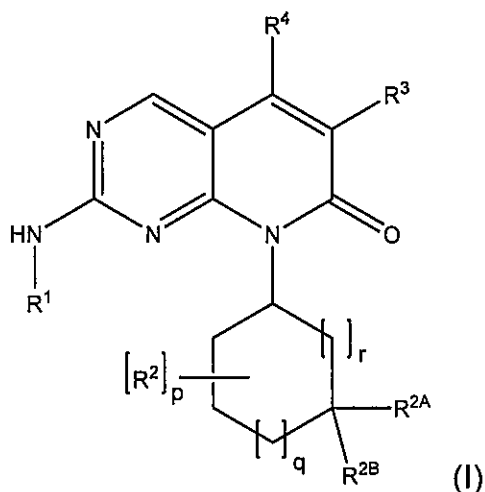


Claims

5 1. A compound of Formula (I):



or a pharmaceutically acceptable salt thereof,

wherein:

10 R^1 is 3-10 membered heterocyclyl substituted by R^{5A} or C_3 - C_8 cycloalkyl substituted by R^{5B} , where said 3-10 membered heterocyclyl and C_3 - C_8 cycloalkyl are optionally further substituted by one or more R^6 ;

each R^2 is independently F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

15 R^{2A} and R^{2B} are independently H, F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

where each said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl in R^2 , R^{2A} and R^{2B} is independently optionally substituted by OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

20 R^3 is H, F, Cl, NH_2 , C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH, CN, C_1 - C_4 alkoxy, C_1 - C_4 fluoroalkoxy, $CONH_2$ and $COOH$;

R^4 is H, C_1 - C_2 alkyl or C_1 - C_2 fluoroalkyl;

R^{5A} is SO_2R^7 , $SO_2NR^8R^9$, $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

R^{5B} is $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

25 each R^6 is independently F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

R^7 is C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, -L-(C_3 - C_8 cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl);

R^8 and R^9 are independently H, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, -L-(C_3 - C_8 cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl); or

R^8 and R^9 may be taken together with the nitrogen atom to which they are attached to form a 5-6 membered heterocyclyl;

5 where each said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl in R^7 , R^8 and R^9 is optionally substituted by OH, C_1 - C_4 alkoxy, C_1 - C_4 fluoroalkoxy or SO_2Me , and each said C_3 - C_8 cycloalkyl, 5-6 membered heterocyclyl and 5-6 membered heteroaryl in R^7 , R^8 and R^9 is optionally substituted by C_1 - C_4 alkyl, OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

10 L is a bond or C_1 - C_4 alkylene, where said C_1 - C_4 alkylene is optionally substituted by OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

p is 0, 1, 2, 3 or 4;

q is 0, 1, 2 or 3; and

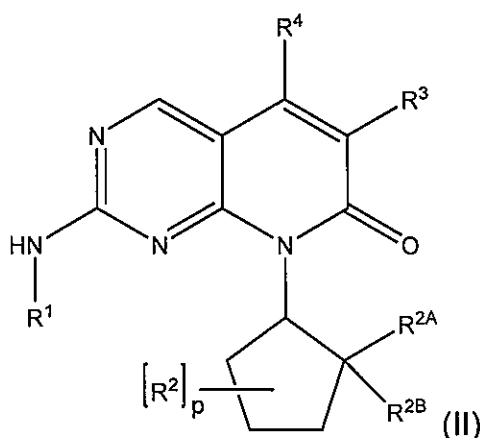
r is 0, 1 or 2.

15 2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is 3-10 membered heterocyclyl substituted by R^{5A} and optionally further substituted by one or more R^6 ; and R^{5A} is SO_2R^7 or $SO_2NR^8R^9$.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^3 is F, Cl, C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH.

20 4. The compound of claim 1, 2 or 3, or a pharmaceutically acceptable salt thereof, wherein R^{2A} and R^{2B} are independently H, OH or C_1 - C_4 alkyl.

