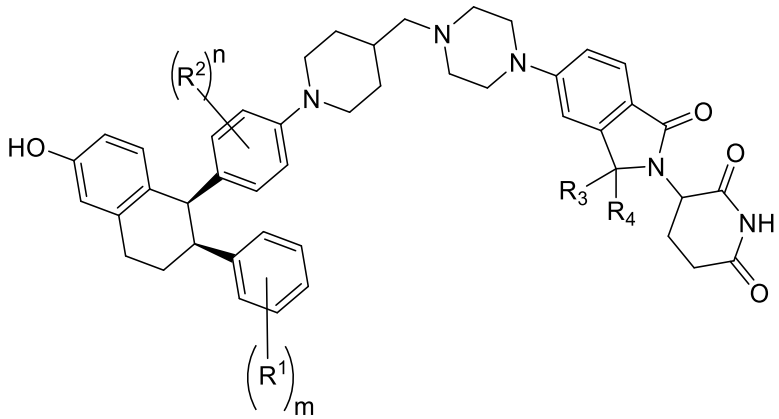
intervals [CI] 9.7-18.8%) and for the 250 mg dose was 14.6% (CI 10.5-19.4%) (Astra Zeneca Faslodex Full Prescribing Information, revised 03/2019).

Summary of the Disclosure

[0007a] In an aspect of the present disclosure, there is provided a use of a compound in the manufacture of a medicament for treating breast cancer in a subject in need thereof, the compound having a Formula (I),



(I), or a pharmaceutically acceptable salt thereof, wherein:

each R^1 and each R^2 is independently selected from halogen, OR_5, $N(R_5)(R_6)$, NO_2, CN, $SO_2(R_5)$, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R_3 and R_4 are either both hydrogen or

R_3 and R_4, taken together with the carbon to which they are attached, form a carbonyl;

each R_5 and each R_6 is independently selected from hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

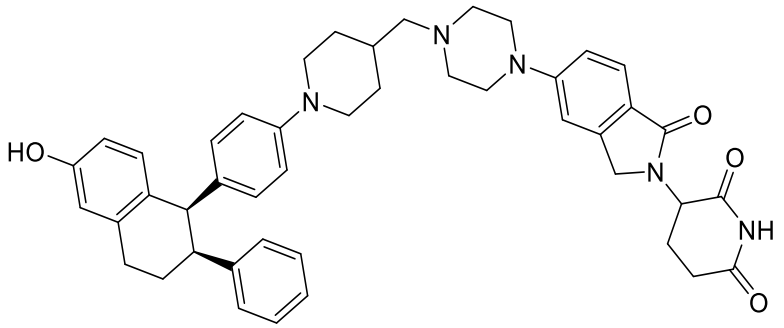
m is 0, 1, 2, 3, 4, or 5; and

n is 0, 1, 2, 3, or 4,

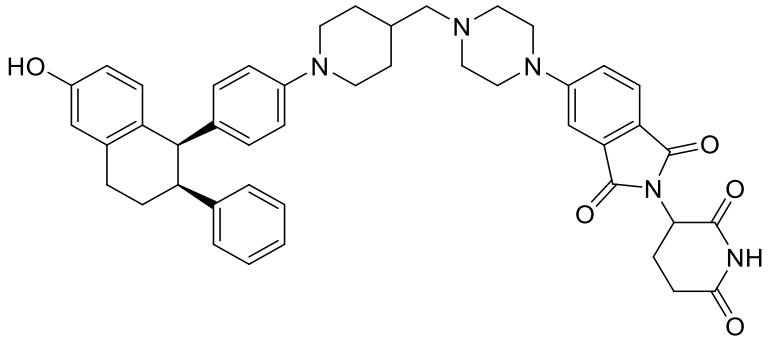
wherein an effective amount of the compound is to be administered to the subject, and

wherein the effective amount of the compound of Formula (I) is about 10 mg to about 1000 mg.

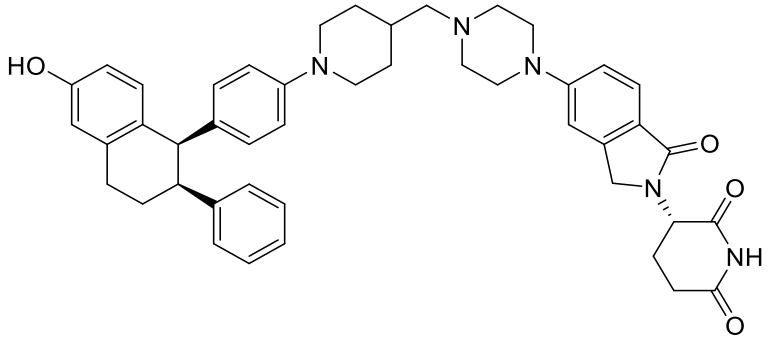
[0007b] In another aspect of the present disclosure, there is provided a use of a compound of Formula (I) in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein an effective amount of the compound of Formula (I) is to be administered orally once a day to the subject, and wherein the compound of Formula (I) is:



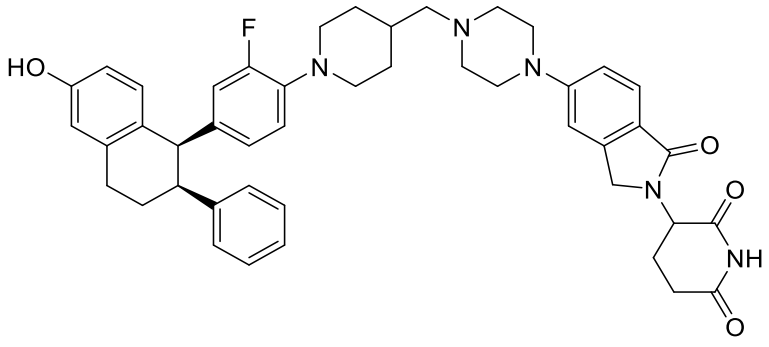
(I-a);



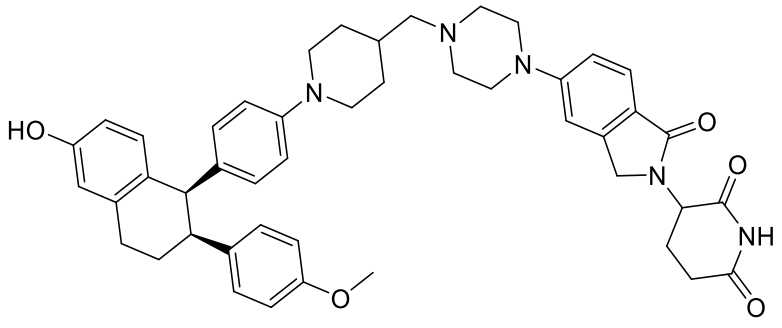
(I-b);



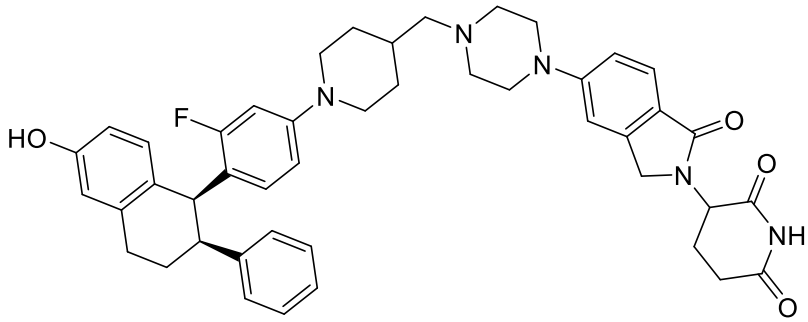
(I-c);



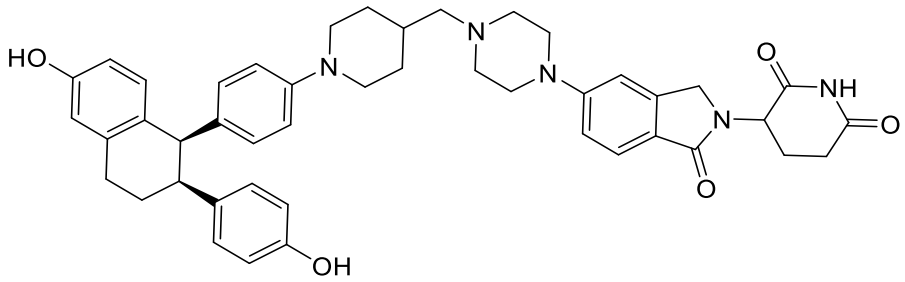
(I-d);



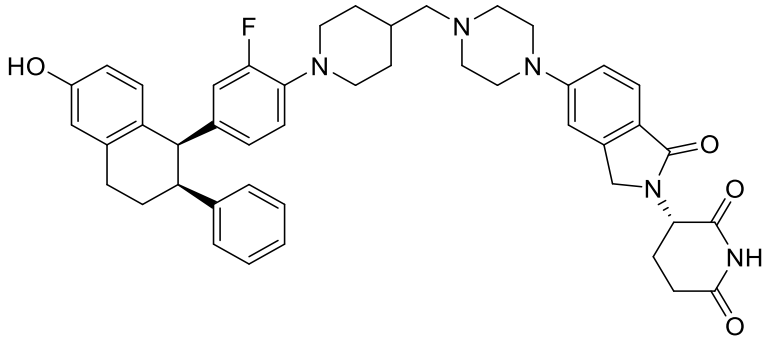
(I-e);



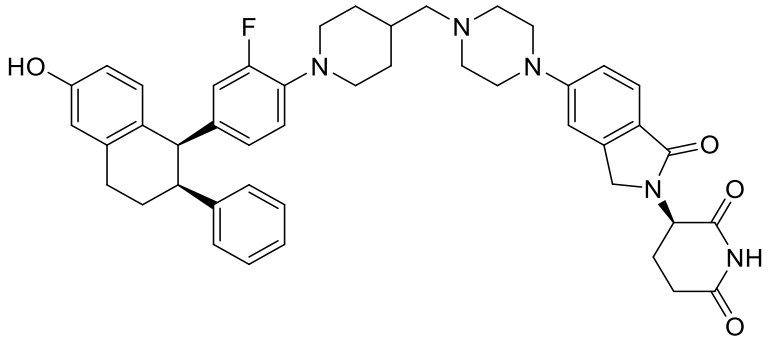
(I-f);



(I-g);



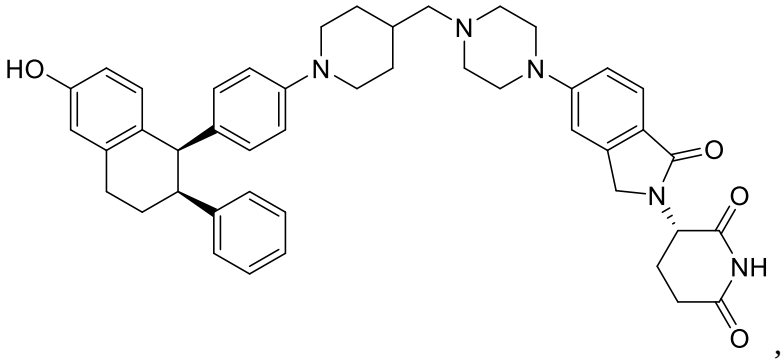
(I-h); or



(I-i);

or a pharmaceutically acceptable salt thereof.

