R^{13}, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocycle optionally substituted with one, two, or three R^{20};

R^{14} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, and C_{1-6} haloalkyl;

R^{15} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{17} and R^{17a} are each independently selected at each occurrence from C_{1-6} alkyl and C_{3-6} cycloalkyl, wherein C_{1-6} alkyl and C_{3-6} cycloalkyl are optionally substituted with one, two or three R^{20}; or R^{17} and R^{17a}, together with the phosphorous atom to which they are attached, form a 3- to 10-membered heterocycle;

R^{20} is independently selected at each occurrence from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, -CH_2-(C_{3-10} carbocycle), 3- to 10-membered heterocycle, -CH_2-(3- to 10-membered heterocycle), -OR^{21}, -SR^{21}, -$N(R^{22})(R^{23})$, -$C(O)OR^{22}$, -$C(O)N(R^{22})(R^{23})$, -$C(O)C(O)N(R^{22})(R^{23})$, -$OC(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)OR^{25}$, -$N(R^{24})C(O)R^{25}$, -$N(R^{24})S(O)_2R^{25}$, -$C(O)R^{25}$, -$S(O)_2R^{25}$, -$S(O)_2N(R^{22})(R^{23})$, -$OCH_2C(O)OR^{22}$, and -$OC(O)R^{25}$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, -CH_2-(C_{3-10} carbocycle), 3- to 10-membered heterocycle, and -CH_2-(3- to 10-membered heterocycle) are optionally substituted with one, two, or three groups independently selected from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, -OR^{21}, -SR^{21}, -$N(R^{22})(R^{23})$, -$C(O)OR^{22}$, -$C(O)N(R^{22})(R^{23})$, -$C(O)C(O)N(R^{22})(R^{23})$, -$OC(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)OR^{25}$, -$N(R^{24})C(O)R^{25}$, -$N(R^{24})S(O)_2R^{25}$, -$C(O)R^{25}$, -$S(O)_2R^{25}$, -$S(O)_2N(R^{22})(R^{23})$, and -$OC(O)R^{25}$;

R^{21} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6}alkyl;

R^{22} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6}alkyl;

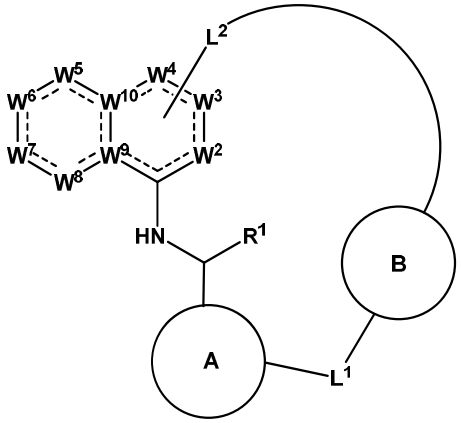
R^{23} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{24} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{25} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-10} carbocycle, and 3- to 10-membered heterocycle; and

------ indicates a single or double bond such that all valences are satisfied.

[009a] In one aspect, there is provided a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein:



is selected from C_{5-7} carbocycle and 5- to 7-membered heterocycle, each of which is optionally substituted with one or more R^{11};



is absent or selected from C_{3-8} carbocycle and 3- to 8-membered heterocycle, each of which is optionally substituted with one or more R^{11a};

L^1 is selected from a bond, C_{1-6} alkylene, and C_{1-6} haloalkylene;

L^2 is selected from C_{5-25} alkylene, C_{5-25} alkenylene, C_{5-25} alkynylene, 5- to 25-membered heteroalkylene, and 5- to 25-membered heteroalkenylene, each of which is optionally substituted with one or more R^{11b}, wherein L^2 is covalently bound to one of W^3, W^4, W^5, W^6, or W^7;

W^2 is N;

W^3 is selected from $N(R^{3b})$, N, $C(R^3)$, and C(O);

W^4 is selected from $N(R^{4b})$, N, $C(R^4)$, and C(O);

W^5 is selected from $N(R^{5b})$, N, and $C(R^5)$;

W^6 is selected from $C(R^6)$ and C(O);

W^7 is $C(R^7)$;

W^8 is $C(R^8)$;

W^9 is C;

W^{10} is C;

R^1 is C_{1-3} alkyl optionally substituted with one or more R^{11c};

R^8 is selected from hydrogen, halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^3, R^4, R^5, R^6, and R^7 are each independently selected from a bond to L^2, hydrogen, halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, -

$OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^{3b}, R^{4b} and R^{5b} are each independently selected from a bond to L^2, hydrogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^{11} and R^{11a} are each independently selected at each occurrence from halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, $-CH_2S(O)_2N(R^{12})(R^{13})$, $-CH_2N(R^{12})S(O)_2(R^{13})$, and $-P(O)(R^{17})(R^{17a})$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{11b} is independently selected at each occurrence from halogen, oxo, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, $-CH_2S(O)_2N(R^{12})(R^{13})$, $-CH_2N(R^{12})S(O)_2(R^{13})$, and $-P(O)(R^{17})(R^{17a})$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{11c} is independently selected at each occurrence from halogen, $-OR^{12}$, and $-N(R^{12})(R^{13})$;

R^{12} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{13} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, and C_{1-6} haloalkyl; or R^{12} and R^{13}, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocycle optionally substituted with one, two, or three R^{20};

R^{14} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, and C_{1-6} haloalkyl;

R^{15} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{17} and R^{17a} are each independently selected at each occurrence from C_{1-6} alkyl and C_{3-6} cycloalkyl, wherein C_{1-6} alkyl and C_{3-6} cycloalkyl are optionally substituted with one, two or three R^{20}; or R^{17} and R^{17a}, together with the phosphorous atom to which they are attached, form a 3- to 10-membered heterocycle;

R^{20} is independently selected at each occurrence from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, $-CH_2-(C_{3-10}$ carbocycle), 3- to 10-membered heterocycle, $-CH_2-$(3- to 10-membered heterocycle), $-OR^{21}$, $-SR^{21}$, $-N(R^{22})(R^{23})$, $-C(O)OR^{22}$, $-C(O)N(R^{22})(R^{23})$, $-C(O)C(O)N(R^{22})(R^{23})$, $-OC(O)N(R^{22})(R^{23})$,

