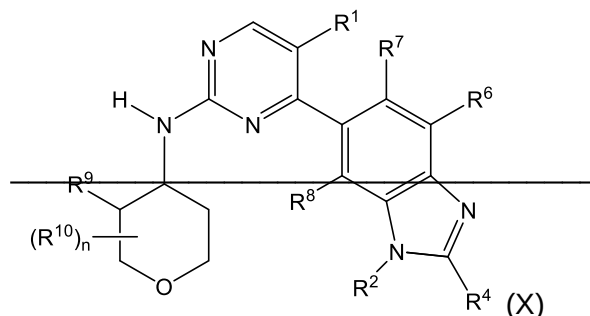


Claims

1. A compound of Formula (X):



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H, F, Cl, CN, C_1 - C_2 alkyl or C_1 - C_2 fluoroalkyl, where each said C_1 - C_2 alkyl and C_1 - C_2 fluoroalkyl is optionally substituted by R^{20} ;

R^2 is H, C_1 - C_5 alkyl, C_1 - C_5 fluoroalkyl, C_3 - C_8 cycloalkyl or 3-6 membered heterocyclyl, where each said C_1 - C_5 alkyl and C_1 - C_5 fluoroalkyl is optionally substituted by R^{20} and each said C_3 - C_8 cycloalkyl and 3-6 membered heterocyclyl is optionally substituted by R^{21} ;

R^4 is H, 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, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy and C_1 - C_4 fluoroalkoxy is optionally substituted by R^{20} ;

R^6 is H, F, Cl, CN, CH_3 , CH_2F , CHF_2 or CF_3 ;

R^7 and R^8 are independently H, F, Cl, CN, C_1 - C_2 alkyl, C_1 - C_2 fluoroalkyl, C_1 - C_2 alkoxy or C_1 - C_2 fluoroalkoxy, where each said C_1 - C_2 alkyl, C_1 - C_2 fluoroalkyl, C_1 - C_2 alkoxy and C_1 - C_2 fluoroalkoxy is optionally substituted by R^{20} ;

R^9 is H, OH, NH_2 , $NHCH_3$ or $N(CH_3)_2$;

each R^{10} is independently F, CN, C_1 - C_2 alkyl or C_1 - C_2 fluoroalkyl, where each said C_1 - C_2 alkyl and C_1 - C_2 fluoroalkyl is optionally substituted by R^{20} ;

each R^{20} is independently OH, C_1 - C_2 alkoxy, C_1 - C_2 fluoroalkoxy, CN or $NR^{22}R^{23}$;

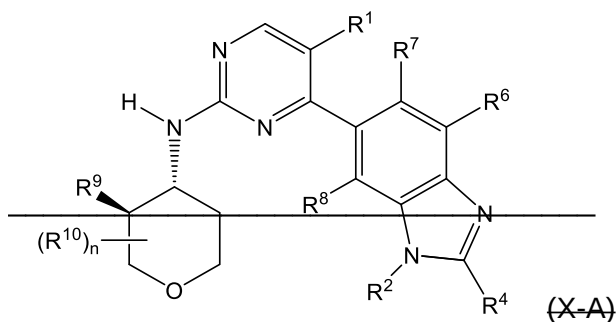
each R^{21} is independently F, OH, CN, $NR^{22}R^{23}$, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy or C_1 - C_4 fluoroalkoxy, where each said C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, C_1 - C_4 alkoxy and C_1 - C_4 fluoroalkoxy is optionally further substituted by OH, NH_2 , $NHCH_3$ or $N(CH_3)_2$;

each R^{22} and R^{23} is independently H, C_1 - C_2 alkyl or C_1 - C_2 fluoroalkyl; or

R^{22} and R^{23} may be taken together with the nitrogen atom to which they are attached to form an azetidiny ring, which is optionally substituted by F or OH; and

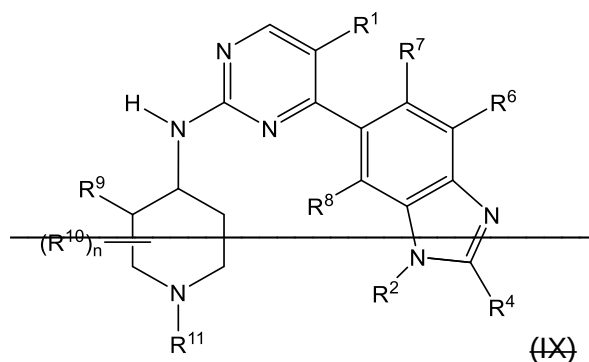
n is 0, 1, 2, 3 or 4.

