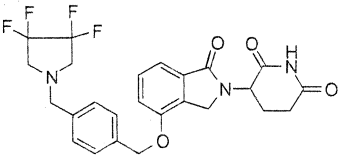


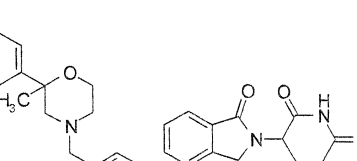


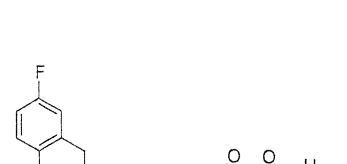


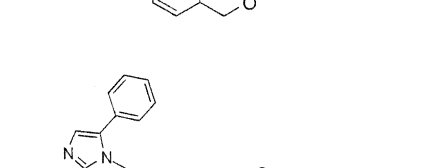


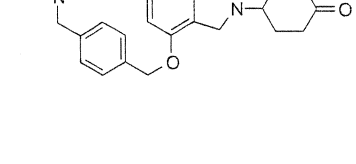


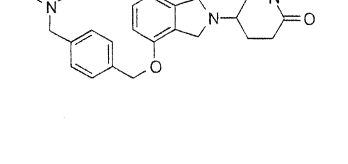




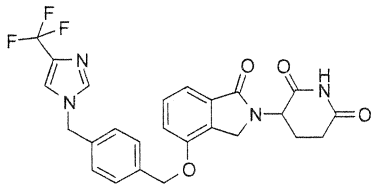


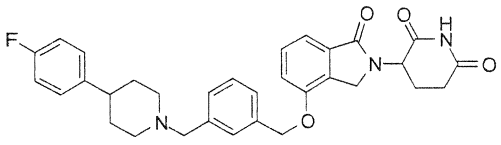


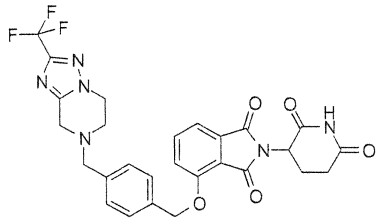


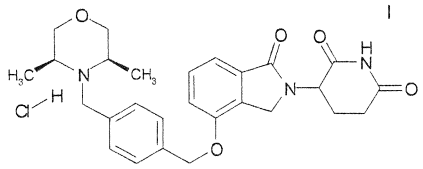


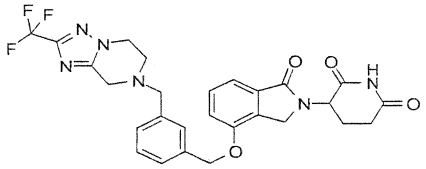
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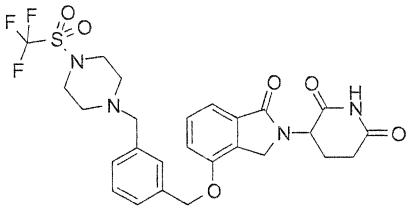