$-N(R^{24})C(O)N(R^{22})(R^{23})$, $-N(R^{24})C(O)OR^{25}$, $-N(R^{24})C(O)R^{25}$, $-N(R^{24})S(O)_2R^{25}$, $-C(O)R^{25}$, $-S(O)_2R^{25}$, $-S(O)_2N(R^{22})(R^{23})$, $-OCH_2C(O)OR^{22}$, and $-OC(O)R^{25}$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, $-CH_2-(C_{3-10}$ carbocycle), 3- to 10-membered heterocycle, and $-CH_2-$(3- to 10-membered heterocycle) are optionally substituted with one, two, or three groups independently selected from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, $-OR^{21}$, $-SR^{21}$, $-N(R^{22})(R^{23})$, $-C(O)OR^{22}$, $-C(O)N(R^{22})(R^{23})$, $-C(O)C(O)N(R^{22})(R^{23})$, $-OC(O)N(R^{22})(R^{23})$, $-N(R^{24})C(O)N(R^{22})(R^{23})$, $-N(R^{24})C(O)OR^{25}$, $-N(R^{24})C(O)R^{25}$, $-N(R^{24})S(O)_2R^{25}$, $-C(O)R^{25}$, $-S(O)_2R^{25}$, $-S(O)_2N(R^{22})(R^{23})$, and $-OC(O)R^{25}$;

R^{21} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

R^{22} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

R^{23} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{24} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{25} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-10} carbocycle, and 3- to 10-membered heterocycle; and

$\overline{\text{------}}$ indicates a single or double bond such that all valences are satisfied.

[010] The compound of Formula (I) may be a compound of Formula (I-A)

-CH_2-(C_{3-10} carbocycle), 3- to 10-membered heterocycle, and -CH_2-(3- to 10-membered heterocycle) are optionally substituted with one, two, or three groups independently selected from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, -OR^{21}, -SR^{21}, -$N(R^{22})(R^{23})$, -$C(O)OR^{22}$, -$C(O)N(R^{22})(R^{23})$, -$C(O)C(O)N(R^{22})(R^{23})$, -$OC(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)OR^{25}$, -$N(R^{24})C(O)R^{25}$, -$N(R^{24})S(O)_2R^{25}$, -$C(O)R^{25}$, -$S(O)_2R^{25}$, -$S(O)_2N(R^{22})(R^{23})$, and -$OC(O)R^{25}$;

R^{21} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

R^{22} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

R^{23} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{24} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{25} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-10} carbocycle, and 3- to 10-membered heterocycle; and

------ indicates a single or double bond such that all valences are satisfied.

[036] In certain aspects, the present disclosure provides a compound described herein, or a pharmaceutically acceptable salt or solvate thereof. In certain aspects, the present disclosure provides a pharmaceutical composition comprising a compound described herein, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.

[037] In certain aspects, the present disclosure provides a method of treating cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound described herein, or a pharmaceutically acceptable salt or solvate thereof. In some embodiments, the cancer is a solid tumor or a hematological cancer. In some embodiments, the subject is administered with an additional agent or therapy.

[037a] In one aspect, there is provided a use of a compound described herein or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of cancer.

[038] In certain aspects, the present disclosure provides a method of reducing Ras signaling output, comprising contacting a SOS1 protein with an effective amount of a compound described herein, or a pharmaceutically acceptable salt or solvate thereof, thereby reducing the Ras signaling output. In some embodiments, the compound disrupts interaction between a Ras protein and SOS1. In some embodiments, the Ras protein is a wildtype K-Ras or a mutant K-Ras.

[039] In certain aspects, the present disclosure provides a method of inhibiting cell growth, comprising administering a cell expressing SOS1 with an effective amount of a compound described herein, or a pharmaceutically acceptable salt or solvate thereof, thereby inhibiting growth of said cells.

[039a] In one aspect, there is provided a compound described herein or a pharmaceutically acceptable salt or solvate thereof for use in inhibiting cell growth in a cell that expresses SOS1.

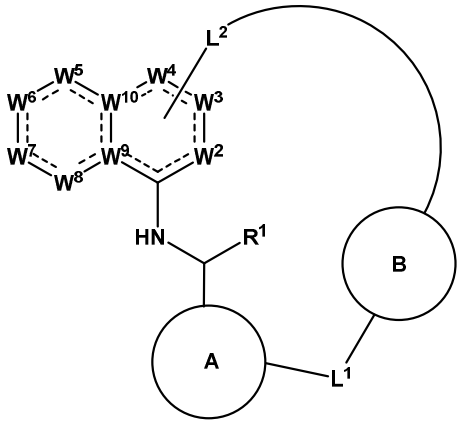
[040] In certain aspects, the present disclosure provides a method of reducing Ras signaling output of a cell,

comprising contacting the cell with an effective amount of a compound described herein, or a pharmaceutically acceptable salt or solvate thereof, in combination with an additional agent, wherein the additional agent is a chemotherapeutic agent, a radioactive agent, an immune modulator, or an inhibitor against one or more targets selected from: MEK, epidermal growth factor receptor (EGFR), FGFR1, FGFR2, FGFR3, FGFR4, mitotic kinase,

CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein:



is selected from C_{5-7} carbocycle and 5- to 7-membered heterocycle, each of which is optionally substituted with one or more R^{11};



is absent or selected from C_{3-8} carbocycle and 3- to 8-membered heterocycle, each of which is optionally substituted with one or more R^{11a};

L^1 is selected from a bond, C_{1-6} alkylene, and C_{1-6} haloalkylene;

L^2 is selected from C_{5-25} alkylene, C_{5-25} alkenylene, C_{5-25} alkynylene, 5- to 25-membered heteroalkylene, and 5- to 25-membered heteroalkenylene, each of which is optionally substituted with one or more R^{11b}, wherein L^2 is covalently bound to one of W^3, W^4, W^5, W^6, or W^7;

W^2 is N;

W^3 is selected from $N(R^{3b})$, N, $C(R^3)$, and C(O);

W^4 is selected from $N(R^{4b})$, N, $C(R^4)$, and C(O);

W^5 is selected from $N(R^{5b})$, N, and $C(R^5)$;

W^6 is selected from $C(R^6)$ and C(O);

W^7 is $C(R^7)$;

W^8 is $C(R^8)$;

W^9 is C;

W^{10} is C;

R^1 is C_{1-3} alkyl optionally substituted with one or more R^{11c};

R^8 is selected from hydrogen, halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^3, R^4, R^5, R^6, and R^7 are each independently selected from a bond to L^2, hydrogen, halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^{3b}, R^{4b} and R^{5b} are each independently selected from a bond to L^2, hydrogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, and $-CH_2S(O)_2N(R^{12})(R^{13})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle and 3- to 10-membered heterocycle is independently optionally substituted with one, two, or three R^{20};