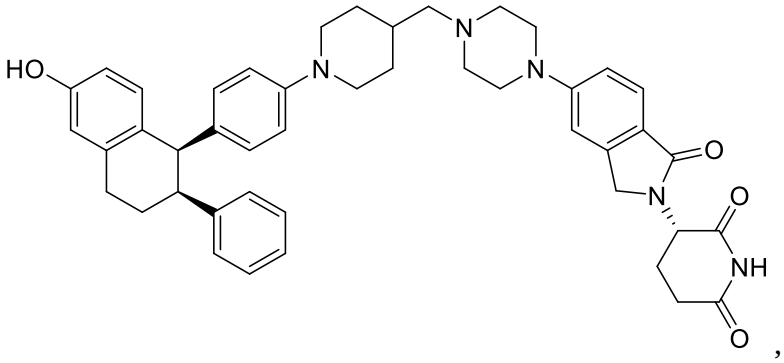
[0007c] In a further aspect of the present disclosure, there is provided a use of a compound of Formula (I-c),



,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and wherein palbociclib is to be further administered orally once a day.

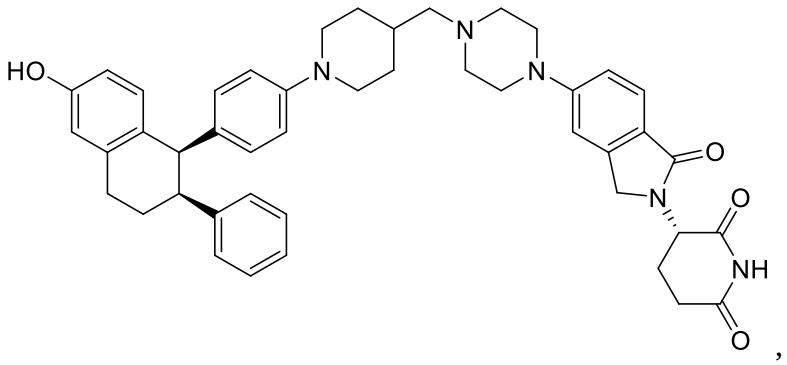
[0007d] In another aspect of the present disclosure, there is provided a use of a compound of Formula (I-c),



,

in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein a therapeutically effective amount of the compound is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

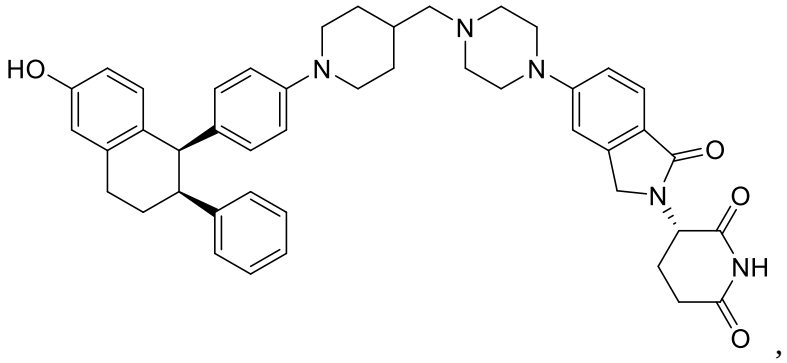
[0007e] In a further aspect of the present disclosure, there is provided a use of a compound of Formula (I-c),



,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for selective estrogen receptor degradation in a patient, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

[0007f] In another aspect of the present disclosure, there is provided a use of a compound of Formula (I-c),

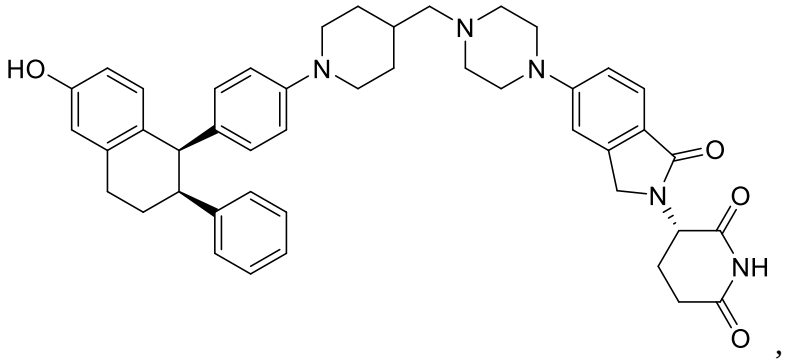


,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inhibiting a cyclin-dependent kinase in a subject in need thereof, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

[0007g] In a further aspect of the present disclosure, there is provided a kit comprising:

(i) a compound of Formula (I-c),

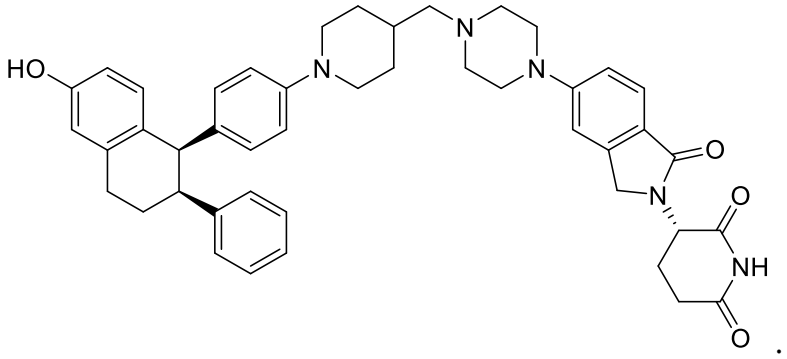


,

(ii) palbociclib, and

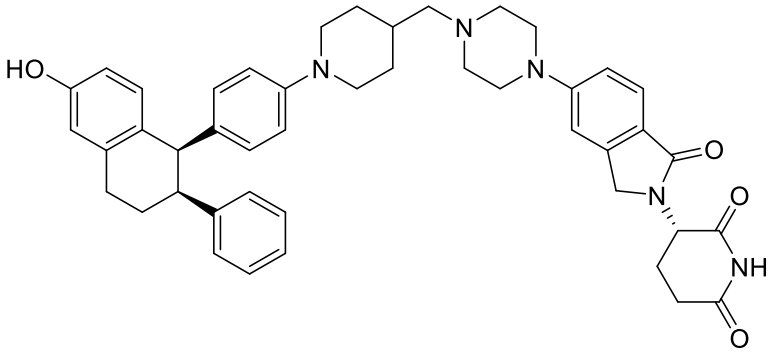
(iii) instructions for use.

[0007h] In another aspect of the present disclosure, there is provided a liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c):



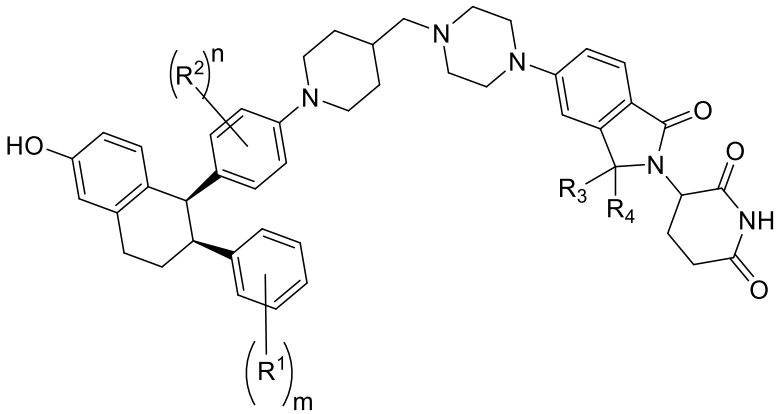
.

[0007i] In a further aspect of the present disclosure, there is provided a method of making a liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c):



comprising the step of adding the solvent to a pre-aliquoted volume of the surfactant.

[0008] In one example, this application pertains to a method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I),



(I), or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, wherein:

each R^1 and each R^2 is independently selected from the group consisting of halo, OR_5, $N(R_5)(R_6)$, NO_2, CN, $SO_2(R_5)$, C_1-C_6 alkyl and C_3-C_6 cycloalkyl;

R_3 and R_4 are either both hydrogen or, taken together with the carbon to which they are attached, form a carbonyl;

each R_5 and each R_6 is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_3-C_6 cycloalkyl;

m is 0, 1, 2, 3, 4, or 5; and

n is 0, 1, 2, 3, or 4.

[0009] In one example, the breast cancer is ER+, HER2-.

[0010] In one example, the breast cancer is metastatic or locally advanced.

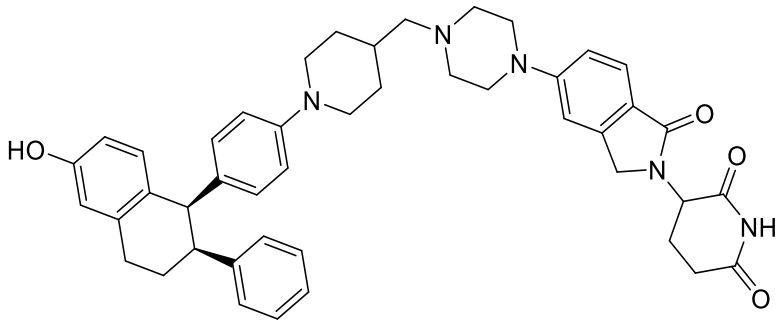
[0011] In one example, each R^1 and each R^2 is independently selected from the group consisting of halo and OR_5.

[0012] In one example, R_3 and R_4 are both hydrogen.

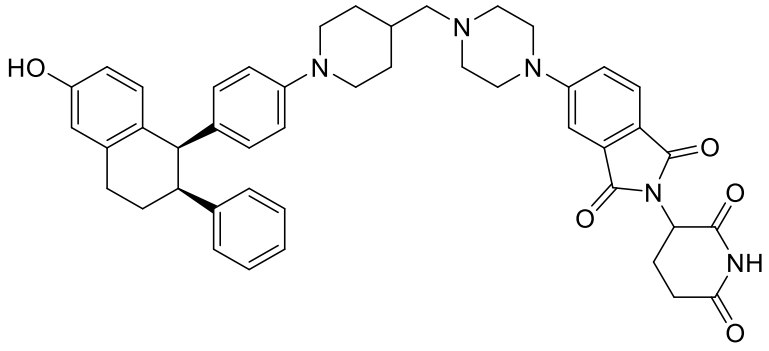
[0013] In one example, R_3 and R_4, taken together with the carbon to which they are attached, form a carbonyl.