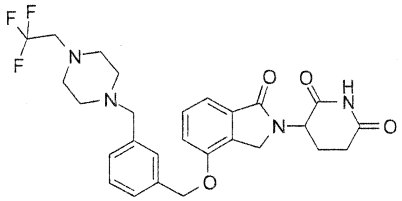


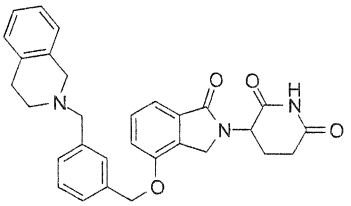


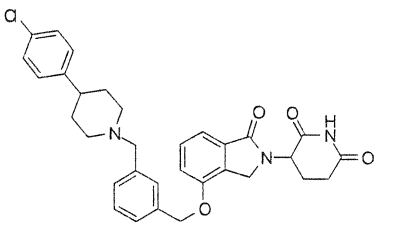


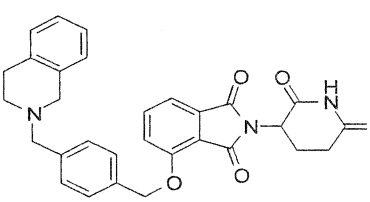


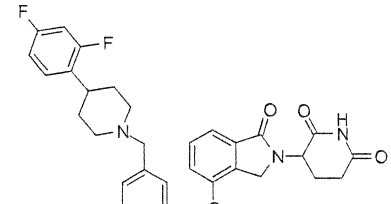


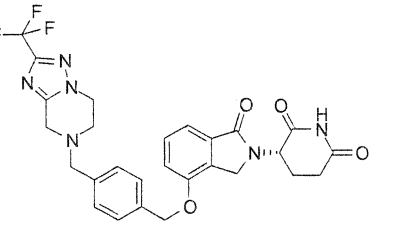


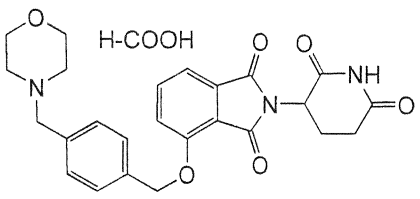


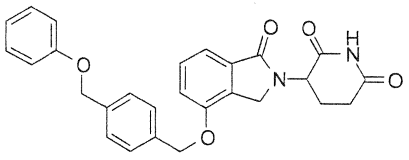


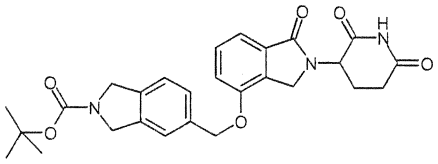






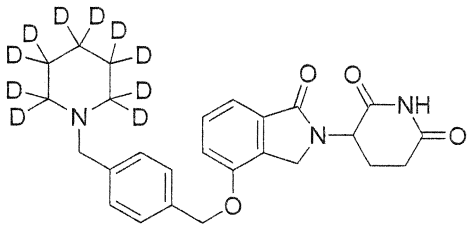




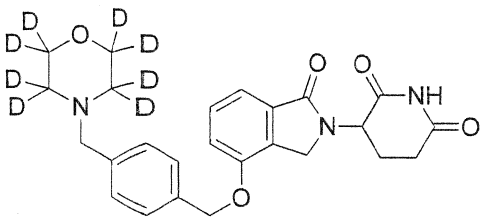


or a pharmaceutically acceptable salt or stereoisomer thereof.

5. A deuterium-enriched compound of the formula:



,



,

or a pharmaceutically acceptable salt or stereoisomer thereof, for use in treating, managing, or preventing a disease or disorder, wherein the disease or disorder is cancer, a disorder associated with angiogenesis, pain, macular degeneration or a related syndrome, a skin disease, a pulmonary disorder, an asbestos-related disorder, a parasitic disease, an immunodeficiency disorder, a CNS disorder, CNS injury, atherosclerosis or a related disorder, dysfunctional sleep or a related disorder, an infectious disease, hemoglobinopathy or a related disorder, or a TNFα related disorder.

6. The compound for use of any one of claims 1-5, wherein the cancer is a cancer of the skin.

7. The compound for use of claim 6, wherein the cancer of the skin is melanoma.

8. The compound for use of claim 7, wherein the melanoma is metastatic melanoma.

9. The compound for use of any one of claims 1-5, wherein the cancer is rectal adenocarcinoma, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, peritoneal carcinoma, papillary serous carcinoma, unresectable hepatocellular carcinoma, papillary thyroid carcinoma, follicular thyroid carcinoma or medullary thyroid carcinoma.

10. The compound for use of any one of claims 1-5, wherein the cancer is Kaposi's sarcoma, gynecologic sarcoma, soft tissue sarcoma, resected high-risk soft tissue sarcoma or leiomyosarcoma.

11. The compound for use of any one of claims 1-5, wherein the cancer is a cancer of the blood or bone marrow.

12. The compound for use of claim 11, wherein the cancer of the blood or bone marrow is leukemia or lymphoma.

13. The compound for use of claim 12, wherein the leukemia is chronic lymphocytic leukemia, chronic myelocytic leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia or acute myeloblastic leukemia.

14. The compound for use of claim 12, wherein the lymphoma is Hodgkin's lymphoma.

15. The compound for use of claim 12, wherein the lymphoma is Non-Hodgkin's lymphoma.

16. The compound for use of claim 15, wherein the Non-Hodgkin's lymphoma is cutaneous T cell lymphoma, cutaneous B cell lymphoma, diffuse large cell B cell lymphoma, Waldenstrom's macrogliobineima, mantle cell lymphoma or follicular lymphoma.

17. The compound for use of claim 11, wherein the cancer of the blood or bone marrow is multiple myeloma, smoldering myeloma or indolent myeloma.

18. The compound for use of claim 11, wherein the cancer of the blood or bone marrow is a precancerous condition selected from the group consisting of myelodysplastic syndrome and myeloproliferative disease.