R^{11} and R^{11a} are each independently selected at each occurrence from halogen, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, $-CH_2S(O)_2N(R^{12})(R^{13})$, $-CH_2N(R^{12})S(O)_2(R^{13})$, and $-P(O)(R^{17})(R^{17a})$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{11b} is independently selected at each occurrence from halogen, oxo, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})(R^{13})$, $-C(O)OR^{12}$, $-OC(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)OR^{15}$, $-N(R^{14})S(O)_2R^{15}$, $-C(O)R^{15}$, $-S(O)R^{15}$, $-OC(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-C(O)C(O)N(R^{12})(R^{13})$, $-N(R^{14})C(O)R^{15}$, $-S(O)_2R^{15}$, $-S(O)_2N(R^{12})(R^{13})$, $-S(=O)(=NH)N(R^{12})(R^{13})$, $-CH_2C(O)N(R^{12})(R^{13})$, $-CH_2N(R^{14})C(O)R^{15}$, $-CH_2S(O)_2R^{15}$, $-CH_2S(O)_2N(R^{12})(R^{13})$, $-CH_2N(R^{12})S(O)_2(R^{13})$, and $-P(O)(R^{17})(R^{17a})$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{11c} is independently selected at each occurrence from halogen, $-OR^{12}$, and $-N(R^{12})(R^{13})$;

R^{12} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{13} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, and C_{1-6} haloalkyl; or R^{12} and R^{13}, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocycle optionally substituted with one, two, or three R^{20};

R^{14} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, and C_{1-6} haloalkyl;

R^{15} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20};

R^{17} and R^{17a} are each independently selected at each occurrence from C_{1-6} alkyl and C_{3-6} cycloalkyl, wherein C_{1-6} alkyl and C_{3-6} cycloalkyl are optionally substituted with one, two or three R^{20}; or R^{17} and R^{17a}, together with the phosphorous atom to which they are attached, form a 3- to 10-membered heterocycle;

R^{20} is independently selected at each occurrence from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, -CH_2-(C_{3-10} carbocycle), 3- to 10-membered heterocycle, -CH_2-(3- to 10-membered heterocycle), -OR^{21}, -SR^{21}, -$N(R^{22})(R^{23})$, -$C(O)OR^{22}$, -$C(O)N(R^{22})(R^{23})$, -$C(O)C(O)N(R^{22})(R^{23})$, -$OC(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)OR^{25}$, -$N(R^{24})C(O)R^{25}$, -$N(R^{24})S(O)_2R^{25}$, -$C(O)R^{25}$, -$S(O)_2R^{25}$, -$S(O)_2N(R^{22})(R^{23})$, -$OCH_2C(O)OR^{22}$, and -$OC(O)R^{25}$, wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, -CH_2-(C_{3-10} carbocycle), 3- to 10-membered heterocycle, and -CH_2-(3- to 10-membered heterocycle) are optionally substituted with one, two, or three groups independently selected from halogen, oxo, =NH, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, -OR^{21}, -SR^{21}, -$N(R^{22})(R^{23})$, -$C(O)OR^{22}$, -$C(O)N(R^{22})(R^{23})$, -$C(O)C(O)N(R^{22})(R^{23})$, -$OC(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)N(R^{22})(R^{23})$, -$N(R^{24})C(O)OR^{25}$, -$N(R^{24})C(O)R^{25}$, -$N(R^{24})S(O)_2R^{25}$, -$C(O)R^{25}$, -$S(O)_2R^{25}$, -$S(O)_2N(R^{22})(R^{23})$, and -$OC(O)R^{25}$;

R^{21} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

R^{22} is independently selected at each occurrence from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen and C_{1-6} alkyl;

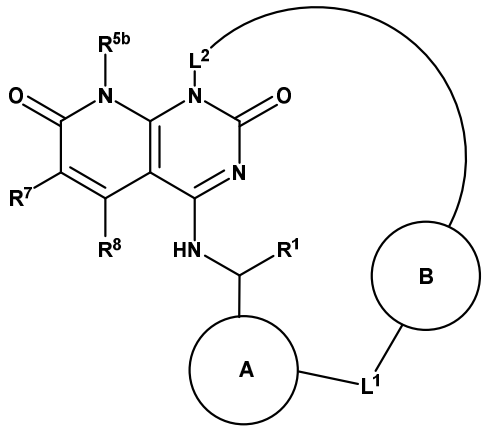
R^{23} is independently selected at each occurrence from H and C_{1-6} alkyl;

R^{24} is independently selected at each occurrence from H and C_{1-6} alkyl;

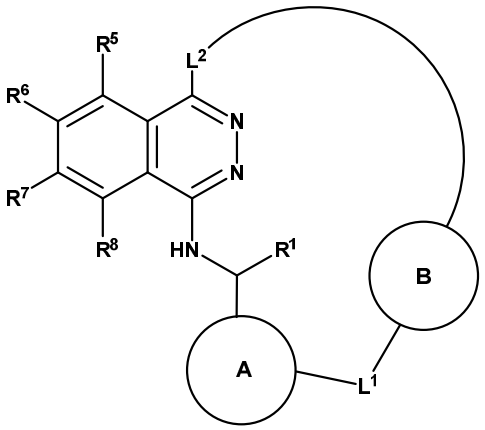
R^{25} is independently selected at each occurrence from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-10} carbocycle, and 3- to 10-membered heterocycle; and

------ indicates a single or double bond such that all valences are satisfied.

2. The compound of claim 1 having the structure of Formula (I-B1) or (I-B2):



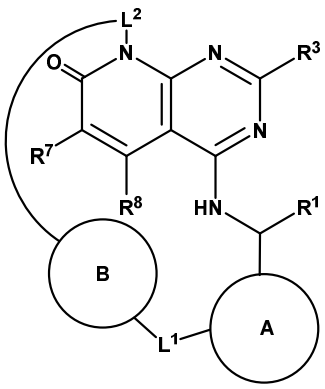
(I-B1) or

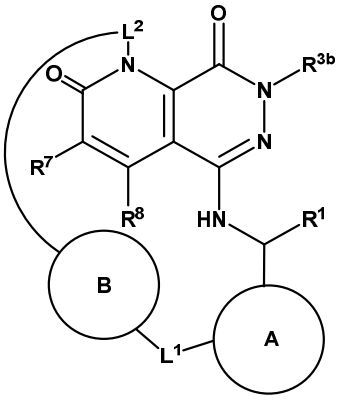


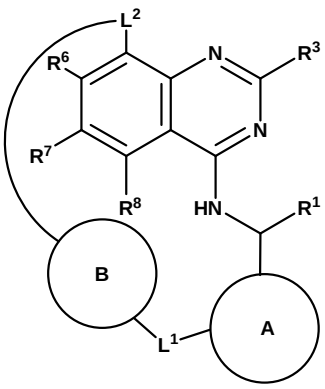
(I-B2),

or a pharmaceutically acceptable salt or solvate thereof.

