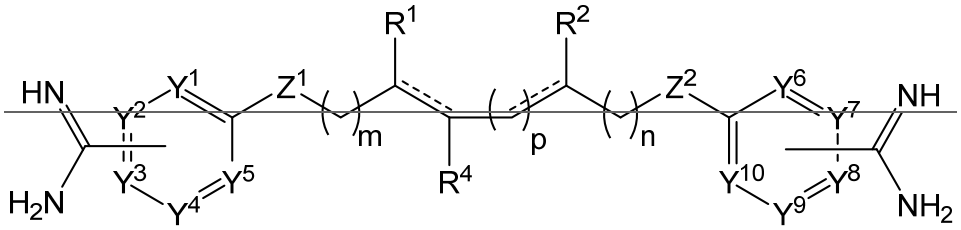
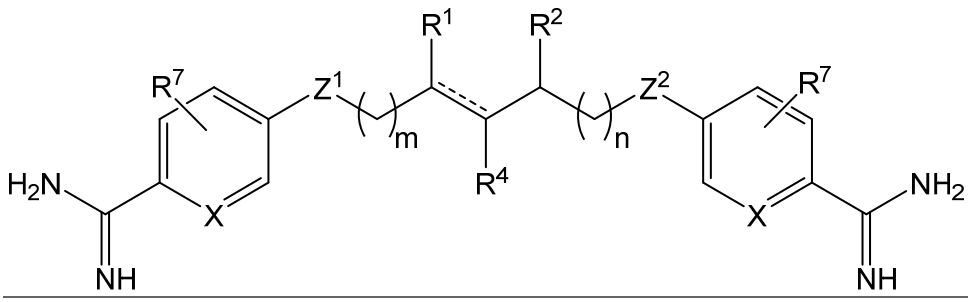
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (~~A~~II):



~~Formula (A)~~



Formula (II)

or a pharmaceutically acceptable salt thereof, wherein:

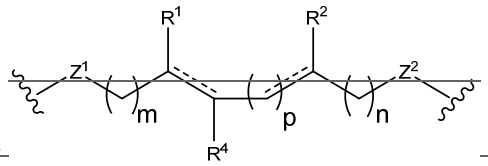
represents a single or double bond;

m or *n* is independently an integer of 0, 1, 2 or 3;

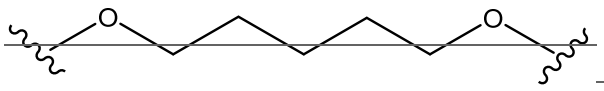
~~p is 0 or 1;~~

Z^1 or Z^2 is independently O, S, SO_2, NR^3, or CR^5R^6;

only one X is N and the other X is CR_7; ~~Y^1-Y^{10} are each independently N or CR^7, wherein at least one of Y^1-Y^{10} is N, provided that~~



~~when the moiety~~ ~~is taken together to form the moiety~~



~~one Y^1-Y^5 is N and one of Y^8-Y^{10} is N and the remaining Y^1-Y^{10} are each CH, then Y^1-Y^5 are taken together with the amidine substituent to~~

~~form an amidine substituted pyridine ring that is different than the amidine substituted pyridine ring formed by Y^8-Y^{10};~~

R^1 and R^2 are each independently hydrogen or halo,

or R^1 taken together with R^2 forms a saturated~~, unsaturated~~ or partially unsaturated 3-9 membered cyclic group, wherein the cyclic group is optionally substituted by halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino~~, provided that when R^1 is taken together with R^2 to form a phenyl group, both of Z^1 and Z^2 are O, and one of Y^1-Y^5 is N and one of Y^8-Y^{10} is N and the remaining Y^1-Y^{10} are each CH, then Y^1-Y^5 are taken together with the amidine substituent to form an amidine substituted pyridine ring that is different than the amidine substituted pyridine ring formed by Y^8-Y^{10}~~;

R^3 is hydrogen, alkyl, cycloalkyl, aryl, or heteroaryl;

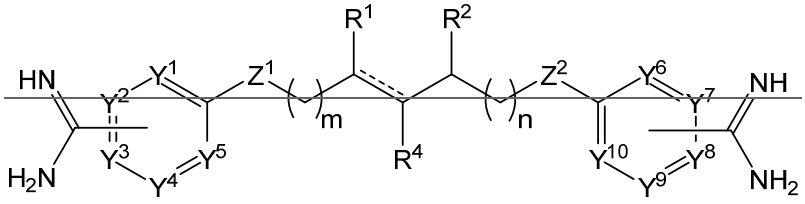
R^4 is hydrogen, halo, cycloalkyl, aryl, or heteroaryl;

