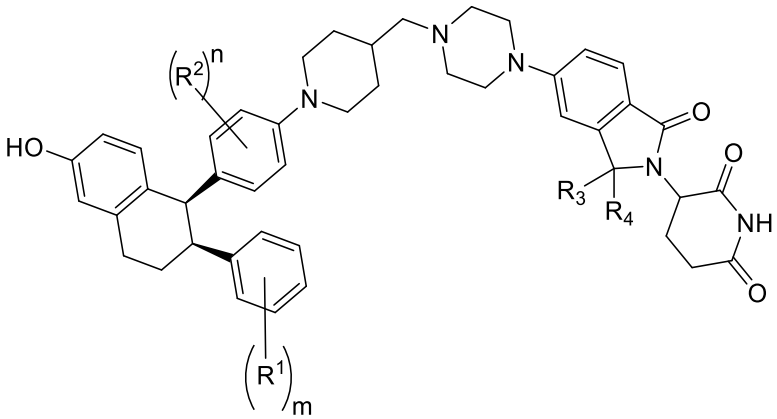
intervals [CI] 9.7-18.8%) and for the 250 mg dose was 14.6% (CI 10.5-19.4%) (Astra Zeneca Faslodex Full Prescribing Information, revised 03/2019).

Summary of the Disclosure

[0007a] In an aspect of the present disclosure, there is provided a use of a combination comprising palbociclib and a compound of Formula (I),



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

each R^1 and 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 taken together with the carbon to which they are attached, form a carbonyl;

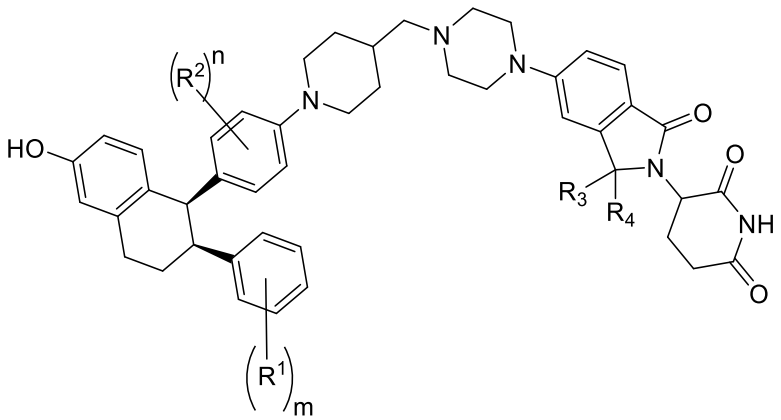
each R_5 and R_6 is independently selected from hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

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

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

in the manufacture of a medicament for the treatment of breast cancer in a subject, wherein about 10 mg to about 1000 mg of the compound of Formula (I), or pharmaceutically acceptable salt thereof, and the palbociclib are to be administered to the subject.

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



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

each R^1 and 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, taken together with the carbon to which they are attached, form a carbonyl;

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

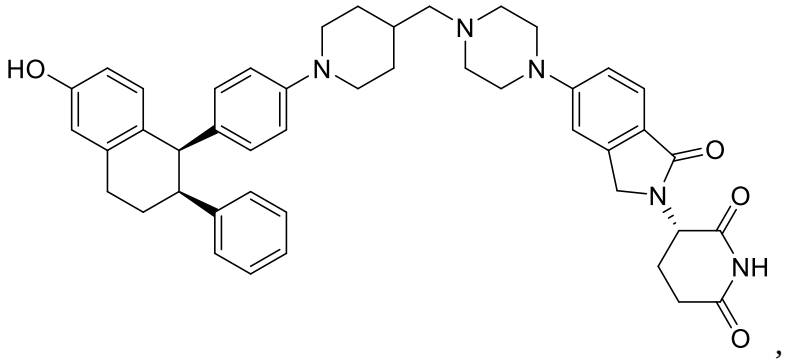
m is 0, 1, 2, 3, 4, or 5; and

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

in the manufacture of a medicament for the treatment of breast cancer in a subject, wherein about 10 mg to about 1000 mg of the compound of Formula (I), or pharmaceutically acceptable salt thereof, and palbociclib are to be co-administered to the subject.