2. The compound of claim 1, having the Formula (X-A):



or a pharmaceutically acceptable salt thereof.

3. A compound of Formula (IX):



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H, F, Cl, CN, C_1-C_2 alkyl or C_1-C_2 fluoroalkyl, where each said C_1-C_2 alkyl and C_1-C_2 fluoroalkyl is optionally substituted by R^{20} ;

R^2 is H, C_1-C_5 alkyl, C_1-C_5 fluoroalkyl, C_3-C_8 cycloalkyl or 3-6 membered heterocyclyl, where each said C_1-C_5 alkyl and C_1-C_5 fluoroalkyl is optionally substituted by R^{20} and each said C_3-C_8 cycloalkyl and 3-6 membered heterocyclyl is optionally substituted by R^{21} ;

R^4 is H, 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, C_1-C_4 fluoroalkyl, C_1-C_4 alkoxy and C_1-C_4 fluoroalkoxy is optionally substituted by R^{20} ;

R^6 is H, F, Cl, CN, CH_3 , CH_2F , CHF_2 or CF_3 ;

R^7 and R^8 are independently H, F, Cl, CN, C_1-C_2 alkyl, C_1-C_2 fluoroalkyl, C_1-C_2 alkoxy or C_1-C_2 fluoroalkoxy, where each said C_1-C_2 alkyl, C_1-C_2 fluoroalkyl, C_1-C_2 alkoxy and C_1-C_2 fluoroalkoxy is optionally substituted by R^{20} ;

R^9 is H, OH, NH_2 , $NHCH_3$ or $N(CH_3)_2$;

each R^{10} is independently F, CN, C_1-C_2 alkyl or C_1-C_2 fluoroalkyl, where each said C_1-C_2 alkyl and C_1-C_2 fluoroalkyl is optionally substituted by R^{20} ;

R^{11} is H, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, SO₂R¹⁴, SO₂NR¹⁵R¹⁶, COR¹⁷, COOR¹⁷ or CONR¹⁸R¹⁹;

R¹⁴ is C₁-C₄ alkyl or C₁-C₄ fluoroalkyl;

each R¹⁵ and R¹⁶ is independently H or CH₃;

R¹⁷ is C₁-C₄ alkyl or C₁-C₄ fluoroalkyl, where each said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl is optionally substituted by R²⁰;

each R¹⁸ and R¹⁹ is independently H, C₁-C₄ alkyl or C₁-C₄ fluoroalkyl, where each said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl is optionally substituted by R²⁰;

each R²⁰ is independently OH, C₁-C₂ alkoxy, C₁-C₂ fluoroalkoxy, CN or NR²²R²³;

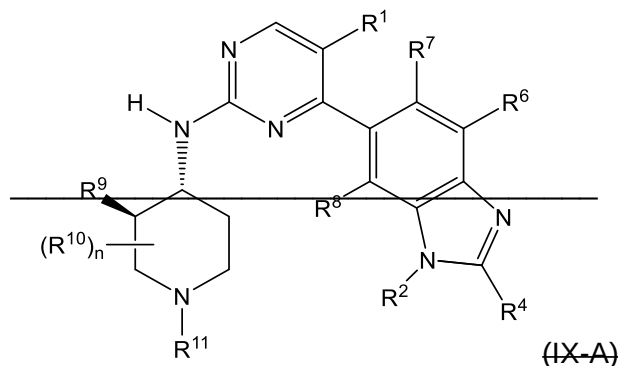
each R²¹ is independently F, OH, CN, NR²²R²³, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, C₁-C₄ alkoxy or C₁-C₄ fluoroalkoxy, where each said C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, C₁-C₄ alkoxy and C₁-C₄ fluoroalkoxy is optionally further substituted by OH, NH₂, NHCH₃ or N(CH₃)₂;

each R²² and R²³ is independently H, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl; or