R^5 or R^6 is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, amino,

or R^5 taken together with R^6 forms a saturated or partially unsaturated 3-9 membered ring; and

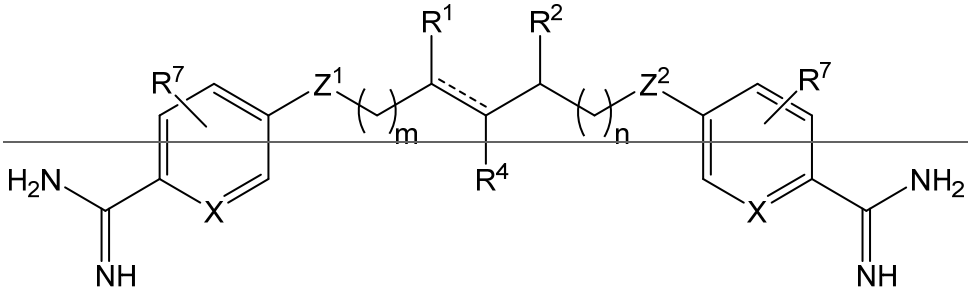
R^7 is hydrogen. ~~R^7 is independently hydrogen, halo, or amidine (-Am)~~ .

~~2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula (I):~~



~~**Formula (I); or**~~

~~wherein the compound is of Formula (II):~~



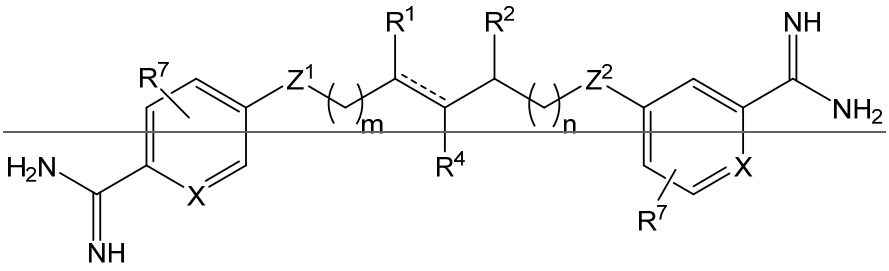
~~Formula (II)~~

~~wherein:~~

~~X is independently N or CR^7, provided that at least one X is N; and~~

~~R^7 is independently hydrogen or halo; or~~

~~wherein the compound is of Formula (III):~~



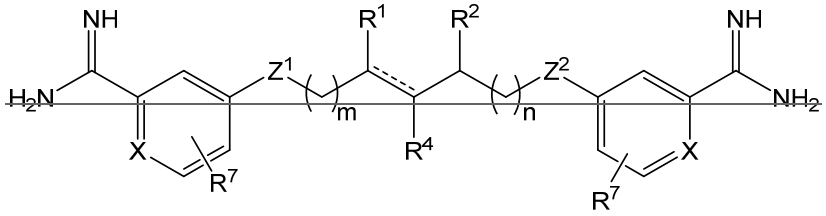
~~Formula (III)~~

~~wherein:~~

~~X is independently N or CR^7, provided that at least one X is N; and~~

~~R^7 is independently hydrogen or halo; or~~

~~wherein the compound is of Formula (IV):~~



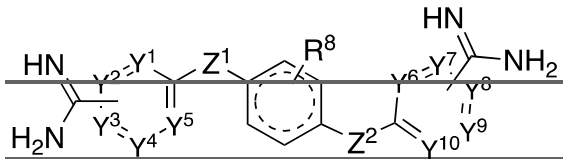
~~Formula (IV)~~

~~wherein:~~

~~X is independently N or CR^7, provided that at least one X is N; and~~

~~R^7 is independently hydrogen or halo.~~

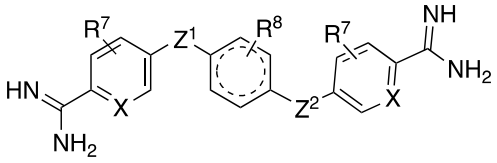
~~3.~~2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, ~~wherein the compound is of Formula (V):~~



~~Formula (V)~~

~~wherein R^8 is y hydrogen, halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino; or~~

wherein the compound is of Formula (VI):