[0014] In one example, m and n are each 0. In one example, m and n are each 1. In one example, one of m and n is 0 and the other is 1. For example, in one example m is 0 and n is 1. In another example, m is 0 and n is 1.

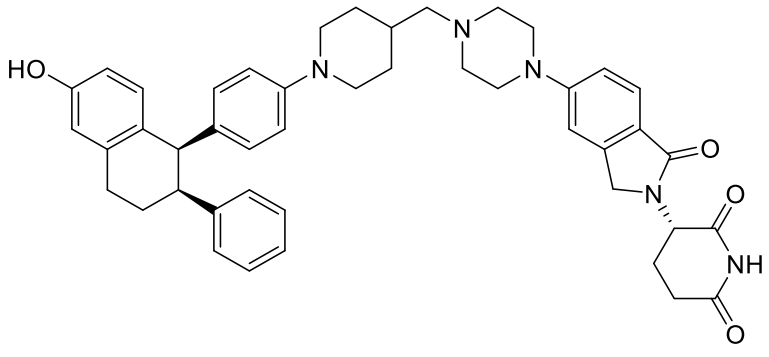
[0015] In one example, the compound of Formula (I) is:



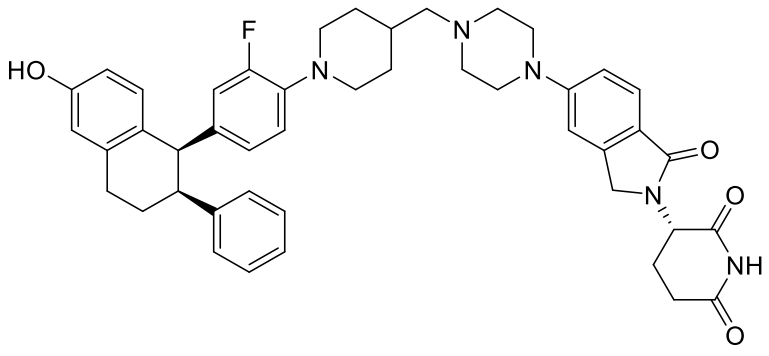
(I-a);



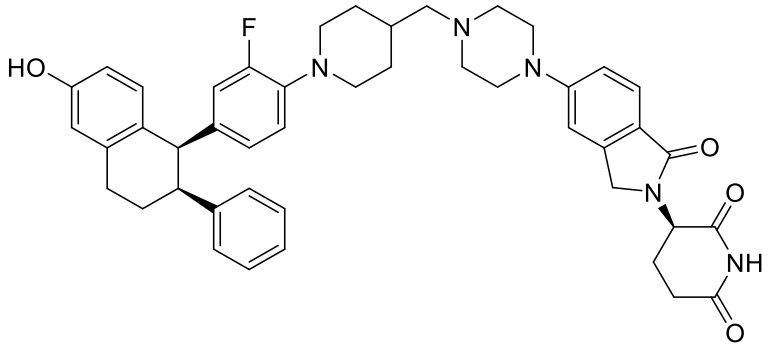
(I-b);



(I-c);



(I-h); or



(I-i);

or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug of any of the foregoing.

[0016] In one example, the method comprises administering to the subject a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, or isotopic derivative thereof.

[0017] In one example, the compound of Formula (I) is administered orally to the subject.

[0018] In one example, the therapeutically effective amount of the compound of Formula (I) is administered to the subject once a day, twice a day, three times a day, or four times a day. In one example, the therapeutically effective amount of the compound of Formula (I) is administered to the subject once a day. In one example, the therapeutically effective amount of the compound of Formula (I) is administered to the subject all at once or is administered in two, three, or four portions.

[0019] In one example, the therapeutically effective amount of the compound of Formula (I) is about 3 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, or 30 mg.

[0020] In one example, the therapeutically effective amount of the compound of Formula (I) is about 10 mg to about 1000 mg.

[0021] In one example, the therapeutically effective amount of the compound of Formula (I) is about 20 mg to about 700 mg.

[0022] In one example, the therapeutically effective amount of the compound of Formula (I) is about 30 mg to about 500 mg.

[0023] In one example, the therapeutically effective amount of the compound of Formula (I) is about 30 mg to about 120 mg.

[0024] In one example, the therapeutically effective amount of the compound of Formula (I) is about 10 to about 40 mg, about 20 to about 50 mg, about 30 to about 60 mg, about 40 to about 70 mg, about 50 to about 80 mg, about 60 to about 90 mg, about 70 to about 100 mg, about 80 to about 110 mg, about 90 to about 120 mg, about 100 to about 130 mg, about 110 to about 140 mg, about 120 to about 150 mg, about 130 to about 160 mg, about 140 to about 170 mg, about 150 to about 180 mg, about 160 to about 190 mg, about 170 to about 200 mg, about 180 to about 210 mg, about 190 to about 220 mg, about 200 to about 230 mg, about 210 to about 240 mg, about 220 to about 250 mg, about 230 to about 260 mg, about 240 to about 270 mg, about 250 to about 280 mg, about 260 to about 290 mg, about 270 to about 300 mg, about 280 to about 310 mg, about 290 to about 320 mg, about 300 to about 330 mg, about 310 to about 340 mg, about 320 to about 350 mg, about 330 to about 360 mg, about 340 to about 370 mg, about 350 to about 380 mg, about 360 to about 390 mg, or about 370 to about 400 mg.

[0025] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,500 ng*hr/mL, about 3,600 ng*hr/mL, about 3,700 ng*hr/mL, about 3,800 ng*hr/mL, about 3,900 ng*hr/mL, about 4,000 ng*hr/mL, about 4,100 ng*hr/mL, about 4,200 ng*hr/mL, about 4,300 ng*hr/mL, 4,400 ng*hr/mL, about 4,500 ng*hr/mL, about 4,600 ng*hr/mL, about 4,700 ng*hr/mL, about 4,800 ng*hr/mL, about 4,900 ng*hr/mL, or about 5,000 ng*hr/mL.

[0026] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,500 ng*hr/mL and less than about 4,000 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,600 ng*hr/mL and less than about 4,100 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,700 ng*hr/mL and less than about 4,200 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,800 ng*hr/mL and less than about 4,300 ng*hr/mL. In one example, the therapeutically effective amount of

the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,900 ng*hr/mL and less than about 4,400 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,000 ng*hr/mL and less than about 4,500 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,100 ng*hr/mL and less than about 4,600 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,200 ng*hr/mL and less than about 4,700 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,300 ng*hr/mL and less than about 4,800 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,400 ng*hr/mL and less than about 4,900 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,500 ng*hr/mL and less than about 5,000 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,600 ng*hr/mL and less than about 5,100 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,700 ng*hr/mL and less than about 5,200 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,800 ng*hr/mL and less than about 5,300 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,900 ng*hr/mL and less than about 5,400 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 5,000 ng*hr/mL and less than about 5,500 ng*hr/mL.

[0027] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,000 ng*hr/mL and less than about 4,200 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,900 ng*hr/mL and less than about 4,300 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,800 ng*hr/mL and less than about 4,400 ng*hr/mL. In one example, the therapeutically effective amount of the

compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,700 ng*hr/mL and less than about 4,500 ng*hr/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,600 ng*hr/mL and less than about 4,600 ng*hr/mL.

[0028] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 200 ng/mL, about 205 ng/mL, about 210 ng/mL, about 215 ng/mL, about 220 ng/mL, about 225 ng/mL, about 230 ng/mL, about 235 ng/mL, about 240 ng/mL, about 245 ng/mL, or about 250 ng/mL.

[0029] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 200 ng/mL and less than about 220 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 205 ng/mL and less than about 225 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 210 ng/mL and less than about 230 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 215 ng/mL and less than about 235 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 220 ng/mL and less than about 240 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 225 ng/mL and less than about 245 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 230 ng/mL and less than about 250 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 235 ng/mL and less than about 255 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 240 ng/mL and less than about 260 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 245 ng/mL and less than about 265 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 250 ng/mL and less than about 270 ng/mL.

[0030] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 214 ng/mL and less than about 236 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 213 ng/mL and less than about 237 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 212 ng/mL and less than about 238 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 211 ng/mL and less than about 239 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 210 ng/mL and less than about 240 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 205 ng/mL and less than about 245 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 200 ng/mL and less than about 250 ng/mL.

[0031] In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 223 ng/mL and less than about 225 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 222 ng/mL and less than about 226 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 221 ng/mL and less than about 227 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 220 ng/mL and less than about 228 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 219 ng/mL and less than about 229 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 218 ng/mL and less than about 230 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 217 ng/mL and less than about 231 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 216 ng/mL and less than about 232 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a

mean day 15 C_{max} of greater than about 215 ng/mL and less than about 233 ng/mL. In one example, the therapeutically effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 214 ng/mL and less than about 234 ng/mL.

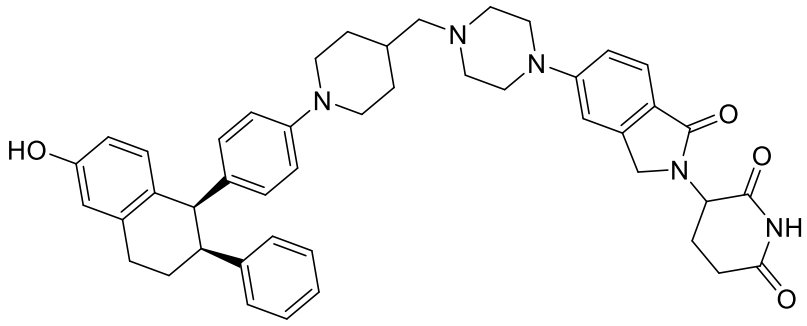
[0032] In one example, the compound of Formula (I) is formulated as a tablet. In one example, the tablet comprises a compound of Formula (I) and, optionally, one or more of the following: emulsifier; surfactant; binder; disintegrant; glidant; and lubricant. In one example, the emulsifier is hypromellose. In one example, the surfactant is Vitamin E polyethylene glycol succinate. In one example, the binder is microcrystalline cellulose or lactose monohydrate. In one example, the disintegrant is croscarmellose sodium. In one example, the glidant is silicon dioxide. In one example, the lubricant is sodium stearyl fumarate. In one example, the subject in need of treatment is in a fed state. In one example, the subject in need of treatment is in a fasted state.

[0033] In one example, this application pertains to a method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I) as defined herein, further comprising the administration of a therapeutically effective amount of a CDK4/6 inhibitor to the subject in need thereof. In one example, the CDK4/6 inhibitor is SHR6390, trilaciclib, lerociclib, AT7519M, dinaciclib, ribociclib, abemaciclib, or palbociclib. In one example, the CDK4/6 inhibitor is palbociclib.