5. A compound of Formula (II):



or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is 3-10 membered heterocyclyl substituted by R^{5A} or C_3-C_8 cycloalkyl substituted by R^{5B} , where said 3-10 membered heterocyclyl and C_3-C_8 cycloalkyl are optionally further substituted by one or more R^6 ;

each R^2 is independently F, OH, C_1-C_4 alkyl, C_1-C_4 fluoroalkyl, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy;

R^{2A} and R^{2B} are independently H, F, OH, C_1-C_4 alkyl, C_1-C_4 fluoroalkyl, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy;

where each said C_1-C_4 alkyl and C_1-C_4 fluoroalkyl in R^2 , R^{2A} and R^{2B} is independently optionally substituted by OH, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy;

R^3 is H, F, Cl, NH_2 , C_1-C_4 alkyl or C_1-C_4 fluoroalkyl, where said C_1-C_4 alkyl and C_1-C_4 fluoroalkyl are optionally substituted by OH, CN, C_1-C_4 alkoxy, C_1-C_4 fluoroalkoxy, $CONH_2$ and $COOH$;

R^4 is H, C_1-C_2 alkyl or C_1-C_2 fluoroalkyl;

R^{5A} is SO_2R^7 , $SO_2NR^8R^9$, $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

R^{5B} is $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

each R^6 is independently F, OH, C_1-C_4 alkyl, C_1-C_4 fluoroalkyl, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy;

R^7 is C_1-C_4 alkyl, C_1-C_4 fluoroalkyl, $-L-(C_3-C_8$ cycloalkyl), $-L-(5-6$ membered heterocyclyl) or $-L-(5-6$ membered heteroaryl);

R^8 and R^9 are independently H, C_1-C_4 alkyl, C_1-C_4 fluoroalkyl, $-L-(C_3-C_8$ cycloalkyl), $-L-(5-6$ membered heterocyclyl) or $-L-(5-6$ membered heteroaryl); or

R^8 and R^9 may be taken together with the nitrogen atom to which they are attached to form a 5-6 membered heterocyclyl;

where each said C_1-C_4 alkyl and C_1-C_4 fluoroalkyl in R^7 , R^8 and R^9 is optionally substituted by OH, C_1-C_4 alkoxy, C_1-C_4 fluoroalkoxy or SO_2Me , and each said C_3-C_8 cycloalkyl, 5-6 membered heterocyclyl and 5-6 membered heteroaryl in R^7 , R^8 and R^9 is optionally substituted by C_1-C_4 alkyl, OH, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy;

L is a bond or C_1-C_4 alkylene, where said C_1-C_4 alkylene is optionally substituted by OH, C_1-C_4 alkoxy or C_1-C_4 fluoroalkoxy; and

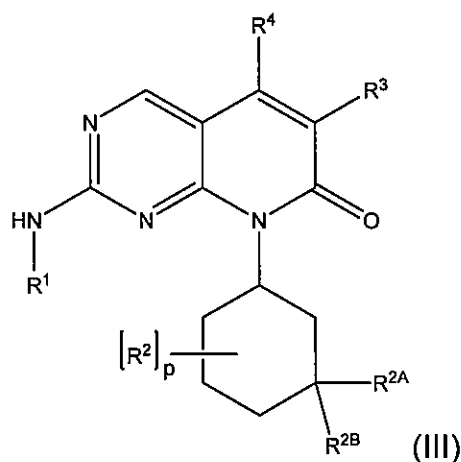
p is 0, 1, 2, 3 or 4.

6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein R^1 is 3-10 membered heterocyclyl substituted by R^{5A} and optionally further substituted by one or more R^6 ; and R^{5A} is SO_2R^7 or $SO_2NR^8R^9$.

7. The compound of claim 5 or 6, or a pharmaceutically acceptable salt thereof, wherein R^3 is F, Cl, C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH.

8. The compound of claims 5, 6 or 7, or a pharmaceutically acceptable salt thereof, wherein R^{2A} and R^{2B} are independently H, OH or C_1 - C_4 alkyl.