3. The compound of claim 1 having the structure of Formula (I-C1), (I-C2), or (I-C3):



(I-C1),


(I-C2), or


(I-C3),

or a pharmaceutically acceptable salt or solvate thereof.

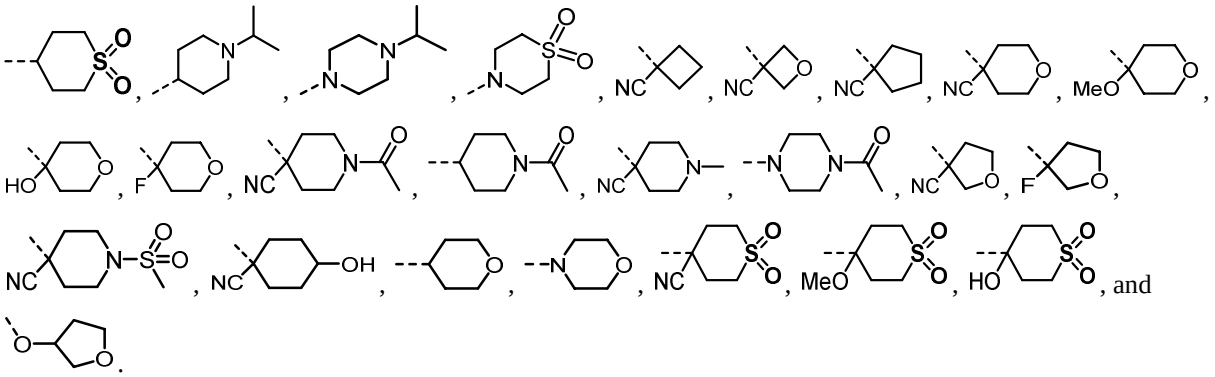
4. The compound, salt, or solvate of any one of claims 1 to 3, wherein R^1 is $-CH_3$.

5. The compound, salt, or solvate of any one of claims 1 to 4, wherein R^3 is selected from hydrogen, halogen, -CN, $-OR^{12}$, and C_{1-6} alkyl optionally substituted with one, two, or three R^{20}.

6. The compound, salt, or solvate of any one of claims 1 to 5, wherein R^6 is selected from hydrogen, $-OR^{12}$, and C_{1-6} alkyl optionally substituted with one, two, or three R^{20}, and wherein R^{12} is selected from C_{1-6} alkyl.

7. The compound, salt, or solvate of any one of claims 1 to 6, wherein R^7 is selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocycloalkyl, and $-N(R^{12})(R^{13})$, wherein C_{1-6} alkyl, C_{3-10} cycloalkyl, and 3- to 10-membered heterocycloalkyl are optionally substituted with one, two, or three R^{20}.

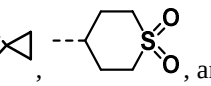
8. The compound, salt, or solvate of any one of claims 1 to 6, wherein R^7 is selected from 

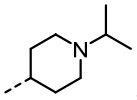
,


, and

.

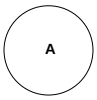
9. The compound, salt, or solvate of claim 8, wherein R^7 is selected from 

, 

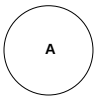
, and


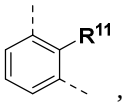
.

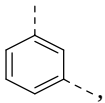
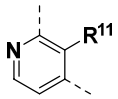
10. The compound, salt, or solvate of any one of claims 1 to 9, wherein R^8 is hydrogen.

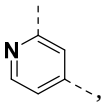
11. The compound, salt, or solvate of any one of claims 1 to 10, wherein 

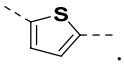
is selected from phenyl and 5- to 7-membered heteroaryl, each of which is optionally substituted with one or more R^{11}.

12. The compound, salt, or solvate of any one of claims 1 to 10, wherein 

is selected from 

, , 

, 

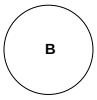
, and 

.

13. The compound, salt, or solvate of claim 11 or 12, wherein R^{11}, when present, is independently selected at each occurrence from fluorine and $-CH_3$.

14. The compound, salt, or solvate of any one of claims 1 to 13, wherein L^1 is C_{1-3} haloalkylene.

15. The compound, salt, or solvate of claim 14, wherein L^1 is selected from $-CF_2-$, $-CF_2CH_2-$, and $-CF_2CH_2CH_2-$.

16. The compound, salt, or solvate of any one of claims 1 to 15, wherein 

is selected from absent, phenyl, and 4- to 8-membered heterocycle, wherein the phenyl and 4- to 8-membered heterocycle are optionally substituted with one or more R^{11a}.

17. The compound, salt, or solvate of claim 16, wherein 

is selected from azetidine, pyrrolidine, and piperidine, each of which is optionally substituted with one or more $-CH_3$.

18. The compound, salt, or solvate of any one of claims 1 to 17, wherein L^2 is selected from C_{6-15} alkylene, C_{6-15} alkenylene, C_{6-15} alkynylene, 6- to 15-membered heteroalkylene, and 6- to 15-membered heteroalkenylene, each of which is optionally substituted with one or more R^{11b}.

19. The compound, salt, or solvate of any one of claims 1 to 17, wherein L^2 is selected from C_{5-10} alkylene, C_{5-10} alkenylene, 5- to 10-membered heteroalkylene, and 5- to 10-membered heteroalkenylene, each of which is optionally substituted with one or more R^{11b}.

20. The compound, salt, or solvate of claim 18 or 19, wherein the alkenylene and heteroalkenylene contain one carbon-carbon double bond.

21. The compound, salt, or solvate of claim 18 or 19, wherein the heteroalkylene and heteroalkenylene comprise at least one oxygen or nitrogen atom.

22. The compound, salt, or solvate of claim 2, wherein:

R^5 is hydrogen;

R^{5b} is $-CH_3$;

R^6 is selected from hydrogen and $-OCH_3$;

R^7 is selected from C_{1-6} alkyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-N(R^{12})(R^{13})$, $-C(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-S(O)_2R^{15}$, and $-SO_2N(R^{12})(R^{13})$, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20}; and

R^8 is hydrogen.