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

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

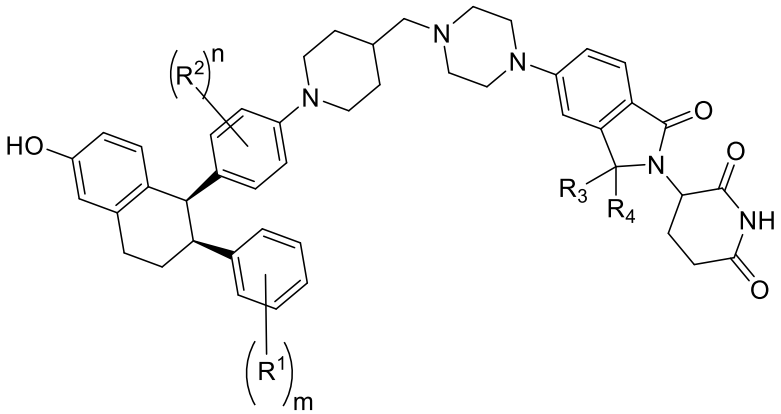


,

(ii) palbociclib, and

(iii) instructions for use.

[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-.

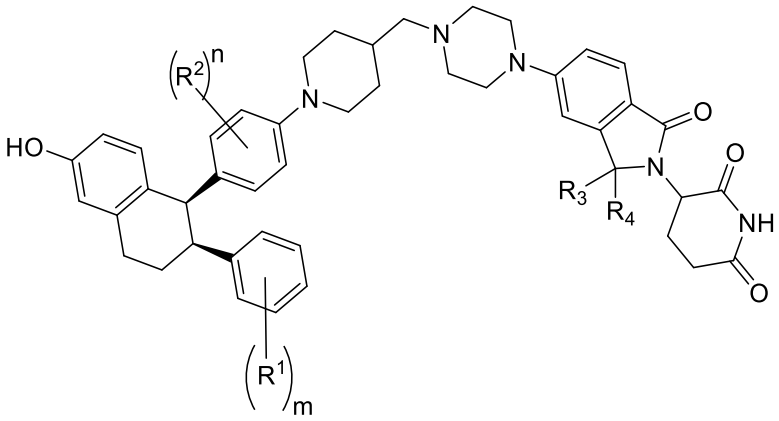
[0010] In one example, the breast cancer is metastatic or locally advanced.

[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.

What is claimed is:

1. Use of a combination comprising palbociclib and a compound of Formula (I),



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

each R^1 and 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, taken together with the carbon to which they are attached, form a carbonyl;

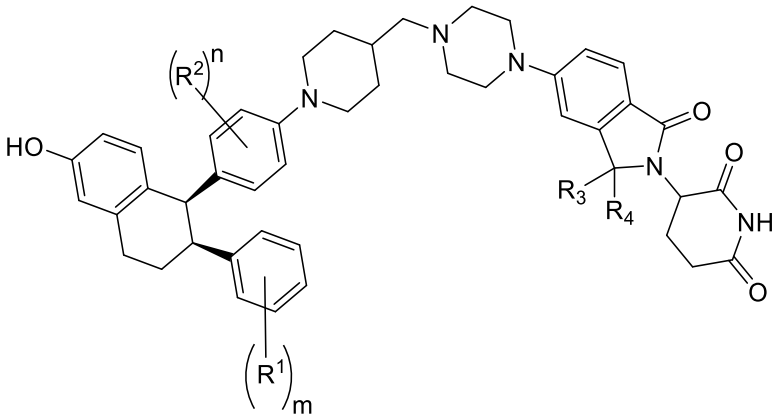
each R_5 and R_6 is independently selected from hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

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

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

in the manufacture of a medicament for the treatment of breast cancer in a subject, wherein about 10 mg to about 1000 mg of the compound of Formula (I), or pharmaceutically acceptable salt thereof, and the palbociclib are to be co-administered to the subject.

2. Use of a compound of Formula (I),



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

each R^1 and 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, taken together with the carbon to which they are attached, form a carbonyl;

each R_5 and 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,

in the manufacture of a medicament for the treatment of breast cancer in a subject, wherein about 10 mg to about 1000 mg of the compound of Formula (I), or pharmaceutically acceptable salt thereof, and palbociclib are to be co-administered to the subject.