9. A compound of Formula (III):



or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is 3-10 membered heterocyclyl substituted by R^{5A} or C_3 - C_8 cycloalkyl substituted by R^{5B} , where said 3-10 membered heterocyclyl and C_3 - C_8 cycloalkyl are optionally further substituted by one or more R^6 ;

each R^2 is independently F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

R^{2A} and R^{2B} are independently H, F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

where each said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl in R^2 , R^{2A} and R^{2B} is independently optionally substituted by OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

R^3 is H, F, Cl, NH_2 , C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH, CN, C_1 - C_4 alkoxy, C_1 - C_4 fluoroalkoxy, $CONH_2$ and $COOH$;

R^4 is H, C_1 - C_2 alkyl or C_1 - C_2 fluoroalkyl;

R^{5A} is SO_2R^7 , $SO_2NR^8R^9$, $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

R^{5B} is $NHSO_2R^7$ or $NHSO_2NR^8R^9$;

each R^6 is independently F, OH, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

5 R^7 is C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, -L-(C_3 - C_8 cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl);

R^8 and R^9 are independently H, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, -L-(C_3 - C_8 cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl); or

10 R^8 and R^9 may be taken together with the nitrogen atom to which they are attached to form a 5-6 membered heterocyclyl;

where each said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl in R^7 , R^8 and R^9 is optionally substituted by OH, C_1 - C_4 alkoxy, C_1 - C_4 fluoroalkoxy or SO_2Me , and each said C_3 - C_8 cycloalkyl, 5-6 membered heterocyclyl and 5-6 membered heteroaryl in R^7 , R^8 and R^9 is optionally substituted by C_1 - C_4 alkyl, OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

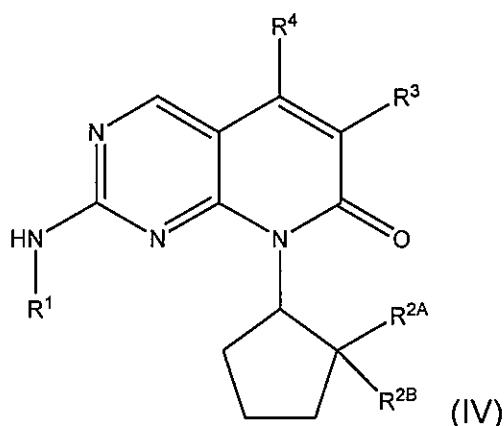
15 L is a bond or C_1 - C_4 alkylene, where said C_1 - C_4 alkylene is optionally substituted by OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy; and
p is 0, 1, 2, 3 or 4.

20 10. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein R^1 is 3-10 membered heterocyclyl substituted by R^{5A} and optionally further substituted by one or more R^6 ; and R^{5A} is SO_2R^7 or $SO_2NR^8R^9$.

25 11. The compound of claim 9 or 10, or a pharmaceutically acceptable salt thereof, wherein R^3 is F, Cl, C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH.

12. The compound of claims 9, 10 or 11, or a pharmaceutically acceptable salt thereof, wherein R^{2A} and R^{2B} are independently H, OH or C_1 - C_4 alkyl.

30 13. A compound of Formula (IV):



or a pharmaceutically acceptable salt thereof,

wherein:

R¹ is 3-10 membered heterocyclyl substituted by R^{5A} or C₃-C₈ cycloalkyl substituted by R^{5B}, where said 3-10 membered heterocyclyl and C₃-C₈ cycloalkyl are optionally further substituted by one or more R⁶;

R^{2A} and R^{2B} are independently H, F, OH, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, C₁-C₄ alkoxy or C₁-C₄ fluoroalkoxy;

where each said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl in R^{2A} and R^{2B} is independently optionally substituted by OH, C₁-C₄ alkoxy or C₁-C₄ fluoroalkoxy; R³ is H, F, Cl, NH₂, C₁-C₄ alkyl or C₁-C₄ fluoroalkyl, where said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl are optionally substituted by OH, CN, C₁-C₄ alkoxy, C₁-C₄ fluoroalkoxy, CONH₂ and COOH;

R⁴ is H, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl;

R^{5A} is SO₂R⁷, SO₂NR⁸R⁹, NHSO₂R⁷ or NHSO₂NR⁸R⁹;

R^{5B} is NHSO₂R⁷ or NHSO₂NR⁸R⁹;

each R⁶ is independently F, OH, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, C₁-C₄ alkoxy or C₁-C₄ fluoroalkoxy;