23. The compound, salt, or solvate of claim 3, wherein:

R^3 is hydrogen or $-CH_3$;

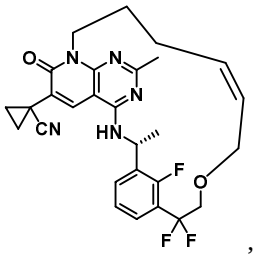
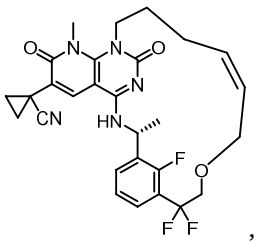
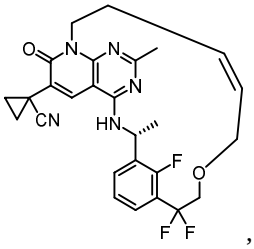
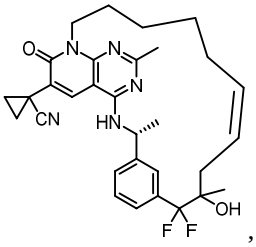
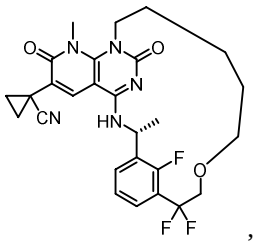
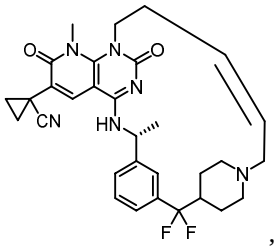
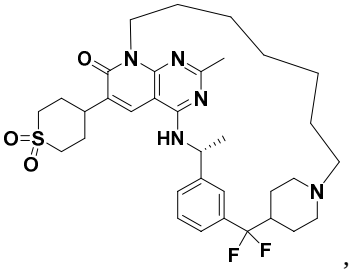
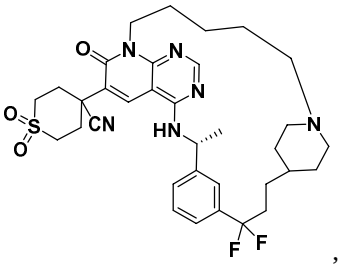
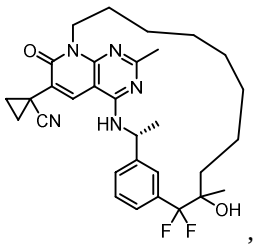
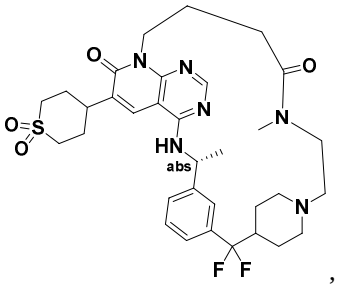
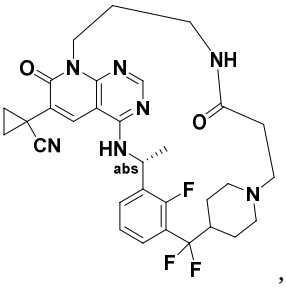
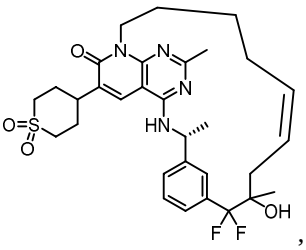
R^{3b} is $-CH_3$;

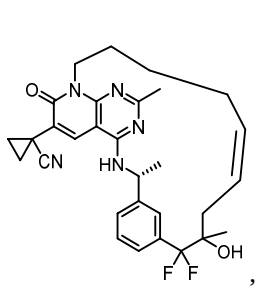
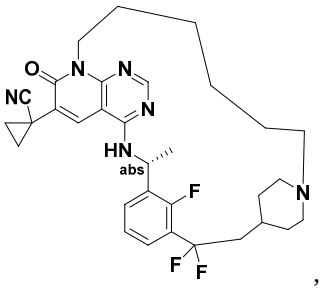
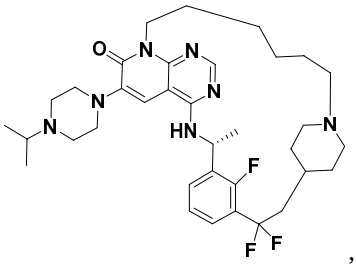
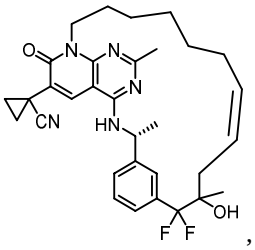
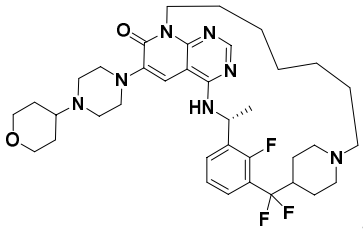
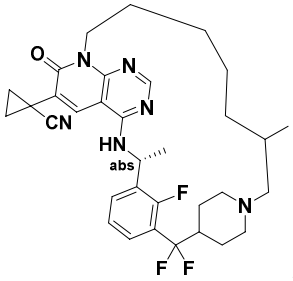
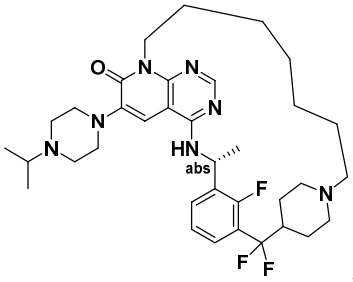
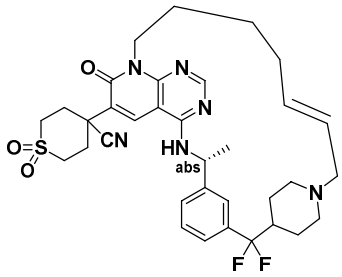
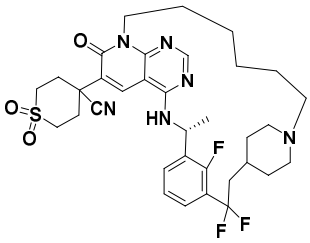
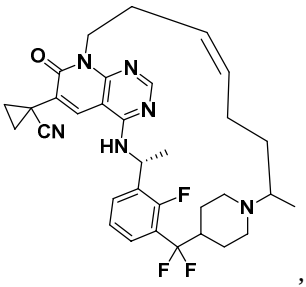
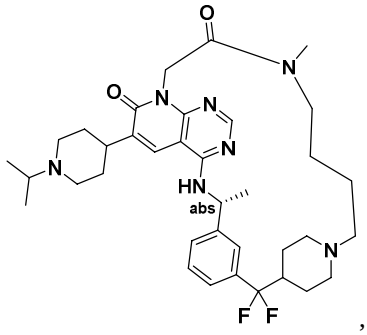
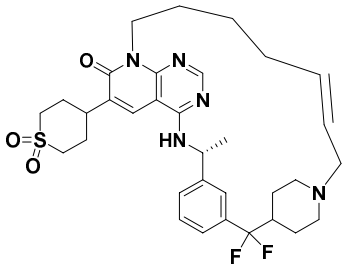
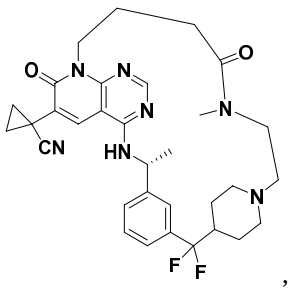
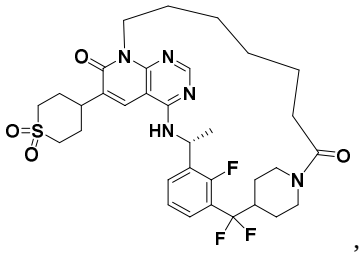
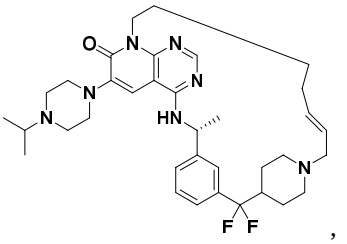
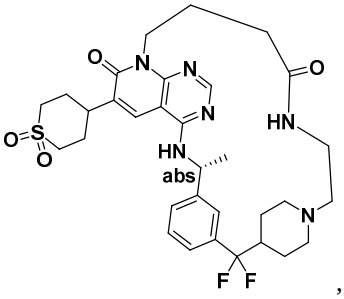
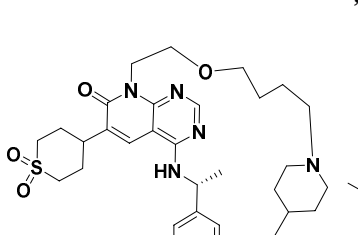
R^6 is selected from hydrogen and $-OCH_3$;