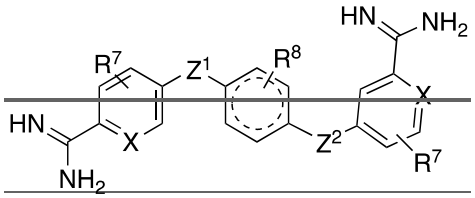
Formula (VI)

wherein:

~~X is independently N or CR^7, provided that at least one X is N; and~~

R^8 is hydrogen, halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino.~~; or~~

~~wherein the compound is of Formula (VII):~~



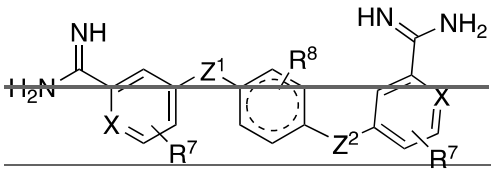
~~Formula (VII)~~

~~wherein:~~

~~X is independently N or CR^7, provided that at least one X is N; and~~

~~R^8 is hydrogen, halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino; or~~

~~wherein the compound is of Formula (VIII):~~



~~**Formula (VIII)**~~

~~wherein:~~

~~X is independently N or CR7, provided that at least one X is N; and~~

~~R8 is hydrogen, halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino.~~

~~4.~~3. The compound of claim 1 ~~or 2~~, or a pharmaceutically acceptable salt thereof, wherein *m* is 1, and *n* is 1; or

wherein *m* is 1, and *n* is 0; or wherein *m* is 0, and *n* is 1; or

wherein *m* is 1, and *n* is 2; or

wherein *m* is 2, and *n* is 1; or

wherein *m* is 2, and *n* is 2; or

wherein *m* is 0, and *n* is 0.

~~5. The compound of claims 1, or 3, or a pharmaceutically acceptable salt thereof, wherein R8 is independently hydrogen, halo, cyano, alkyl, cycloalkyl, aryl, heteroaryl, or amino.~~

~~6.~~4. The compound of any one of claims 1-~~5~~3, or a pharmaceutically acceptable salt thereof, wherein Z^1 or Z^2 is independently selected from the group of ~~N,~~ O, S or NR^3, wherein R^3 is selected from the group of hydrogen, alkyl, cycloalkyl, aryl, and heteroaryl, or CR^5R^6.

~~7.~~5. The compound of any one of claims 1-~~6~~3, or a pharmaceutically acceptable salt thereof, wherein Z^1 is NR^3, wherein R^3 is hydrogen, alkyl, cycloalkyl, aryl, or heteroaryl and Z^2 is CR^5R^6, wherein R^5 or R^6 is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, or amino; or R^5 taken together with R^6 forms a saturated or partially unsaturated 3-9 membered ring; or

wherein Z^1 or Z^2 is independently CR^5R^6, wherein R^5 or R^6 is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, or amino, or R^5 taken together with R^6 forms a saturated or partially unsaturated 3-9 membered ring; or

wherein Z^1 or Z^2 is independently NR^3, wherein R^3 is hydrogen, alkyl, cycloalkyl, aryl, or heteroaryl; or

wherein Z^1 or Z^2 is independently O, S, or SO_2.

~~8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein Y^3 and Y^8 are attached to amidine; or~~

~~wherein Y^3 and Y^7 are attached to amidine; or~~

~~wherein Y^2 and Y^7 are attached to amidine.~~

~~9.~~6. The compound of ~~any one of claims 1-9~~claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 and R^2 are independently hydrogen; or .

~~wherein R^1 taken together with R^2 forms a saturated, unsaturated or partially unsaturated 3-9 membered cyclic group (*e.g.*, ~~~~); or~~

wherein R^1 taken together with R^2 forms 5, 6, or 7 membered cycloalkyl.