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

4. The use of any one of claims 1-3, wherein the breast cancer is metastatic or locally advanced.

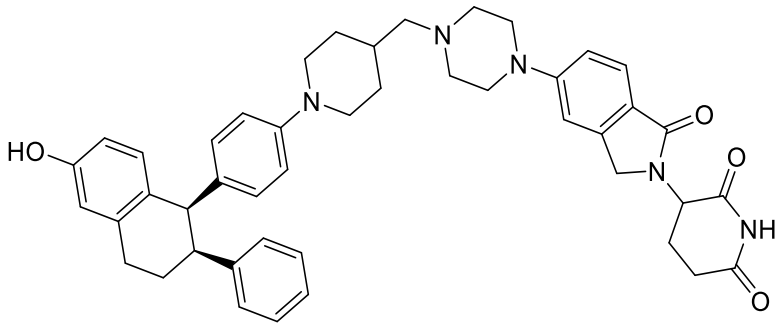
5. The use of any one of claims 1-4, wherein R^1 and R^2 are each independently halogen or OR_5.

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

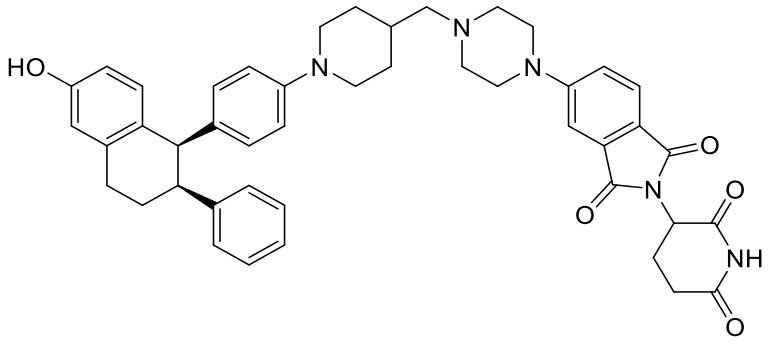
7. The use of any one of claims 1-5, wherein R_3 and R_4, taken together with the carbon to which they are attached, form a carbonyl.

8. The use of any one of claims 1-7, wherein m and n are each 0; or m and n are each 1; or one of m and n is 0 and the other is 1.

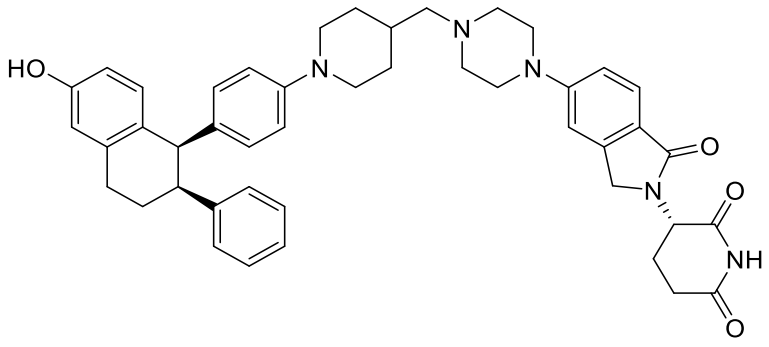
9. The use of any one of claims 1-4, wherein the compound of Formula (I) is:



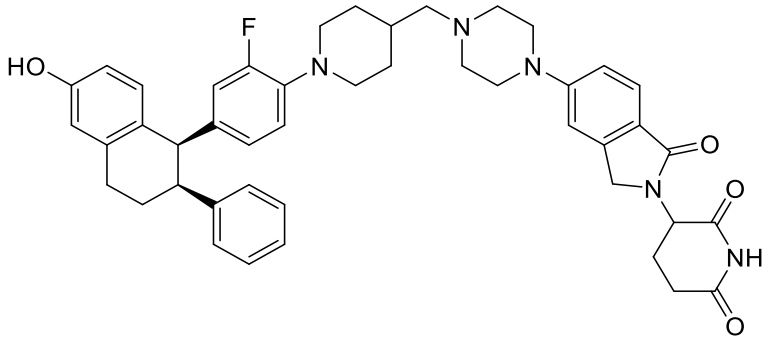
(I-a);



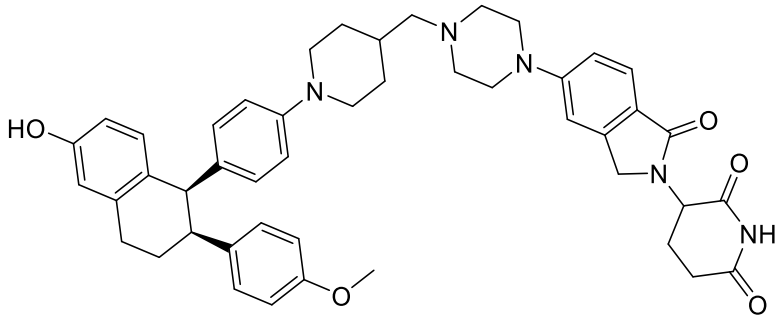
(I-b);