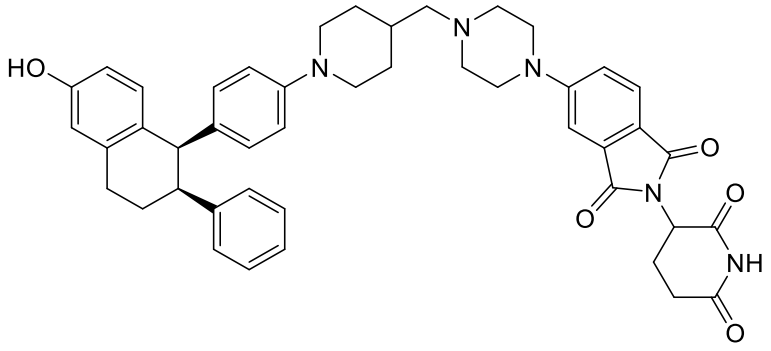
[0034] In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I) and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered to the subject once a day. In one example, the therapeutically effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg. In one example, the palbociclib is administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed by off treatment is repeated one, two, three, four, five, or more times. In one example, the compound of formula (I) is administered once daily for 21 up to consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of formula (I) followed by off treatment is repeated one, two, three, four, five, or more times. In one example, the administration of the compound of Formula (I) and palbociclib to the subject in need thereof occurs when the subject is in a fed state. In one

example, the administration of the compound of Formula (I) and palbociclib to the subject in need thereof occurs when the subject is in a fasted state.

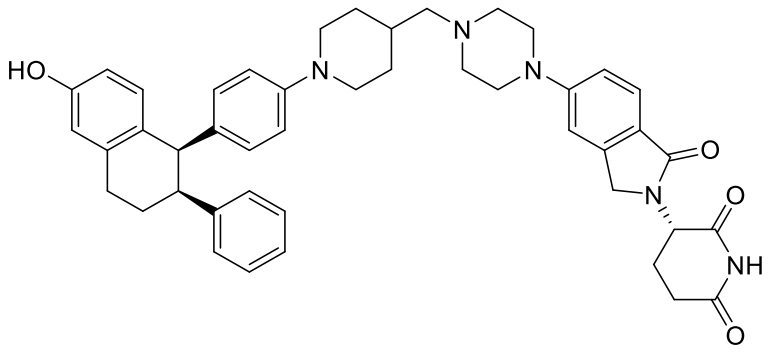
[0035] In one example, this application pertains to a method of treating metastatic breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, wherein the compound of Formula (I), is selected from the group consisting of:



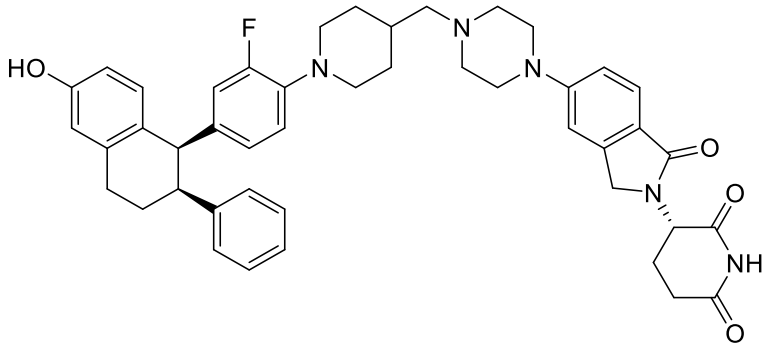
(I-a);



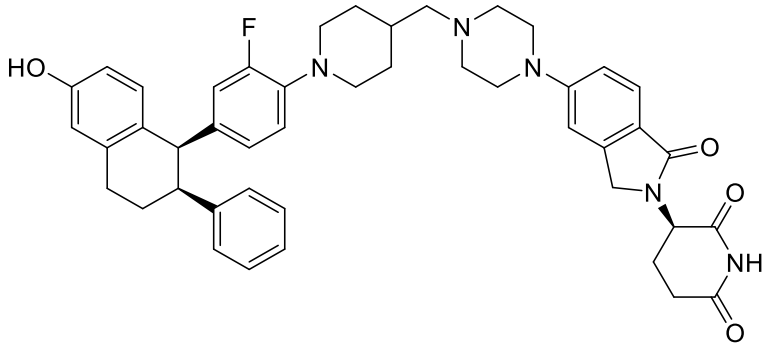
(I-b);



(I-c);



(I-h); and



(I-i).

[0036] In one example, the therapeutically effective amount of the compound of Formula (I) is administered to the subject all at once or is administered in two, three, or four portions.

[0037] In one example, the therapeutically effective amount of the compound of Formula (I) is about 30 mg to about 1000 mg.

[0038] In one example, the therapeutically effective amount of the compound of Formula (I) is about 10 to about 40 mg, about 20 to about 50 mg, about 30 to about 60 mg, about 40 to about 70 mg, about 50 to about 80 mg, about 60 to about 90 mg, about 70 to about 100 mg, about 80 to about 110 mg, about 90 to about 120 mg, about 100 to about 130 mg, about 110 to about 140 mg, about 120 to about 150 mg, about 130 to about 160 mg, about 140 to about 170 mg, about 150 to about 180 mg, about 160 to about 190 mg, about 170 to about 200 mg, about 180 to about 210 mg, about 190 to about 220 mg, about 200 to about 230 mg, about 210 to about 240 mg, about 220 to about 250 mg, about 230 to about 260 mg, about 240 to about 270 mg, about 250 to about 280 mg, about 260 to about 290 mg, about 270 to about 300 mg, about 280 to about 310 mg, about 290 to about 320 mg, about 300 to about 330 mg, about 310 to about 340 mg, about 320 to about 350 mg, about 330 to about 360 mg, about 340 to about 370 mg, about 350 to about 380 mg, about 360 to about 390 mg, or about 370 to about 400 mg.

[0039] In one example, the compound of Formula (I) is formulated as a tablet.

[0040] In one example, this application pertains to a method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I), wherein the compound of Formula (I) is a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), Formula (I-i), or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, further comprising the administration of a therapeutically effective amount of a CDK4/6 inhibitor to the subject in need thereof. In one example, the CDK4/6 inhibitor is SHR6390, trilaciclib, lerociclib, AT7519M, dinaciclib, ribociclib, abemaciclib, or palbociclib. In one example, the CDK4/6 inhibitor is palbociclib.

[0041] In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered at the same time as the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered prior to the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered after the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In some examples for the method of treating breast cancer in a subject in need thereof, comprising administering to

the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i) and the administration of palbociclib are separated in time such that the two compounds, and their respective excipients (if present), do not mix in the subject's stomach.

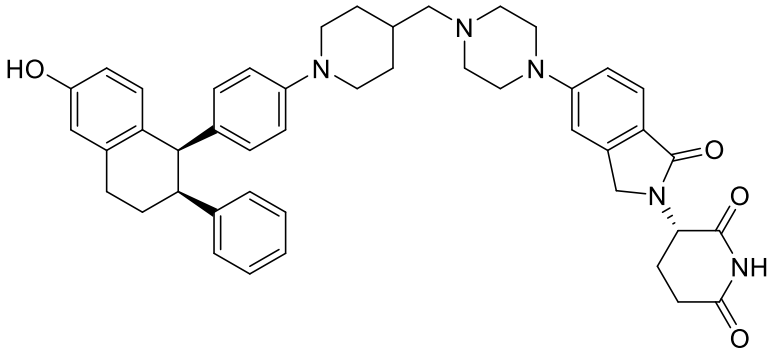
[0042] In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered at least 5, at least 10, at least 15, at least 20, at least 25, or at least 30 minutes prior to the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered at least 30 minutes prior to the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered between 30 and 60 minutes prior to the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i).

[0043] In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered at least 5, at least 10, at least 15, at least 20, at least 25, or at least 30 minutes after the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered at least 30 minutes after the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i). In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered between 30 and 60 minutes after the administration of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i).

[0044] In one example, for the method of treating breast cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i), and further comprising the administration of a therapeutically effective amount of palbociclib, the therapeutically effective amount of palbociclib is administered to the subject once a day. In one example, the therapeutically effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg. In one example, the palbociclib is administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed by off treatment is repeated one, two, three, four,

five, or more times. In one example, the compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i) is administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i) followed by off treatment is repeated one, two, three, four, five, or more times. In one example, the administration of the compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i) and palbociclib to the subject in need thereof occurs when the subject is in a fed state. In one example, the administration of the compound of Formula (I-a), Formula (I-b), Formula (I-c), Formula (I-d), Formula (I-e), Formula (I-f), Formula (I-g), Formula (I-h), or Formula (I-i) and palbociclib to the subject in need thereof occurs when the subject is in a fasted state.

[0045] In one example, this application pertains to a method of treating breast cancer in a subject in need thereof, comprising: (i) once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c),



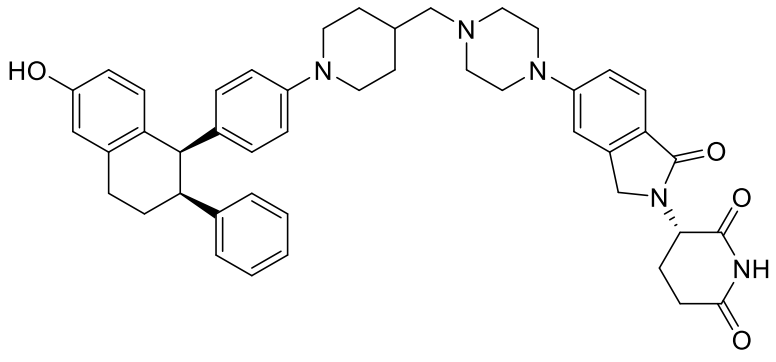
, or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, and (ii) once a day, oral administration of palbociclib. In one example, this application pertains to a method of treating breast cancer in a subject in need thereof, comprising: (i) once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and (ii) once a day, oral administration of palbociclib. In one example, the therapeutically effective amount of the compound of Formula (I-c) is about 30 mg to about 1000 mg. In one example, the therapeutically effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg. In one example, the palbociclib is administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed

by off treatment is repeated one, two, three, four, five, or more times. In one example, the compound of formula (I-c) is administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of formula (I-c) followed by off treatment is repeated one, two, three, four, five, or more times. In one example, the administration of the compound of Formula (I-c) and palbociclib to the subject in need thereof occurs when the subject is in a fed state. In one example, the administration of the compound of Formula (I-c) and palbociclib to the subject in need thereof occurs when the subject is in a fasted state.

[0046] In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the administration of a compound of Formula (I-c) and the administration of palbociclib are separated in time such that the two compounds, and their respective excipients (if present), do not mix in the subject's stomach. In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered prior to the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered at least 5, at least 10, at least 15, at least 20, at least 25, or at least 30 minutes prior to the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered at least 30 minutes prior to the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered between 30 and 60 minutes prior to the administration of a compound of Formula (I-c).