~~10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein $Y^{1, 2, 4, 5, 6, \text{ and } 8}$ are CR^7 (*e.g.*, CH); Y^2 is N; and Y^3 and Y^7 attached to amidine; or~~

~~wherein $Y^{1, 4, 5, 6, \text{ and } 7}$ are CH; Y^2 is N; and Y^3 and Y^8 are CR^7, wherein R^7 is amidine; or~~

~~wherein $Y^{1, 4, 5, 6, \text{ and } 8}$ are CH; Y^3 is N; and Y^2 and Y^7 are CR^7, wherein R^7 is amidine; or~~

~~wherein $Y^{1, 4, 5, 6, \text{ and } 8}$ are CH; Y^3 is N; and Y^2 and Y^7 are CR^7, wherein R^7 is amidine, wherein *m* is 1, and *n* is 0; or~~

~~wherein $Y^{1, 4, 5, \text{ and } 6}$ are CH; Y^3 and Y^8 are N; and Y^2 and Y^7 are CR^7, wherein R^7 is amidine, and wherein *m* is 1, and *n* is 0.~~

~~11.~~7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

5-(5-(4-carbamimidoylphenoxy)pentyloxy)picolinimidamide;

~~6-((5-(4-carbamimidoylphenoxy)pentyl)oxy)nicotinimidamide;~~

~~5-((5-(4-carbamimidoylphenoxy)pentyl)oxy)pyrimidine-2-carboximidamide;~~

~~5-((5-(4-carbamimidoylphenoxy)pentyl)oxy)pyrazine-2-carboximidamide;~~

5-(4-(4-carbamimidoylphenoxy)butoxy)picolinimidamide;

5-(4-(4-carbamimidoylphenoxy)butoxy)picolinimidamide;

~~5,5'-(pentane-1,5-diylbis(oxy))bis(pyrazine-2-carboximidamide);~~

~~6,6' (heptane-1,7-diyl)dipicolinimidamide;~~

~~5,5' (heptane-1,7-diyl)dinicotinimidamide;~~

~~6,6' (heptane-1,7-diyl)dinicotinimidamide;~~

~~5-(5-(3-carbamimidoylphenoxy)pentyloxy)picolinimidamide;~~

~~4-({5-[(6-cyanopyridin-3-yl)oxy]pentyl}oxy)pyridine-2-carbonitrile;~~

5-(((1r, 4r)-4-(4-carbamimidoylphenoxy)cyclohexyl)oxy)picolinimidamide;

5-(((1s, 4s)-4-(4-carbamimidoylphenoxy)cyclohexyl)oxy)picolinimidamide;

~~4-(5-(3-carbamimidoylphenoxy)pentyloxy)picolinimidamide;~~

~~5,5' (butane-1,4-diylbis(oxy))dipicolinimidamide;~~

5-(3-(4-carbamimidoylphenoxy)propoxy)picolinimidamide; and

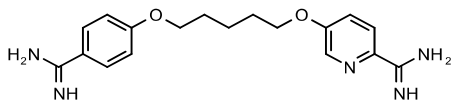
5-{2-[(1R,3S)-3-[2-(4-carbamimidoylphenyl)ethyl]cyclohexyl]ethyl}pyridine-2-carboximidamide~~;~~.

~~4-{[5-(4-carbamimidoylphenoxy)pentyl]oxy}pyridine-2-carboximidamide;~~

~~5-({5-[(6-carbamimidoylpyridin-3-yl)oxy]pentyl}oxy)pyridine-2-carboximidamide; and~~

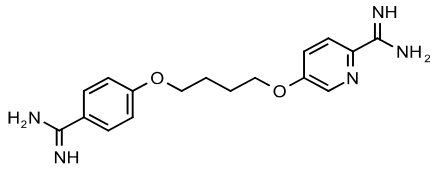
~~4-({5-[(2-carbamimidoylpyridin-4-yl)oxy]pentyl}oxy)pyridine-2-carboximidamide.~~

~~12.~~8. A compound having a structure as follows:



, or a pharmaceutically acceptable salt thereof.~~, or~~

9. ~~a~~A compound having a structure as follows:



, or a pharmaceutically acceptable salt thereof.

~~13.~~10. A pharmaceutical composition comprising a compound of any one of claims 1-~~12~~ 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~14.~~ 11. A pharmaceutical composition ~~comprising a compound of any one of claims 1-13~~ for use in a method of treating cancer, wherein an effective amount of a compound of any one of claims 1-~~12~~ 9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim ~~13~~10, is to be administered to a subject suffering from cancer, optionally
wherein said cancer is selected from the group consisting of liver cancer, cholangiocarcinoma, osteosarcoma, melanoma, breast cancer, renal cancer, prostate cancer, gastric cancer, colorectal cancer, thyroid cancer, head and neck cancer, ovarian cancer, pancreatic cancer, neuronal cancer, lung cancer, uterine cancer, leukemia, and lymphoma, optionally
wherein said cancer is a solid tumor.