R^7 is selected from C_{1-6} alkyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, $-N(R^{12})(R^{13})$, $-C(O)R^{15}$, $-C(O)N(R^{12})(R^{13})$, $-S(O)_2R^{15}$, and $-SO_2N(R^{12})(R^{13})$, wherein C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are optionally substituted with one, two, or three R^{20}; and

R^8 is hydrogen.

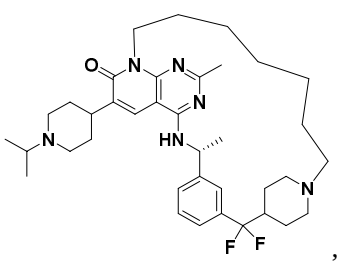
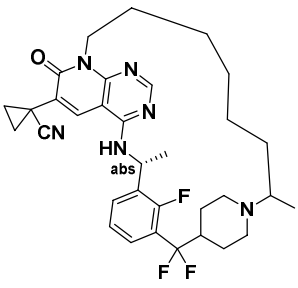
24. A compound selected from :

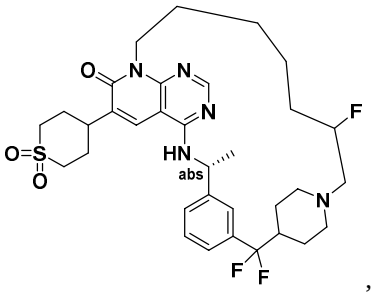
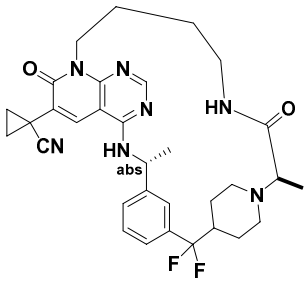
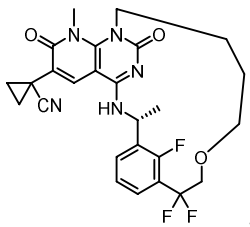
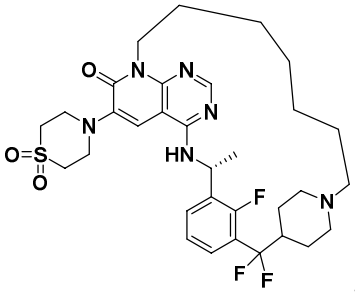
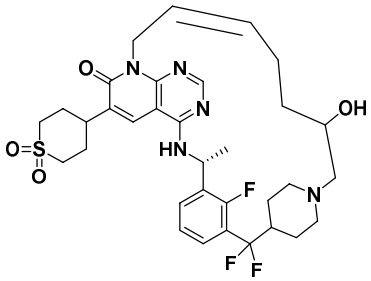
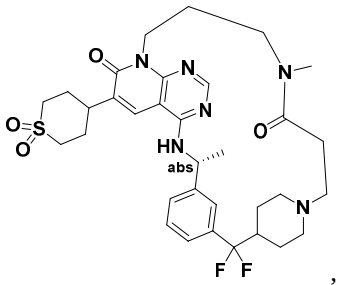
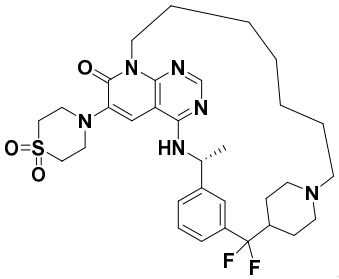
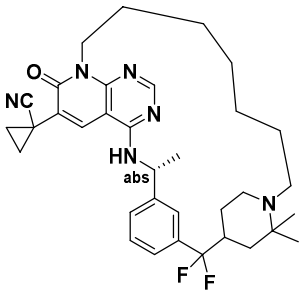
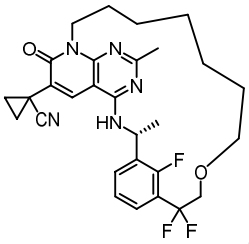
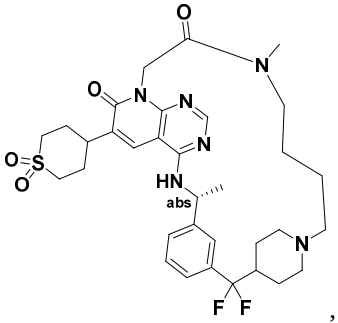
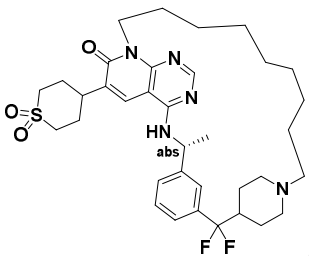
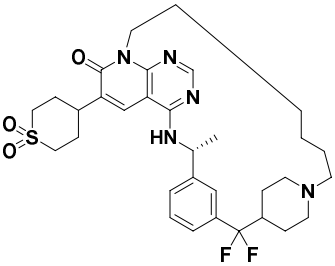
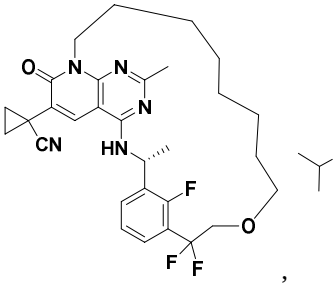
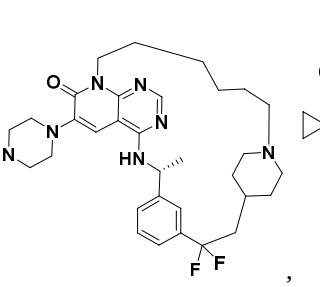
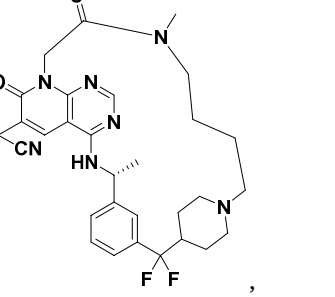