R⁷ is C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, -L-(C₃-C₈ cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl);

R⁸ and R⁹ are independently H, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, -L-(C₃-C₈ cycloalkyl), -L-(5-6 membered heterocyclyl) or -L-(5-6 membered heteroaryl); or

R⁸ and R⁹ may be taken together with the nitrogen atom to which they are attached to form a 5-6 membered heterocyclyl;

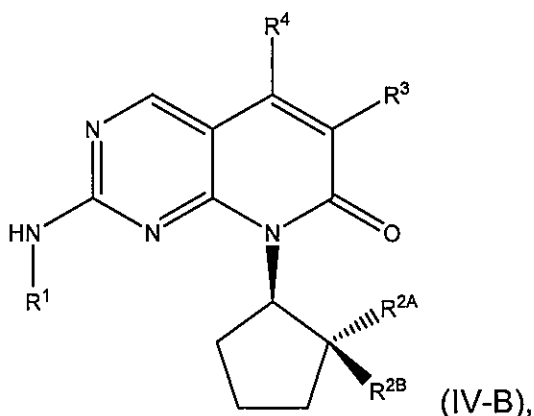
where each said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl in R⁷, R⁸ and R⁹ is optionally substituted by OH, C₁-C₄ alkoxy, C₁-C₄ fluoroalkoxy or SO₂Me, and each said C₃-C₈ cycloalkyl, 5-6 membered heterocyclyl and 5-6 membered

heteroaryl in R^7 , R^8 and R^9 is optionally substituted by C_1 - C_4 alkyl, OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy;

L is a bond or C_1 - C_4 alkylene, where said C_1 - C_4 alkylene is optionally substituted by OH, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy; and

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

14. The compound of claim 13, having the Formula (IV-B):



or a pharmaceutically acceptable salt thereof.

15. The compound of claim 13 or 14, or a pharmaceutically acceptable salt thereof, wherein R^1 is 5-6 membered heterocyclyl substituted by R^{5A} ; and R^{5A} is SO_2R^7 or $SO_2NR^8R^9$.

16. The compound of claim 13, 14 or 15, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_1 - C_4 alkyl or C_1 - C_4 fluoroalkyl, where said C_1 - C_4 alkyl and C_1 - C_4 fluoroalkyl are optionally substituted by OH.

17. The compound of any one of claims 13 to 16, or a pharmaceutically acceptable salt thereof, wherein R^{2A} and R^{2B} are independently H, OH or C_1 - C_4 alkyl, provided at least one of R^{2A} and R^{2B} is not H.

18. The compound of any one of claims 13 to 16, or a pharmaceutically acceptable salt thereof, wherein: (a) R^{2A} is OH and R^{2B} is H; (b) R^{2A} is OH and R^{2B} is CH_3 ; or (c) R^{2A} is H and R^{2B} is CH_3 .

19. A pharmaceutical composition comprising a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

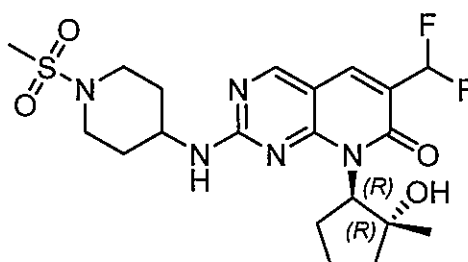
20. A method for the treatment of cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof.

21. The method of claim 20, wherein the cancer is (a) breast cancer or ovarian cancer; (b) characterized by amplification or overexpression of cyclin E1 (CCNE1) or cyclin E2 (CCNE2); or (c) both (a) and (b).

22. Use of a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, for the treatment of cancer in a subject in need thereof.

23. The use of claim 22, wherein the cancer is (a) breast cancer or ovarian cancer; (b) characterized by amplification or overexpression of cyclin E1 (CCNE1) or cyclin E2 (CCNE2); or (c) both (a) and (b).

24. A compound of the formula:



or a pharmaceutically acceptable salt thereof.

25. A pharmaceutical composition comprising a compound of claim 24, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.