[0047] In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered after the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered at least 5, at least 10, at least 15, at least 20, at least 25, or at least 30 minutes after the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered at least 30 minutes after the administration of a compound of Formula (I-c). In one example, for the method of treating breast cancer in a subject in need thereof, comprising once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c) and further once a day, oral administration of palbociclib, the palbociclib is administered between 30 and 60 minutes after the administration of a compound of Formula (I-c).

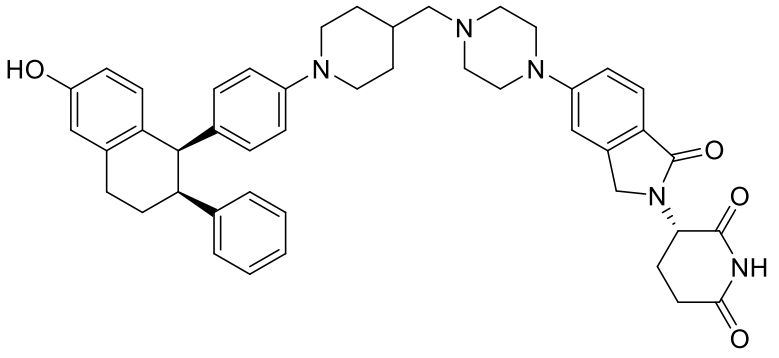
[0048] In one example, this application pertains to a method for selective estrogen receptor degradation in a patient comprising: (i) once a day, oral administration of a therapeutically effective amount of a compound of Formula (I-c),



, or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, and (ii) once a day, oral administration of palbociclib.

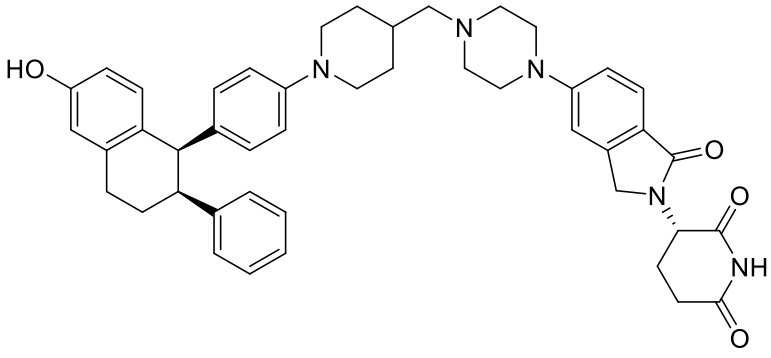
[0049] In one example, this application pertains to a method for inhibiting a cyclin-dependent kinase in a subject in need thereof comprising: (i) once a day, oral administration of a

therapeutically effective amount of a compound of Formula (I-c),



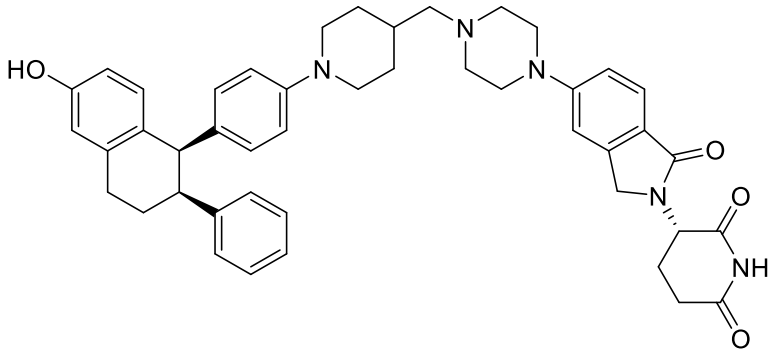
, or a pharmaceutically acceptable salt, enantiomer, stereoisomer, solvate, polymorph, isotopic derivative, or prodrug thereof, and (ii) once a day, oral administration of palbociclib.

[0050] In one example, this application pertains to a kit comprising: a compound of Formula (I-c),



, palbociclib, and instructions for use.

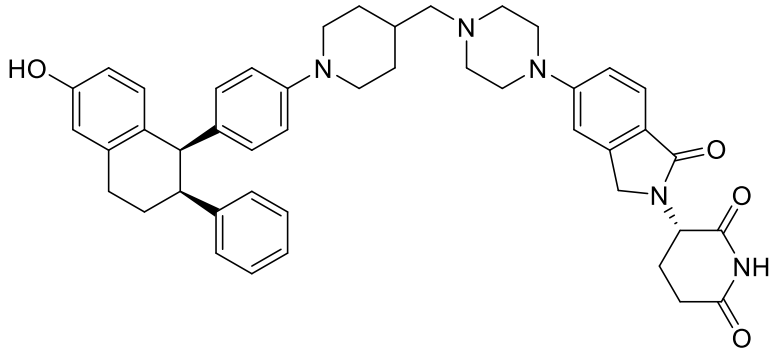
[0051] In one example, this application pertains to a liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c),



. In some examples, the surfactant is a sorbitan derivative. In some examples, the surfactant is Tween 80. In some

examples, the solvent is a low molecular weight polyethylene glycol (PEG). In some examples, the solvent is polyethylene glycol (PEG)-400.

[0052] In one example, this application pertains to method of making a liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c):



comprising the step of adding the solvent to a pre-aliquoted volume of the surfactant. In some examples, the method further comprises the step of adding a compound of Formula (I-c) to a mixture of the solvent and the surfactant. In some examples, the surfactant is a sorbitan derivative. In some examples, the surfactant is Tween 80. In some examples, the solvent is a low molecular weight polyethylene glycol (PEG). In some examples, the solvent is polyethylene glycol (PEG)-400.

Brief Description of the Figures

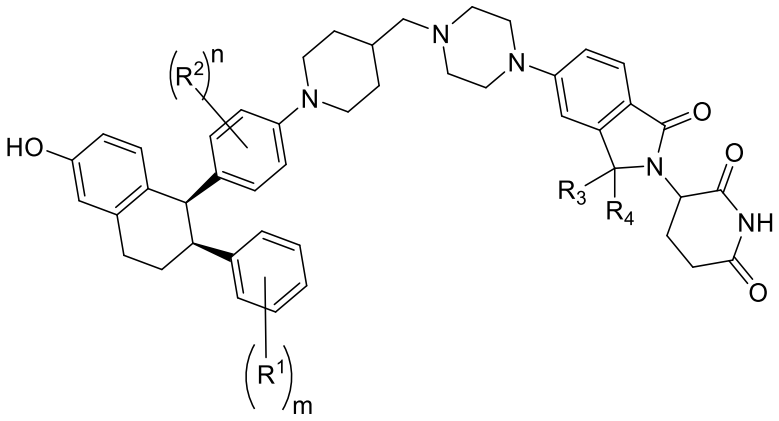
[0053] FIG. 1 shows the results of tumor growth inhibition experiments (mean tumor volume (mm^3) vs. time) associated with oral, once daily administration of Compound (I-c) at doses of 3 mg/kg, 10 mg/kg, and 30 mg/kg compared to vehicle. At doses of 3 mg/kg, 10 mg/kg, and 30 mg/kg of Compound (I-c), tumor growth inhibition (TGI) of 85%, 98%, and 124%, respectively, was observed compared to a control group in a MCF7 xenograft model.

[0054] FIG. 2 is a Western Blot experiment that shows the reduction of ER in MCF7 xenograft tumors in response to dosing of Compound (I-c) of 3 mg/kg, 10 mg/kg, and 30 mg/kg (oral, once daily).

[0055] FIG. 3 is a pair of line graphs which show the mean concentration of the compound of Formula (I-c) (ng/mL) over the course of 24 hours post-dosing on both day 1 and day 15 in a Phase I clinical trial.

What is claimed is:

1. Use of a compound in the manufacture of a medicament for treating breast cancer in a subject in need thereof, the compound having a Formula (I),



(I), or a pharmaceutically acceptable salt thereof, wherein:

each R^1 and each R^2 is independently selected from halogen, OR_5, $N(R_5)(R_6)$, NO_2, CN, $SO_2(R_5)$, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R_3 and R_4 are either both hydrogen or

R_3 and R_4, taken together with the carbon to which they are attached, form a carbonyl;

each R_5 and each R_6 is independently selected from hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

m is 0, 1, 2, 3, 4, or 5; and

n is 0, 1, 2, 3, or 4,

wherein an effective amount of the compound is to be administered to the subject, and

wherein the effective amount of the compound of Formula (I) is about 10 mg to about 1000 mg.

2. The use of claim 1, wherein the breast cancer is ER+, HER2-.

3. The use of claim 1 or 2, wherein the breast cancer is metastatic or locally advanced.

4. The use of any one of claims 1-3, wherein R^1 and R^2 are each independently halo or OR_5.

5. The use of any one of claims 1-4, wherein R_3 and R_4 are both hydrogen.

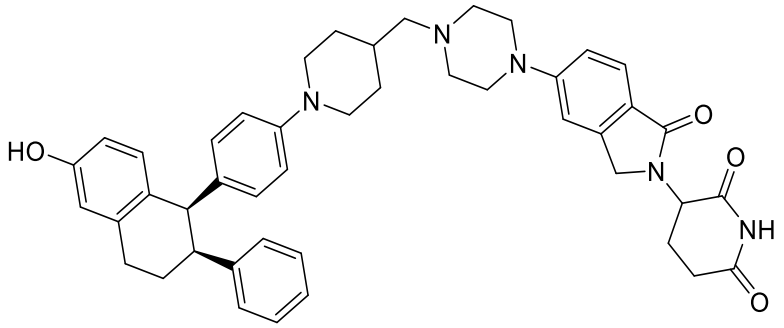
6. The use of any one of claims 1-4, wherein R_3 and R_4, taken together with the carbon to which they are attached, form a carbonyl.

7. The use of any one of claims 1-3, 5, or 6, wherein m and n are each 0.

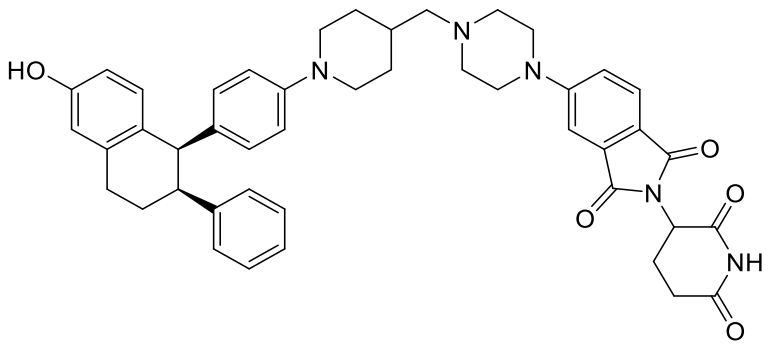
8. The use of any one of claims 1-6, wherein m and n are each 1.