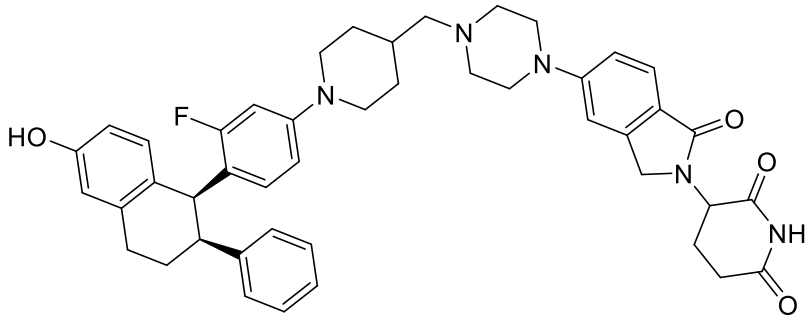
(I-c);



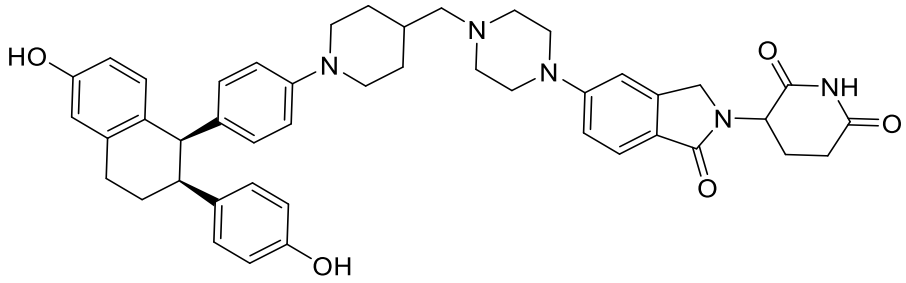
(I-d);



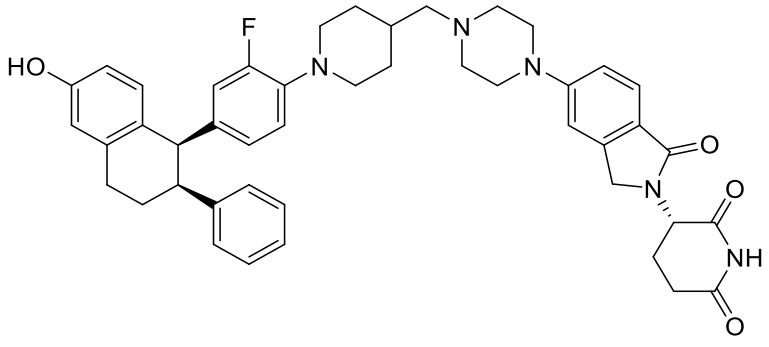
(I-e);



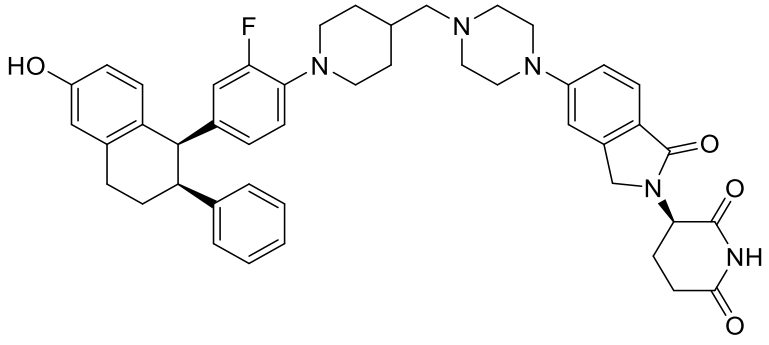
(I-f);



(I-g);



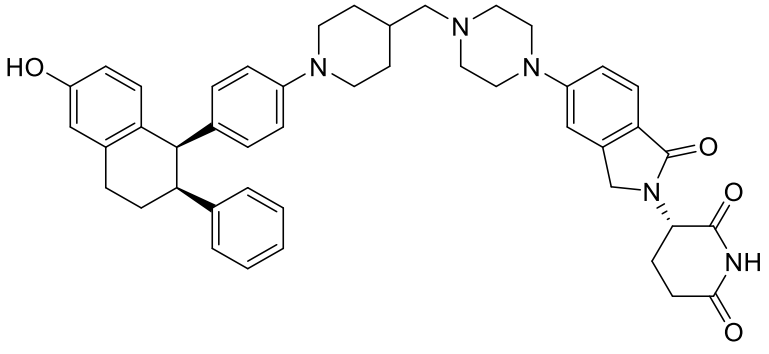
(I-h); or



(I-i);

or a pharmaceutically acceptable salt thereof.

