In another aspect, there is provided a compound selected from the group consisting of compounds 1-102, 104-107, 110-121, 125-127, 131-168, 170-206, 208-209, 212-276, 278-328 and pharmaceutically acceptable salts thereof.

In another aspect, the disclosure provides a pharmaceutical composition comprising the compound disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient. In some examples, the composition is isotopically enriched in deuterium.

In yet another example, the disclosure provides a method of inhibiting Myt1 in a cell expressing Myt1, the method comprising contacting the cell with the compound disclosed herein.

In some examples, the cell is overexpressing CCNE1. In some examples, the cell is in a subject.

In still another example, the disclosure provides a method of treating a subject in need thereof comprising administering to the subject the compound disclosed herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition disclosed herein.

In some examples, the subject is suffering from, and is in need of a treatment for, a disease or condition having the symptom of cell hyperproliferation. In some examples, the disease or condition is a cancer. In some examples, the cancer is a cancer overexpressing CCNE1.

In still another example, the disclosure provides a method of treating a cancer in a subject, the method comprising administering to the subject in need thereof a therapeutically effective amount of a Myt1 inhibitor, wherein the cancer has been previously identified as a cancer overexpressing *CCNE1*.

In another example, the disclosure provides a method of treating a cancer in a subject, the method comprising administering to the subject in need thereof a therapeutically effective amount of a Myt1 inhibitor, wherein the cancer is a cancer overexpressing *CCNE1*.

In yet another example, the disclosure provides a method of inducing cell death in a cancer cell overexpressing *CCNE1*, the method comprising contacting the cell with an effective amount of a Myt1 inhibitor.

In some examples, the cell is in a subject. In some examples, the Myt1 inhibitor is the compound disclosed herein or a pharmaceutically acceptable salt thereof. In some examples, the cancer overexpressing CCNE1 is uterine cancer, ovarian cancer, breast cancer, stomach cancer, esophageal cancer, lung cancer, or endometrial cancer.

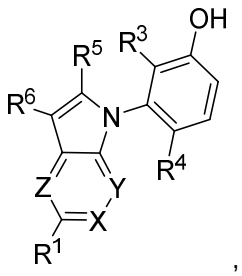
In still another example, the disclosure provides a method of treating a cancer in a subject, the method comprising administering to the subject in need thereof a therapeutically effective amount of a Myt1 inhibitor, wherein the cancer has been previously identified as a cancer having an inactivating mutation in the *FBXW7* gene.

In another example, the disclosure provides a method of treating a cancer in a subject, the method comprising administering to the subject in need thereof a therapeutically effective amount of a Myt1 inhibitor, wherein the cancer has an inactivating mutation in the *FBXW7* gene.

In yet another example, the disclosure provides a method of inducing cell death in an FBXW7-mutated cancer cell, the method comprising contacting the cell with an effective amount of a Myt1 inhibitor.

CLAIMS

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt thereof,

wherein

each of X, Y, and Z is independently N or CR^2;

R^1 and each R^2 are independently hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{3-8} cycloalkenyl, optionally substituted C_{2-9} heterocyclyl, optionally substituted C_{2-9} heterocyclyl C_{1-6} alkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{1-9} heteroaryl, optionally substituted C_{1-9} heteroaryl C_{1-6} alkyl, halogen, cyano, $–N(R^7)_2$, $–OR^7$, $–C(O)N(R^8)_2$, $–SO_2N(R^8)_2$, $–SO_2R^{7A}$, or $–Q–R^{7B}$; or R^1 combines with one R^2 that is *vicinal* to R^1 to form an optionally substituted C_{3-6} alkylene;

each of R^3 and R^4 is independently optionally substituted C_{1-6} alkyl or halogen;

R^5 is H or $–N(R^7)_2$;

R^6 is $–C(O)NH(R^8)$, $–C(O)R^{7A}$, or $–SO_2R^{7A}$;

each R^7 is independently hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl C_{1-6} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{2-9} heterocyclyl, optionally substituted C_{1-9} heteroaryl, optionally substituted C_{1-9} heteroaryl C_{1-6} alkyl, or $–SO_2R^{7A}$; or two R^7 groups, together with the atom to which both are attached, combine to form an optionally substituted C_{2-9} heterocyclyl;

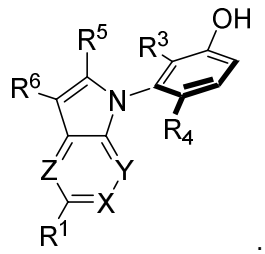
each R^{7A} is independently optionally substituted C_{1-6} alkyl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{6-10} aryl;

each R^{7B} is independently hydroxyl, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{2-9} heterocyclyl, optionally substituted C_{1-9} heteroaryl, $–N(R^7)_2$, $–C(O)N(R^8)_2$, $–SO_2N(R^8)_2$, $–SO_2R^{7A}$, or optionally substituted alkoxy;

each R^8 is independently hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkoxyalkyl, optionally substituted C_{6-10} aryl C_{1-6} alkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{1-9} heteroaryl; or two R^8, together with the atom to which they are attached, combine to form an optionally substituted C_{2-9} heterocyclyl;

Q is optionally substituted C_{1-6} alkylene, optionally substituted C_{2-6} alkenylene, optionally substituted C_{2-6} alkynylene, optionally substituted C_{3-8} cycloalkylene, optionally substituted C_{3-8} cycloalkenylene optionally substituted C_{6-10} arylene, optionally substituted C_{2-9} heterocyclylene, or optionally substituted C_{1-9} heteroarylene.