R²² and R²³ may be taken together with the nitrogen atom to which they are attached to form an azetidiny ring, which is optionally substituted by F or OH; and

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

4. The compound of claim 3, having the Formula (IX-A):



or a pharmaceutically acceptable salt thereof.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R¹ is Cl.

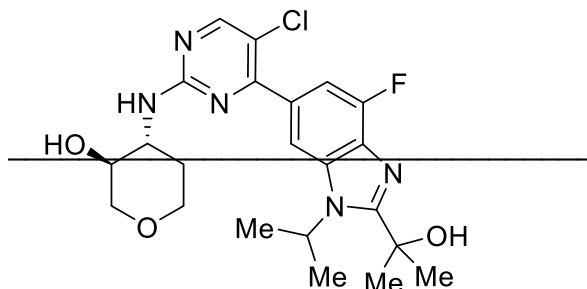
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R² is C₁-C₅ alkyl, where said C₁-C₅ alkyl is optionally substituted by R²⁰.

7. ~~The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R⁴ is C₁-C₄ alkyl, where said C₁-C₄ alkyl is optionally substituted by R²⁰.~~

8. ~~The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R²⁰ is OH.~~

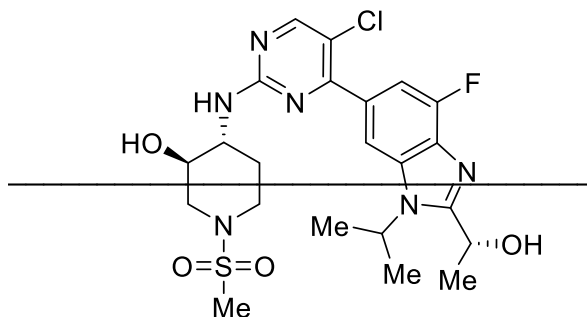
9. ~~The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R⁶ is F, R⁷ is H, and R⁸ is H.~~

10. ~~1,5-anhydro-3-((5-chloro-4-[4-fluoro-2-(2-hydroxypropan-2-yl)-1-(propan-2-yl)-1H-benzimidazol-6-yl]pyrimidin-2-yl)amino)-2,3-dideoxy-D-threo-pentitol, having the structure:~~



~~or a pharmaceutically acceptable salt thereof.~~

11. ~~(3R,4R)-4-[(5-chloro-4-{4-fluoro-2-[(1R)-1-hydroxyethyl]-1-(propan-2-yl)-1H-benzimidazol-6-yl]pyrimidin-2-yl)amino]-1-(methanesulfonyl)piperidin-3-ol, having the structure:~~



~~or a pharmaceutically acceptable salt thereof.~~

12. ~~A pharmaceutical composition comprising the compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.~~

13. A pharmaceutical composition comprising the compound of claim 10, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

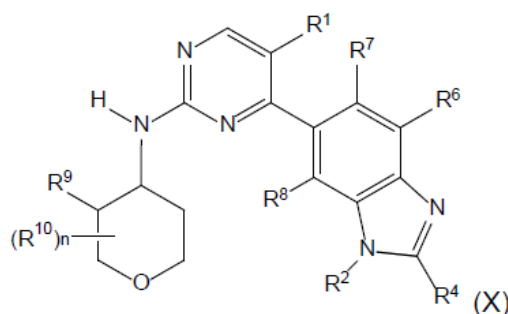
14. A pharmaceutical composition comprising the compound of claim 11, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

15. ~~The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof for use in the treatment of cancer.~~

16. ~~Use of the compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cancer.~~

Claims

1. A compound of Formula (X):



or a pharmaceutically acceptable salt or solvate thereof, wherein:

R₁ is H, F, Cl, CN, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl;

R₂ is H, C₁-C₅ alkyl, C₁-C₅ fluoroalkyl, C₃-C₈ cycloalkyl, oxolanyl, azetidynyl or oxetanyl, where each said C₁-C₅ alkyl and C₁-C₅ fluoroalkyl is optionally substituted by R²⁰ and said C₃-C₈ cycloalkyl is optionally substituted by R²¹;

R₄ is H, C₁-C₄ alkyl, or C₁-C₄ fluoroalkyl, where each said C₁-C₄ alkyl and C₁-C₄ fluoroalkyl is optionally substituted by R²⁰;

R₆ is H, F, or Cl;

R₇ and R₈ are independently H, F, or Cl;

R₉ is OH;

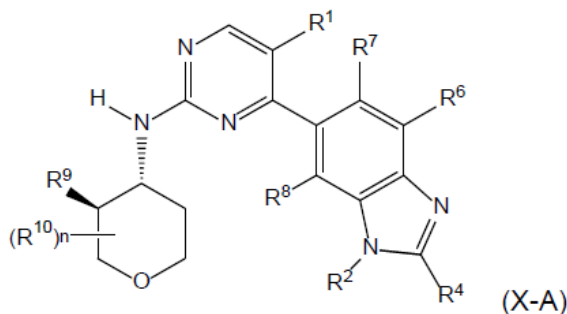
each R¹⁰ is independently F, CN, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl, where each said C₁-C₂ alkyl and C₁-C₂ fluoroalkyl is optionally substituted by R²⁰;

each R²⁰ is independently OH, C₁-C₂ alkoxy or CN;

each R²¹ is independently F; and

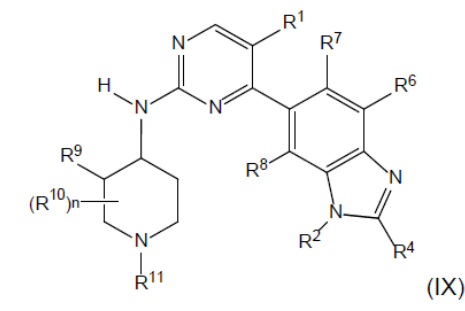
n is 0.

2. The compound of claim 1, having the Formula (X-A):



or a pharmaceutically acceptable salt or solvate thereof.

3. A compound of Formula (IX):



or a pharmaceutically acceptable salt or solvate thereof, wherein:

R₁ is H, F, Cl, CN, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl;

R₂ is H, C₁-C₅ alkyl, C₁-C₅ fluoroalkyl, C₃-C₈ cycloalkyl, oxolanyl, azetidinyI or oxetanyl,

where each said C₁-C₅ alkyl and C₁-C₅ fluoroalkyl is optionally substituted by R²⁰ and said C₃-C₈ cycloalkyl is optionally substituted by R²¹;

R₄ is H, C₁-C₄ alkyl, or C₁-C₄ fluoroalkyl, where each said C₁-C₄ alkyl, and C₁-C₄ fluoroalkyl is optionally substituted by R²⁰;

R₆ is H, F, or Cl;

R₇ and R₈ are independently H, F, or Cl;

R₉ is OH;

each R¹⁰ is independently F, CN, C₁-C₂ alkyl or C₁-C₂ fluoroalkyl, where each said C₁-C₂ alkyl and C₁-C₂ fluoroalkyl is optionally substituted by R²⁰;

R₁₁ is SO₂R¹⁴;