,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

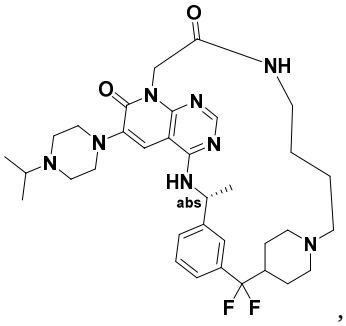
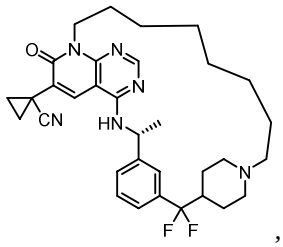
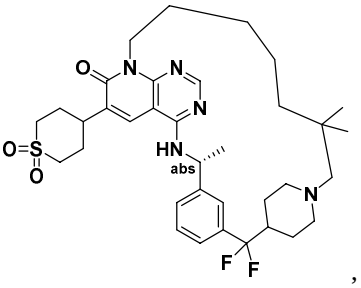
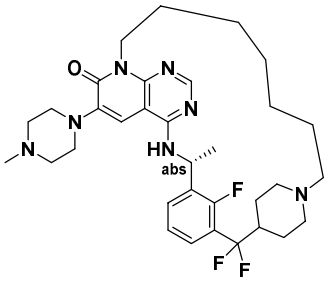
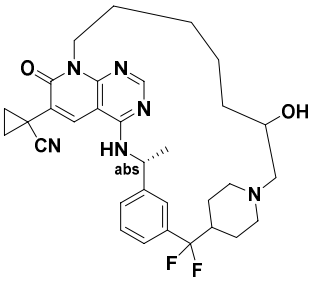
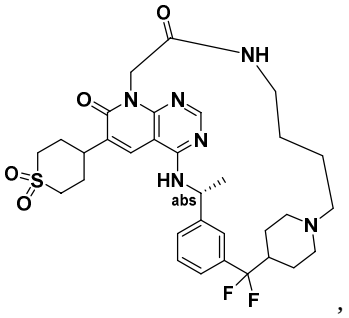
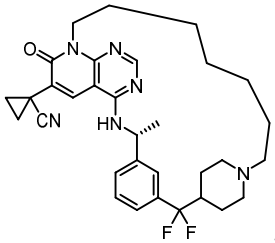
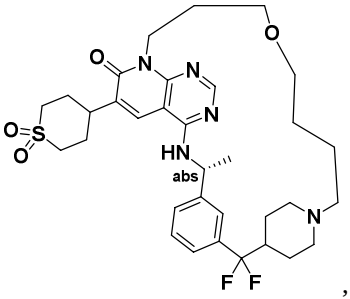
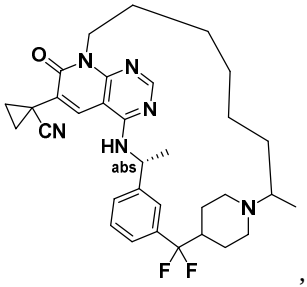
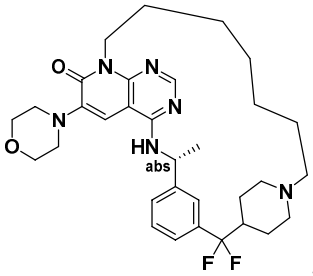
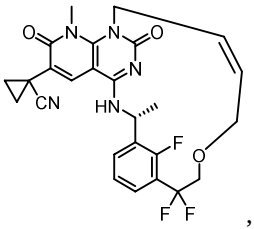
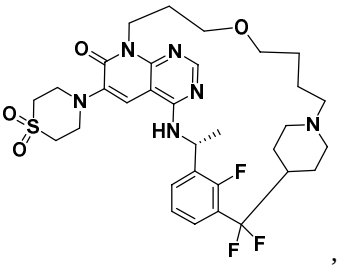
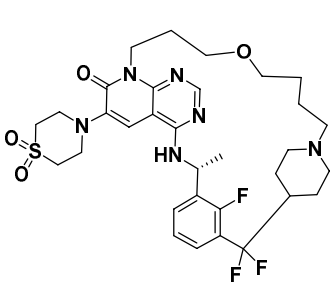
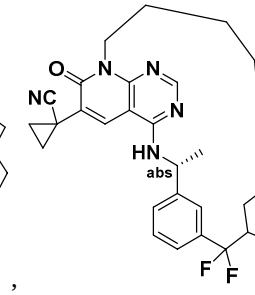
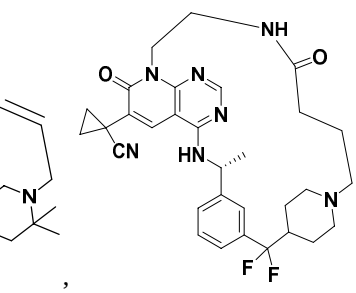
,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