9. The use of any one of claims 1-3, 5, or 6, wherein one of m and n is 0 and the other is 1.

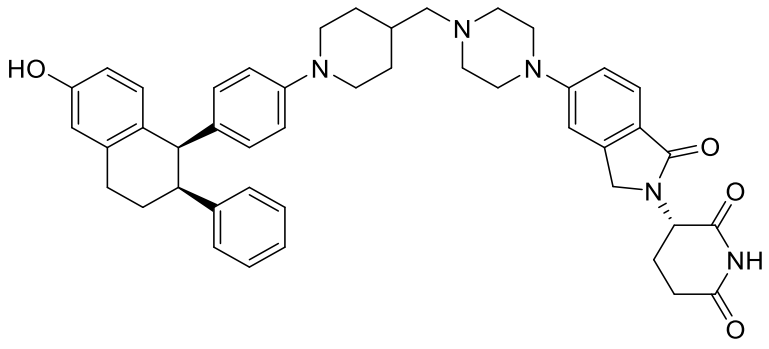
10. The use of any one of claims 1-3, wherein the compound of Formula (I) is:



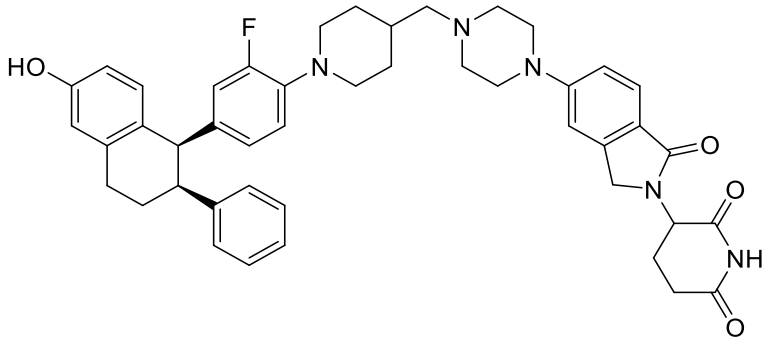
(I-a);



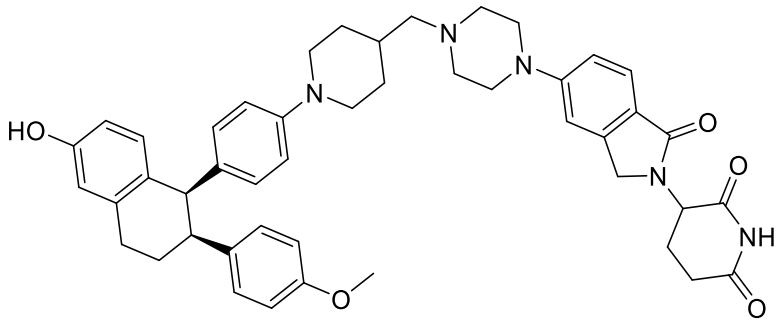
(I-b);



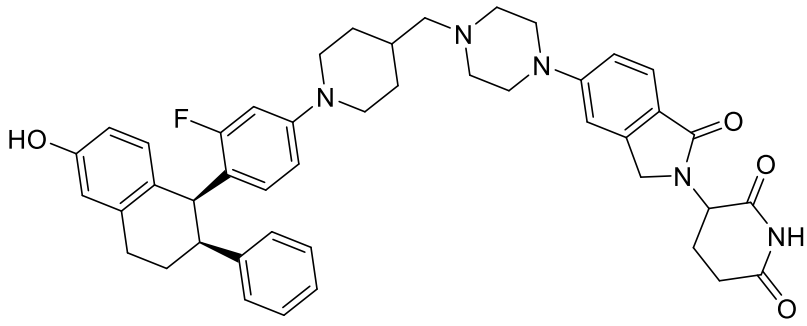
(I-c);



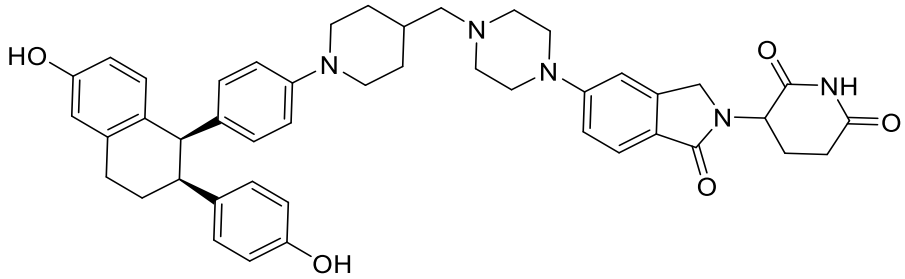
(I-d);



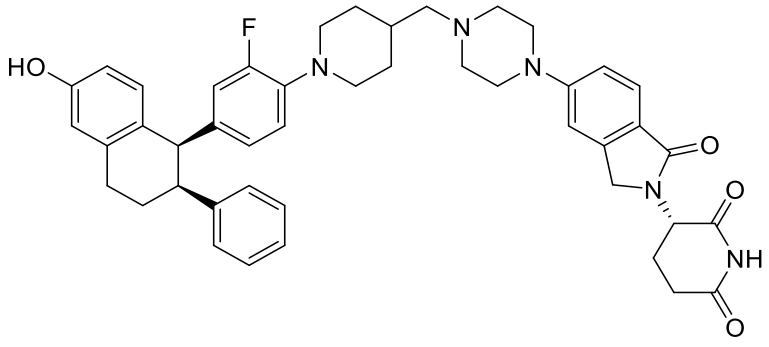
(I-e);



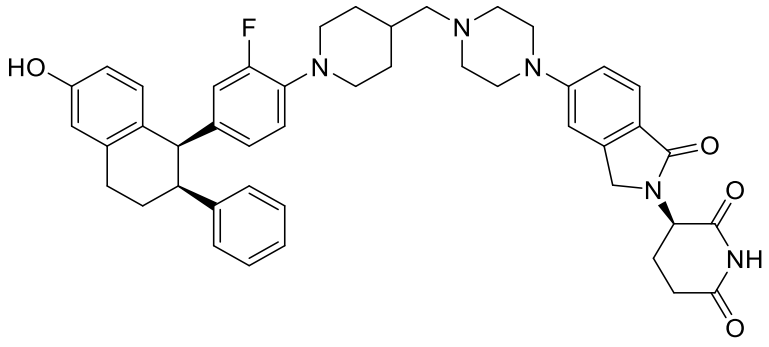
(I-f);



(I-g);



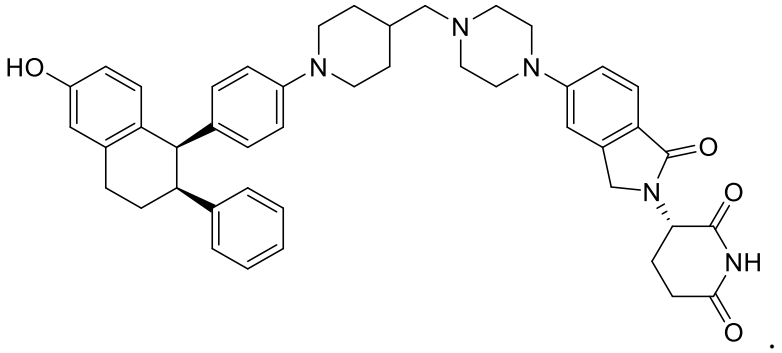
(I-h); or



(I-i);

or a pharmaceutically acceptable salt thereof.

11. The use of any one of claims 1-3, wherein the compound of Formula (I) is a compound of Formula (I-c):



.

12. The use of any one of claims 1-11, wherein the compound of Formula (I) is to be administered orally to the subject.

13. The use of any one of claims 1-12, wherein the effective amount of the compound of Formula (I) is to be administered to the subject once a day, twice a day, three times a day, or four times a day.

14. The use of any one of claims 1-13, wherein the effective amount of the compound of Formula (I) is to be administered to the subject once a day.

15. The use of claims 1-12, wherein the effective amount of the compound of Formula (I) is to be administered to the subject all at once or is to be administered in two, three, or four portions.

16. The use of any one of claims 1-15, wherein the effective amount of the compound of Formula (I) is about 3 mg, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, or about 30 mg.

17. The use of any one of claims 1-15, wherein the effective amount of the compound of Formula (I) is about 20 mg to about 750 mg.

18. The use of any one of claims 1-15, wherein the effective amount of the compound of Formula (I) is about 30 mg to about 500 mg.

19. The use of any one of claims 1-15, wherein the effective amount of the compound of Formula (I) is about 30 mg to about 120 mg.

20. The use of any one of claims 1-19, wherein the effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 3,500 ng*hr/mL, greater than about 3,600 ng*hr/mL, greater than about 3,700 ng*hr/mL, greater than about 3,800 ng*hr/mL, greater than about 3,900 ng*hr/mL, greater than about 4,000 ng*hr/mL, greater than about 4,100 ng*hr/mL, greater than about 4,200 ng*hr/mL, greater than about 4,300 ng*hr/mL, greater than about 4,400 ng*hr/mL, greater than about 4,500 ng*hr/mL, greater than about 4,600 ng*hr/mL, greater than about 4,700 ng*hr/mL, greater than about 4,800 ng*hr/mL, greater than about 4,900 ng*hr/mL, or greater than about 5,000 ng*hr/mL.

21. The use of any one of claims 1-19, wherein the effective amount of the compound of Formula (I) results in a mean day 15 AUC_{TAU} of greater than about 4,000 ng*hr/mL and less than about 4,500 ng*hr/mL.

22. The use of any one of claims 1-21, wherein the effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 200 ng/mL, greater than about 205 ng/mL, greater than about 210 ng/mL, greater than about 215 ng/mL, greater than about 220 ng/mL, greater than about 225 ng/mL, greater than about 230 ng/mL, greater than about 235 ng/mL, greater than about 240 ng/mL, greater than about 245 ng/mL, or greater than about 250 ng/mL.

23. The use of any one of claims 1-21, wherein the effective amount of the compound of Formula (I) results in a mean day 15 C_{max} of greater than about 215 ng/mL and less than about 235 ng/mL.

24. The use of any one of claims 1-23, wherein the compound of Formula (I) is formulated as a tablet.

25. The use of claim 24, wherein the tablet further comprises one or more of an emulsifier; a surfactant; a binder; a disintegrant; a glidant; or lubricant.

26. The use of claim 25, wherein the emulsifier is hypromellose.

27. The use of claim 25, wherein the surfactant is vitamin E polyethylene glycol succinate.

28. The use of claim 25, wherein the binder is microcrystalline cellulose or lactose monohydrate.

29. The use of claim 25, wherein the disintegrant is croscarmellose sodium.

30. The use of claim 25, wherein the glidant is silicon dioxide.

31. The use of claim 25, wherein the lubricant is sodium stearyl fumarate.

32. The use of any one of claims 1-31, wherein a therapeutically effective amount of a CDK4/6 inhibitor is to be further administered to the subject in need thereof.