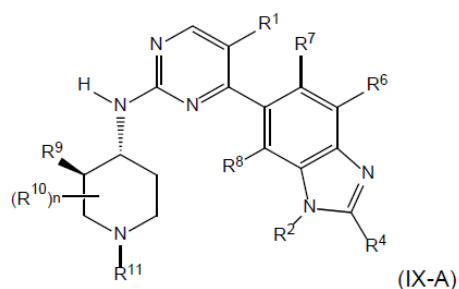
R₁₄ is C₁-C₄ alkyl;

each R²⁰ is independently OH, C₁-C₂ alkoxy or CN;

each R²¹ is independently F; and

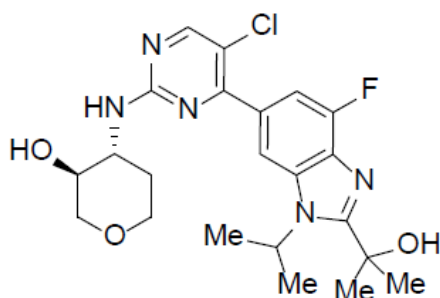
n is 0.

4. The compound of claim 3, having the Formula (IX-A):



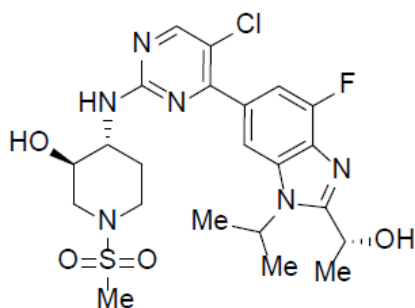
or a pharmaceutically acceptable salt or solvate thereof.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is Cl.
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt or solvate thereof, wherein R^2 is C₁-C₅ alkyl, where said C₁-C₅ alkyl is optionally substituted by R^{20} .
7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt or solvate thereof, wherein R^4 is C₁-C₄ alkyl, where said C₁-C₄ alkyl is optionally substituted by R^{20} .
8. The compound of claim 7, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{20} is OH.
9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt or solvate thereof, wherein R^6 is F, R^7 is H, and R^8 is H.
10. 1,5-anhydro-3-({5-chloro-4-[4-fluoro-2-(2-hydroxypropan-2-yl)-1-(propan-2-yl)-1H-benzimidazol-6-yl]pyrimidin-2-yl}amino)-2,3-dideoxy-D-threo-pentitol, having the structure:



or a pharmaceutically acceptable salt or solvate thereof.

11. (3R,4R)-4-[(5-chloro-4-{4-fluoro-2-[(1R)-1-hydroxyethyl]-1-(propan-2-yl)-1H-benzimidazol-6-yl}pyrimidin-2-yl)amino]-1-(methanesulfonyl)piperidin-3-ol, having the structure:



or a pharmaceutically acceptable salt or solvate thereof.

12. A pharmaceutical composition comprising the compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier or excipient.

13. The pharmaceutical composition of claim 12, to be used for the treatment of cancer in a subject.

14. The pharmaceutical composition of claim 13, wherein the cancer is selected from the group consisting of breast cancer, ovarian cancer, bladder cancer, uterine cancer, prostate cancer, lung cancer, esophageal cancer, head and neck cancer, colorectal cancer, kidney cancer, liver cancer, pancreatic cancer, stomach cancer and thyroid cancer.

15. The pharmaceutical composition of claim 13, wherein the cancer is selected from the group consisting of ER-positive/HR-positive breast cancer, HER2-negative breast cancer, ER-positive/HR-positive breast cancer, HER2-positive breast cancer; triple negative breast cancer (TNBC), and inflammatory breast cancer.

16. The pharmaceutical composition of claim 15, wherein the breast cancer is advanced or metastatic breast cancer.

17. The pharmaceutical composition of claim 13, wherein the cancer is prostate cancer.

18. The pharmaceutical composition of claim 13, wherein the cancer is lung cancer.

19. The pharmaceutical composition of claim 13, wherein the cancer is colorectal cancer.
20. The pharmaceutical composition of any one of claims 13 to 19, to be used for the treatment of cancer in combination with an additional anti-cancer agent.
21. The pharmaceutical composition of claim 20, wherein the additional anti-cancer agent is an endocrine agent selected from the group consisting of an aromatase inhibitor, a selective estrogen receptor downregulator (SERD), and a selective estrogen receptor modulator (SERM).
22. The pharmaceutical composition of claim 21, wherein the endocrine agent is letrozole or fulvestrant.