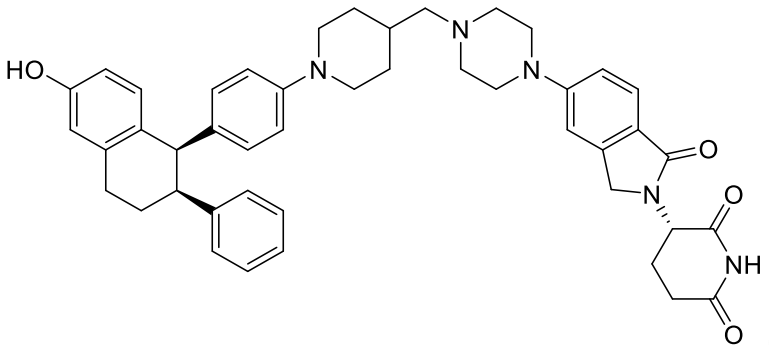
10. The use of any one of claims 1–4, wherein the compound of Formula (I) is a compound of Formula (I-c):



(I-c)

or a pharmaceutically acceptable salt thereof.

11. The use of any one of claims 1-4, wherein the compound of Formula (I) is a compound of Formula (I-c):



(I-c).

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

13. The use of any one of claims 1-12, wherein the compound of Formula (I), or pharmaceutically acceptable salt thereof, 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 compound of Formula (I), or pharmaceutically acceptable salt thereof, is to be administered to the subject all at once or is to be administered in two, three, or four portions.

15. The use of any one of claims 1-14, wherein the amount of the compound of Formula (I) is about 10 mg, about 15 mg, about 20 mg, about 25 mg, or about 30 mg; or
the amount of the compound of Formula (I) is 20 mg to 750 mg; or
the amount of the compound of Formula (I) is 30 mg to 500 mg; or
the amount of the compound of Formula (I) is 30 mg to 120 mg.

16. The use of any one of claims 1-15, wherein the compound of Formula (I), or pharmaceutically acceptable salt thereof, is formulated as a tablet.

17. The use of claim 16, wherein the tablet comprises a compound of Formula (I), or pharmaceutically acceptable salt thereof, and, optionally, one or more of the following: emulsifier; surfactant; binder; disintegrant; glidant; and lubricant.

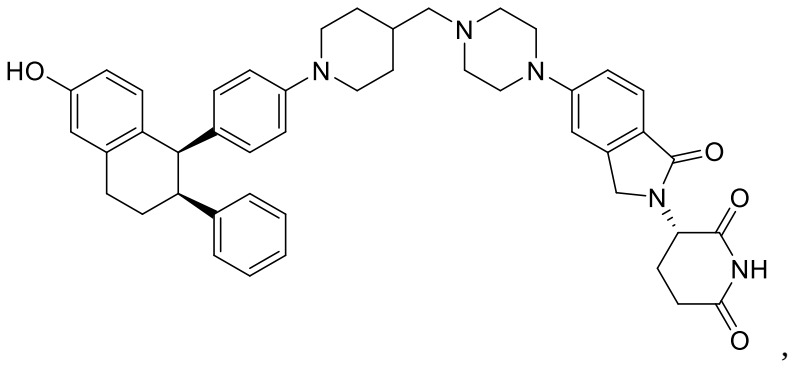
18. The use of claim 17, wherein
the emulsifier is hypromellose;
the surfactant is vitamin E polyethylene glycol succinate;
the binder is microcrystalline cellulose or lactose monohydrate;
the disintegrant is croscarmellose sodium;
the glidant is silicon dioxide; and/or
the lubricant is sodium stearyl fumarate.

19. The use of any one of claims 1-18, wherein the palbociclib is provided in an amount selected from 60 mg, 75 mg, 100 mg, and 125 mg.

20. The use of any one of claims 1-19, 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.

21. The use of any one of claims 1–20, wherein the compound of Formula (I), or pharmaceutically acceptable salt thereof, 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), or pharmaceutically acceptable salt thereof, followed by off treatment is repeated one, two, three, four, five, or more times.

22. A kit comprising:
(i) a compound of Formula (I-c),



,

(ii) palbociclib, and

(iii) instructions for use.