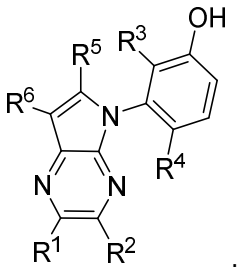
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is enriched for the atropisomer of formula (IA):



(IA)

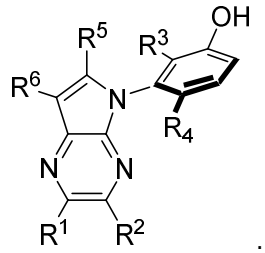
3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is CR^2.

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of formula (II):



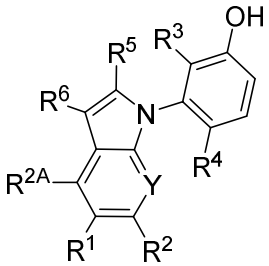
(II)

5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is enriched for the atropisomer of formula (IIA):



(IIA)

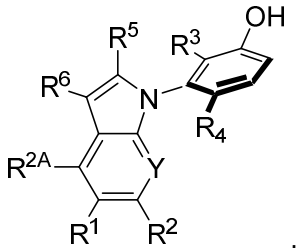
6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of formula (III):



(III)

wherein R^{2A} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{3-8} cycloalkenyl, optionally substituted C_{2-9} heterocyclyl, optionally substituted C_{2-9} heterocyclyl C_{1-6} alkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{1-9} heteroaryl, optionally substituted C_{1-9} heteroaryl C_{1-6} alkyl, halogen, $–N(R^7)_2$, $–OR^7$, $–C(O)N(R^8)_2$, $–SO_2N(R^8)_2$, $–SO_2R^{7A}$, or $–Q–R^{7B}$.

7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein the compound is enriched for the atropisomer of formula (IIIA):



(IIIA)

8. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein R^{2A} is hydrogen, optionally substituted C_{1-6} alkyl, or halogen.

9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^3 is optionally substituted C_{1-6} alkyl or halogen.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 is optionally substituted C_{1-6} alkyl or chlorine.

11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen, optionally substituted methyl, optionally substituted isopropyl, or halogen.

12. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen, chlorine, bromine, optionally substituted methyl, optionally substituted ethyl, optionally substituted isopropyl, optionally substituted butyl, optionally substituted 1,3-thiazolyl, optionally substituted 1,2-thiazolyl, optionally substituted 1,3-oxazolyl, optionally substituted benzo-1,3-thiazolyl, optionally substituted benzo-1,3-oxazolyl, optionally substituted indolyl, optionally substituted benzimidazolyl, optionally substituted pyridyl, optionally substituted imidazolyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted pyrazolyl, optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, optionally substituted cyclohexyl, optionally substituted 1,2,3,6-tetrahydropyridinyl, optionally substituted piperidinyl, optionally substituted morpholinyl, optionally substituted piperazinyl, optionally substituted thiomorpholinyl, optionally substituted oxa-aza-spiro[3,3]heptane, optionally substituted oxa-aza-bicyclo[3.2.1]octane, optionally substituted phenyl, $–Q–R^{7B}$, or diethylamino.

13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is $–Q–R^{7B}$, wherein Q, is optionally substituted C_{2-6} alkynylene, C_{1-6} alkylene, or C_{6-10} arylene; and R^{7B} is optionally substituted C_{2-9} heterocyclyl, or optionally substituted C_{6-10} aryl.

14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is optionally substituted with one, two, or three groups independently selected from the group consisting of methyl, difluoromethyl, trifluoromethyl, fluorine, chlorine, bromine, amino, hydroxyl, cyano, oxo, $-C(O)NH_2$, $-C(O)NH(Me)$, $-C(O)N(Me)_2$, $-(CH_2)_n-C(O)OH$, and $-(CH_2)_n-C(O)Ot-Bu$, wherein n is 0 or 1.

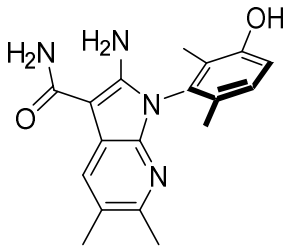
15. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen or $–NH_2$.

16. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–C(O)NH_2$, $–C(O)NH(Me)$ or $–SO_2Me$.

17. A compound selected from the group consisting of compounds 1-102, 104-107, 110-121, 125-127, 131-168, 170-206, 208-209, 212-276, 278-328 and pharmaceutically acceptable salts thereof.

18. The compound of claim 17, wherein the compound is selected from the group consisting of compounds 1-102, 104-107, 110-121, 125-127, 131-168, 170-206, 208-209, 212-276, 278-288 and pharmaceutically acceptable salts thereof.

19. The compound of claim 1, wherein the compound has the structure:



,

or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition comprising the compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.