33. The use of claim 32, wherein the CDK4/6 inhibitor is SHR6390, trilaciclib, lerociclib, AT7519M, dinaciclib, ribociclib, abemaciclib, or palbociclib.

34. The use of claim 32, wherein the CDK4/6 inhibitor is palbociclib.

35. The use of claim 34, wherein the effective amount of palbociclib is to be administered to the subject once a day.

36. The use of claims 34 or 35, wherein the effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg.

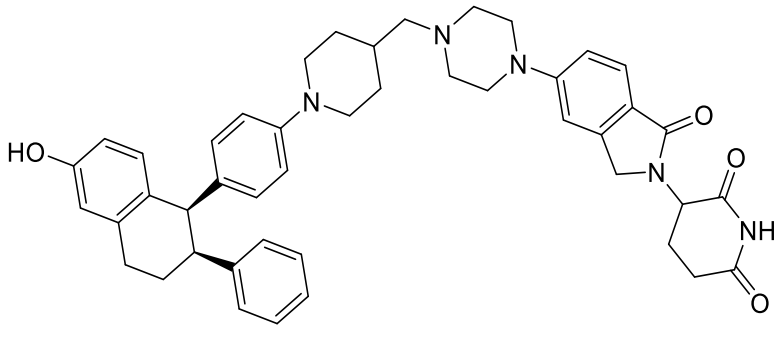
37. The use of any one of claims 33-36, wherein the palbociclib is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed by off treatment is repeated one, two, three, four, five, or more times.

38. The use of any one of claims 1-37, wherein the compound of Formula (I) is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of Formula (I) followed by off treatment is repeated one, two, three, four, five, or more times.

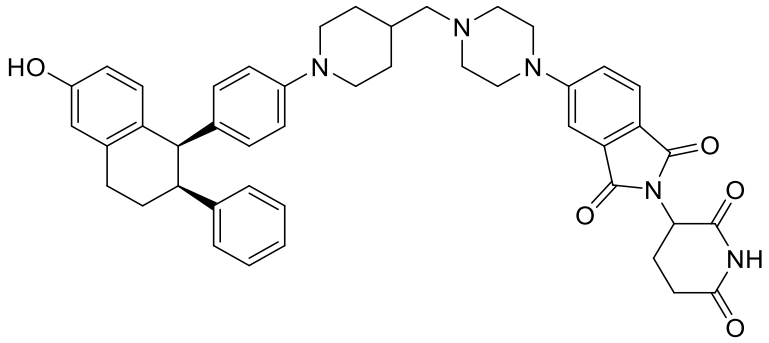
39. The use of any one of claims 1-38, wherein the subject is in a fed state.

40. The use of any one of claims 1-38, wherein the subject is in a fasted state.

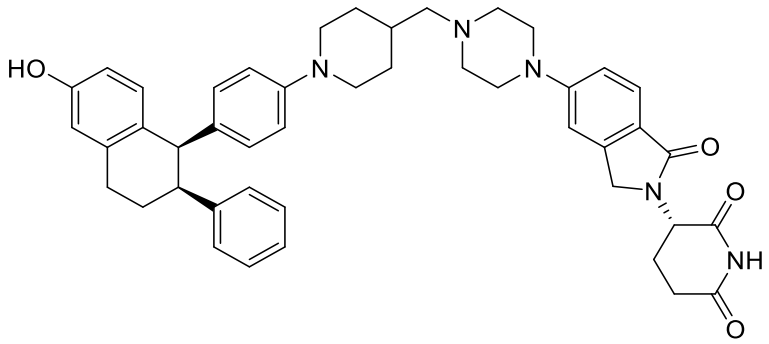
41. Use of a compound of Formula (I) in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein an effective amount of the compound of Formula (I) is to be administered orally once a day to the subject, and wherein the compound of Formula (I) is:



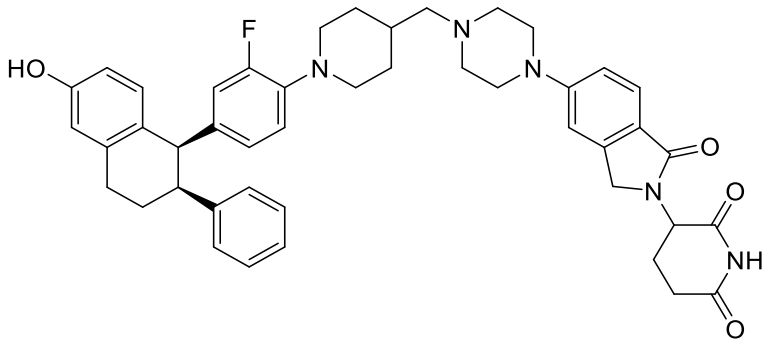
(I-a);



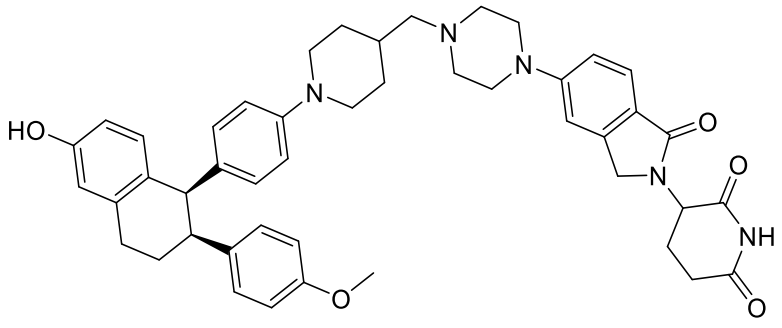
(I-b);

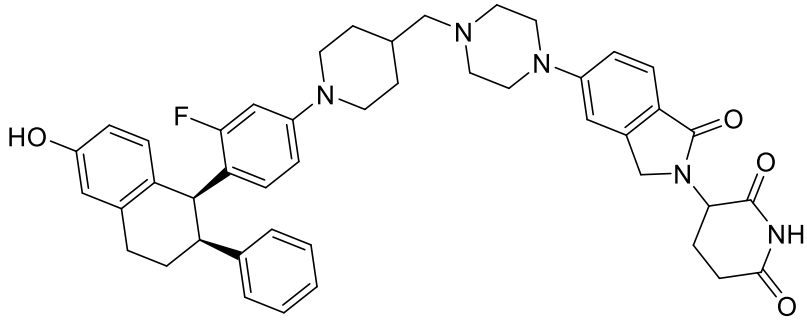


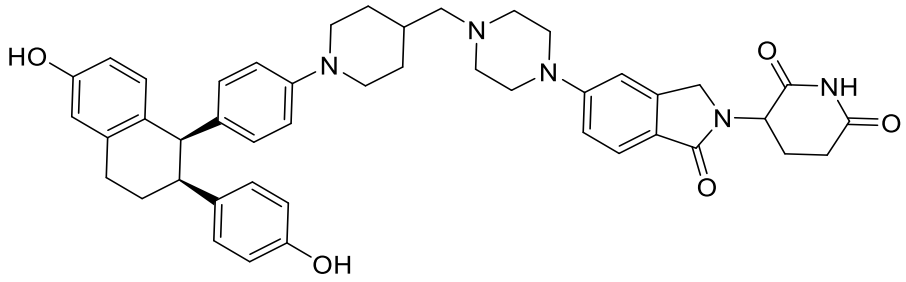
(I-c);

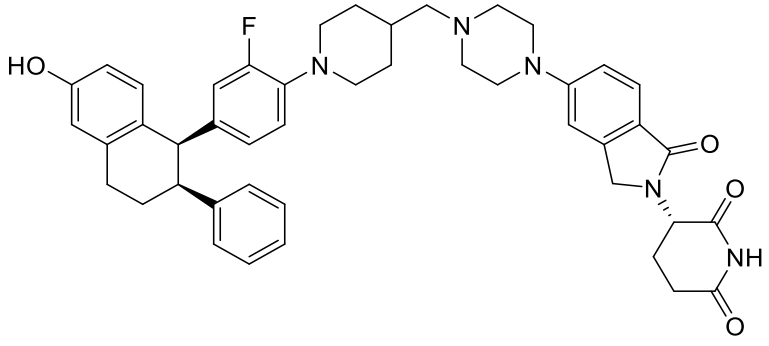


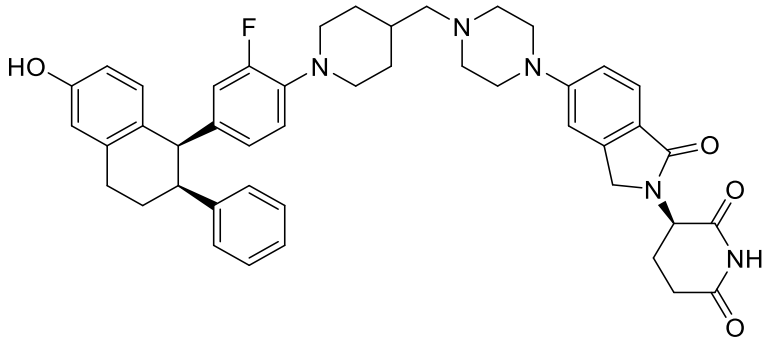
(I-d);


HO
N
N
N
O
O
N
NH
O
O
O
(I-e);


HO
F
N
N
N
O
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NH
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O
(I-f);


HO
N
N
N
O
NH
O
O
O
OH
(I-g);

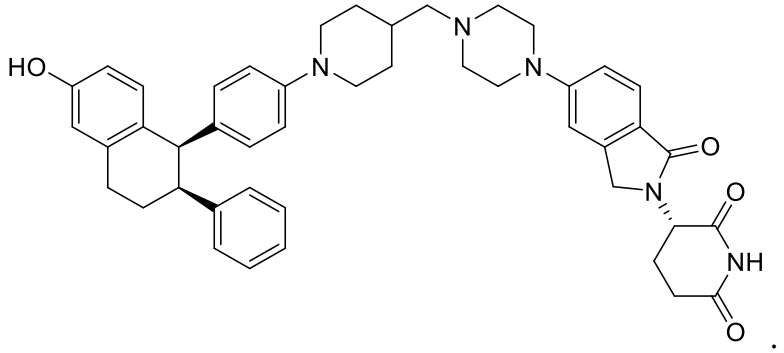

HO
F
N
N
N
O
O
N
NH
O
O
(I-h); or



(I-i);

or a pharmaceutically acceptable salt thereof.

42. The use of claim 41, wherein the compound of Formula (I) is a compound of Formula (I-c):



.

43. The use of claim 41 or 42, wherein the effective amount of the compound of Formula (I) is to be administered to the subject all at once or is to be administered in two, three, or four portions.

44. The use of any one of claims 41-43, wherein the effective amount of the compound of Formula (I) is about 30 mg to about 1000 mg.