~~15.~~ 12. A pharmaceutical composition for use as claimed in Claim ~~14~~ 11 wherein said composition ~~or a pharmaceutically acceptable salt thereof,~~ is to be administered to the subject (*e.g.*, human patient) orally, intravenously or subcutaneously at a dose of about 0.5 mg per kg, 0.6 mg per kg, about 0.7 mg per kg, about 0.8 mg per kg, about 0.9 mg per kg, about 1 mg per kg, about 2 mg per kg, about 3 mg per kg, about 4 mg per kg, about 5 mg per kg, about 6 mg per kg, about 7 mg per kg, about 8 mg per kg, about 9 mg per kg, about 10 mg per kg, about 15 mg per kg, about 20 mg per kg about 30 mg per kg, about 40 mg per kg, about 50 mg per kg, about 60 mg per kg, about 70 mg per kg, about 80 mg per kg, about 90 mg per kg, about 100 mg per kg, about 110 mg per kg, about 120 mg per kg, about 130 mg per kg, about 140 mg per kg, about 150 mg per kg, about 160 mg per kg, about 170 mg per kg, about 180 mg per kg, about 190 mg per kg, about 200 mg per kg, about 210 mg per kg, about 220 mg per kg, about 230 mg per kg, about 240 mg per kg, about 250 mg per kg, about 260 mg per kg, about 270 mg per kg, about 280 mg per kg, about 290 mg per kg, about 300 mg per kg, about 350 mg per kg, about 400 mg per kg, about 450 mg per kg, about 500 mg per kg, or about 600 mg per kg, optionally .
wherein said subject is a human patient, optionally
wherein said subject is to be administered ~~about~~ 1 mg per kg to ~~about~~ 200 mg per kg daily.

~~16.~~ 13. Use of a compound of any one of claims 1-~~13~~ 9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 10, in the manufacture of a medicament for treating cancer, wherein an effective amount of ~~a compound of any one of claims 1-12~~said

compound, or a pharmaceutically acceptable salt thereof, or ~~a~~ said pharmaceutical composition ~~of claim 13~~, is to be administered to a subject suffering from cancer, optionally
wherein said cancer is selected from the group consisting of liver cancer, cholangiocarcinoma, osteosarcoma, melanoma, breast cancer, renal cancer, prostate cancer, gastric cancer, colorectal cancer, thyroid cancer, head and neck cancer, ovarian cancer, pancreatic cancer, neuronal cancer, lung cancer, uterine cancer, leukemia, and lymphoma, optionally
wherein said cancer is a solid tumor.

~~17.~~ 14. The use as claimed in Claim ~~16~~ 13 wherein said ~~composition~~ compound, or a pharmaceutically acceptable salt thereof, or said pharmaceutical composition is to be administered to the subject (*e.g.*, human patient) orally, intravenously or subcutaneously at a dose of about 0.5 mg per kg, 0.6 mg per kg, about 0.7 mg per kg, about 0.8 mg per kg, about 0.9 mg per kg, about 1 mg per kg, about 2 mg per kg, about 3 mg per kg, about 4 mg per kg, about 5 mg per kg, about 6 mg per kg, about 7 mg per kg, about 8 mg per kg, about 9 mg per kg, about 10 mg per kg, about 15 mg per kg, about 20 mg per kg about 30 mg per kg, about 40 mg per kg, about 50 mg per kg, about 60 mg per kg, about 70 mg per kg, about 80 mg per kg, about 90 mg per kg, about 100 mg per kg, about 110 mg per kg, about 120 mg per kg, about 130 mg per kg, about 140 mg per kg, about 150 mg per kg, about 160 mg per kg, about 170 mg per kg, about 180 mg per kg, about 190 mg per kg, about 200 mg per kg, about 210 mg per kg, about 220 mg per kg, about 230 mg per kg, about 240 mg per kg, about 250 mg per kg, about 260 mg per kg, about 270 mg per kg, about 280 mg per kg, about 290 mg per kg, about 300 mg per kg, about 350 mg per kg, about 400 mg per kg, about 450 mg per kg, about 500 mg per kg, or about 600 mg per kg, optionally .
wherein said subject is a human patient, optionally
wherein said subject is to be administered ~~about~~ 1 mg per kg to ~~about~~ 200 mg per kg daily.

~~18~~ 15. A compound of any one of claims 1~~-12~~ 9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim ~~13~~ 10, for use as a medicament.