45. The use of any one of claims 41-44, wherein the compound of Formula (I) is formulated as a tablet.

46. The use of any one of claims 41-45, wherein a therapeutically effective amount of a CDK4/6 inhibitor is to be further administered to the subject in need thereof.

47. The use of claim 46, wherein the CDK4/6 inhibitor is SHR6390, trilaciclib, lerociclib, AT7519M, dinaciclib, ribociclib, abemaciclib, or palbociclib.

48. The use of claim 46, wherein the CDK4/6 inhibitor is palbociclib.

49. The use of claim 48, wherein the effective amount of palbociclib is to be administered to the subject once a day.

50. The use of claims 48 or 49, wherein the effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg.

51. The use of any one of claims 48-50, wherein the palbociclib is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed by off treatment is repeated one, two, three, four, five, or more times.

52. The use of any one of claims 41-51, wherein the compound of Formula (I) is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of Formula (I) followed by off treatment is repeated one, two, three, four, five, or more times.

53. The use of any one of claims 41-52, wherein the subject is in a fed state.

54. The use of any one of claims 41-52, wherein the subject is in a fasted state.

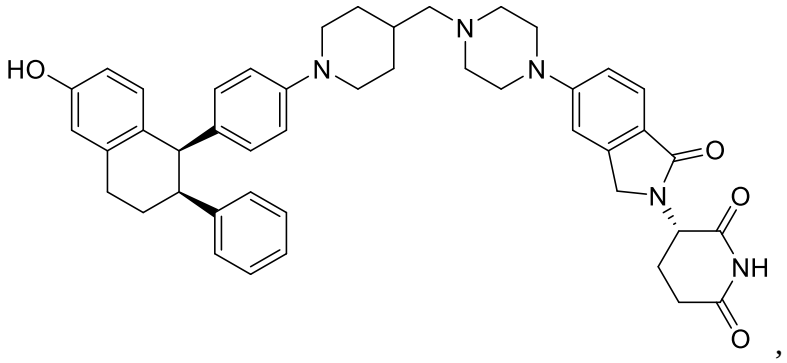
55. The use of any one of claims 46-54, wherein the CDK4/6 inhibitor is to be administered before the compound of Formula (I) is to be administered.

56. The use of claim 55, wherein the CDK4/6 inhibitor is to be administered at least 30 minutes before the compound of Formula (I) is to be administered.

57. The use of any one of claims 46-54, wherein the CDK4/6 inhibitor is to be administered after the compound of Formula (I) is to be administered.

58. The use of claim 57, wherein the CDK4/6 inhibitor is to be administered at least 30 minutes after the compound of Formula (I) is to be administered.

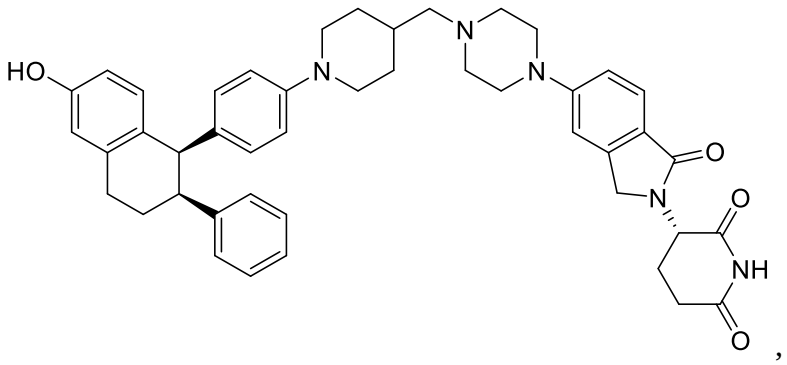
59. Use of a compound of Formula (I-c),



,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and wherein palbociclib is to be further administered orally once a day.

60. Use of a compound of Formula (I-c),



,

in the manufacture of a medicament for treating metastatic breast cancer in a subject in need thereof, wherein a therapeutically effective amount of the compound is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

61. The use of claim 59 or claim 60, wherein the therapeutically effective amount of the compound of Formula (I-c) is about 30 mg to about 1000 mg.

62. The use of any one of claims 59-61, wherein the therapeutically effective amount of palbociclib is 60 mg, 75 mg, 100 mg, or 125 mg.

63. The use of any one of claims 59-62, wherein the palbociclib is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with palbociclib followed by off treatment is repeated one, two, three, four, five, or more times.

64. The use of any one of claims 59-62, wherein the compound of Formula (I-c) is to be administered once daily for up to 21 consecutive days, followed by up to 7 consecutive days off treatment, wherein the cycle of treatment with the compound of Formula (I-c) followed by off treatment is repeated one, two, three, four, five, or more times.

65. The use of any one of claims 59-64, wherein the subject is in a fed state.

66. The use of any one of claims 59-64, wherein the subject is in a fasted state.

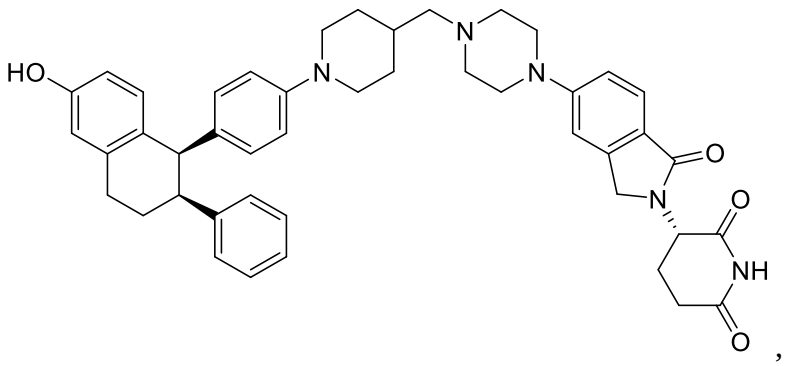
67. The use of any one of claims 59-66, wherein palbociclib is to be administered before the compound of Formula (I-c) is to be administered.

68. The use of claim 67, wherein palbociclib is to be administered at least 30 minutes before the compound of Formula (I-c) is to be administered.

69. The use of any one of claims 59-66, wherein palbociclib is to be administered after the compound of Formula (I-c) is to be administered.

70. The use of claim 69, wherein palbociclib is to be administered at least 30 minutes after the compound of Formula (I-c) is to be administered.

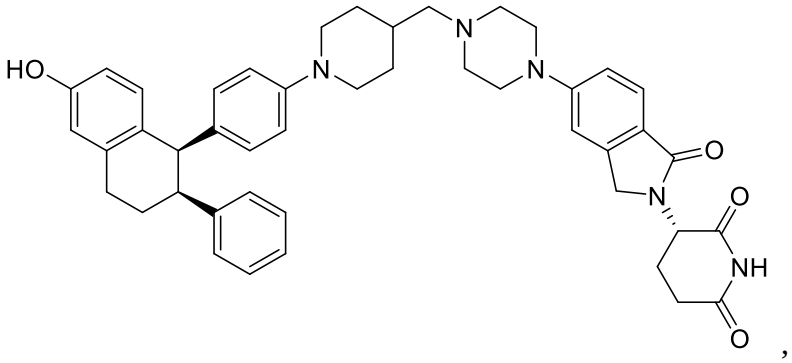
71. Use of a compound of Formula (I-c),



,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for selective estrogen receptor degradation in a patient, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

72. Use of a compound of Formula (I-c),

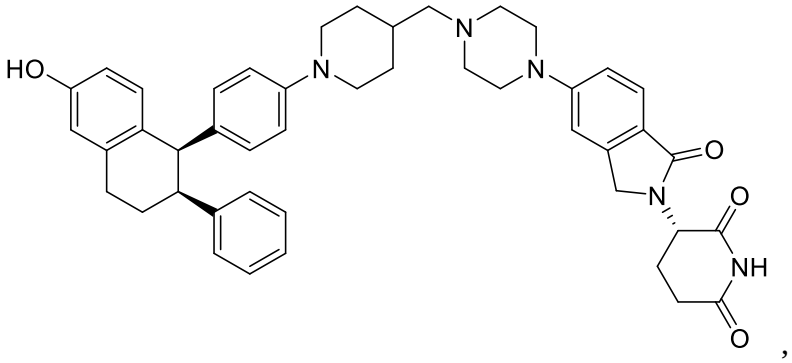


,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inhibiting a cyclin-dependent kinase in a subject in need thereof, wherein a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally once a day, and palbociclib is to be further administered orally once a day.

73. A kit comprising:

(i) a compound of Formula (I-c),

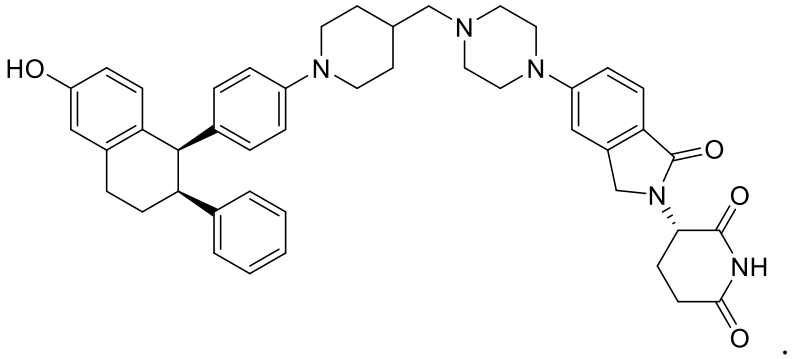


,

(ii) palbociclib, and

(iii) instructions for use.

74. A liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c):

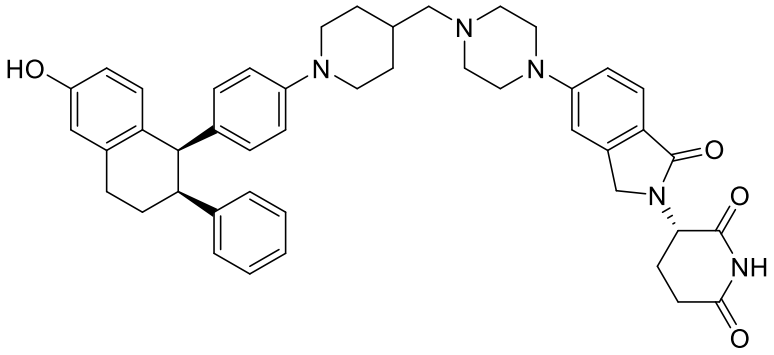


.

75. The liquid composition of claim 74, wherein the surfactant is Tween 80.

76. The liquid composition of claim 74 or 75, wherein the solvent is PEG-400.

77. A method of making a liquid composition comprising a surfactant, a solvent, and a compound of Formula (I-c):



comprising the step of adding the solvent to a pre-aliquoted volume of the surfactant.

78. The method of claim 77, wherein the surfactant is Tween 80.

79. The method of claim 77 or 78, wherein the solvent is PEG-400.