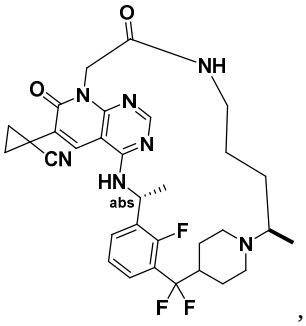
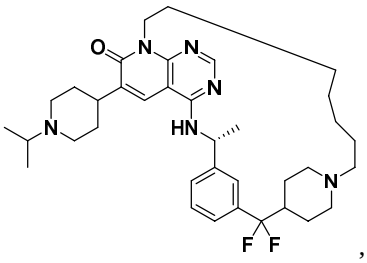
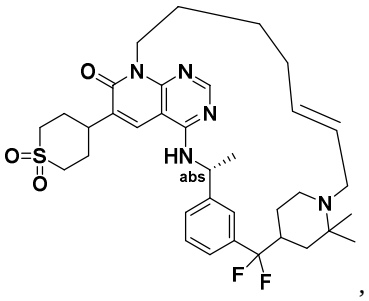
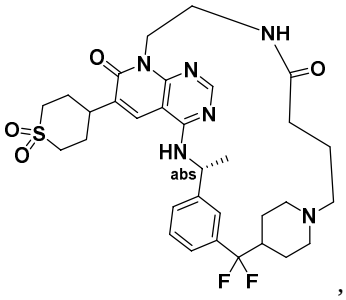
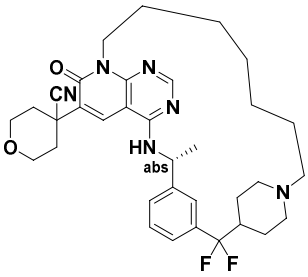
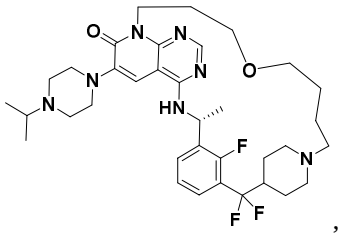
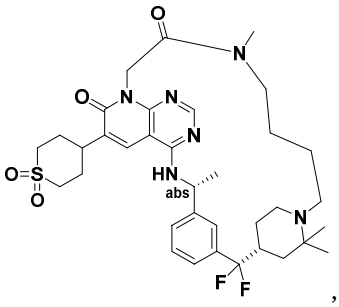
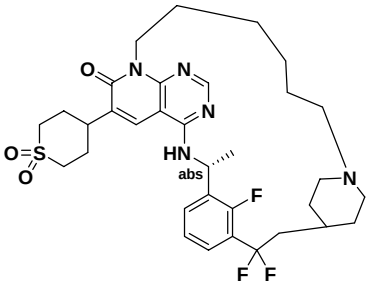
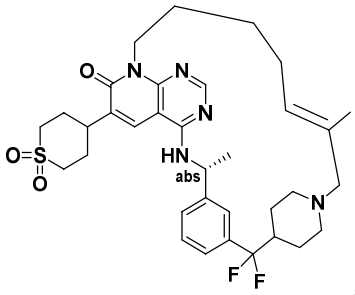
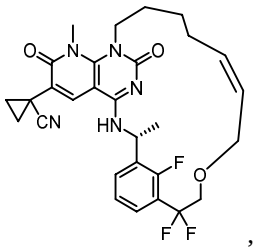
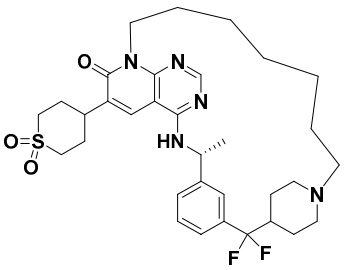
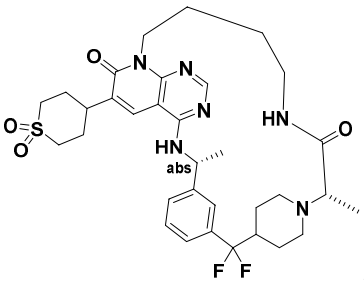
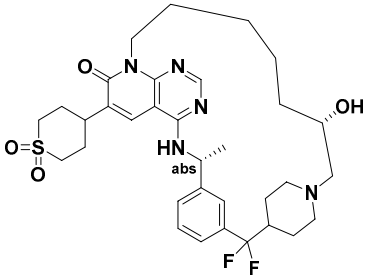
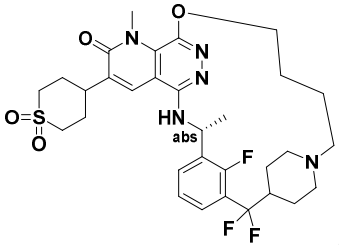
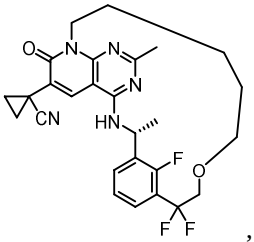
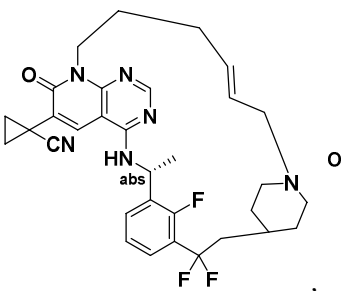
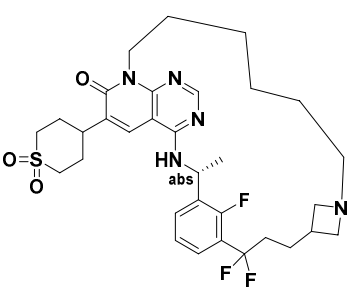
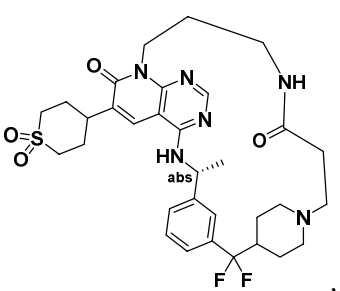
,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

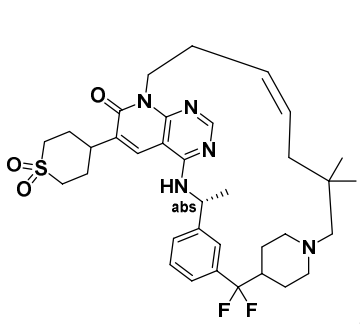
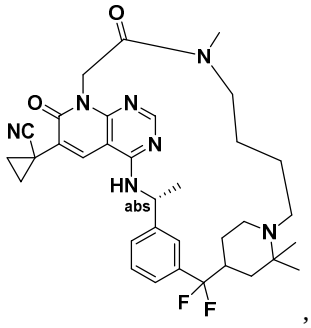
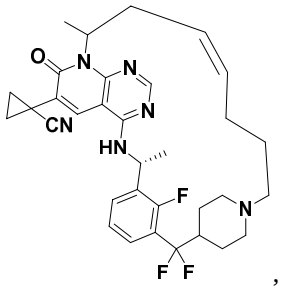
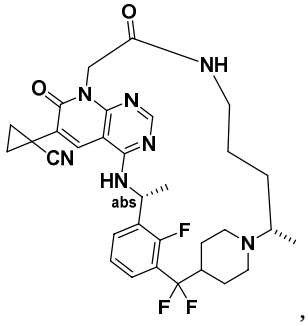
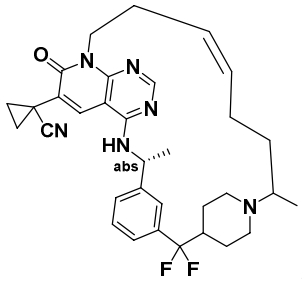
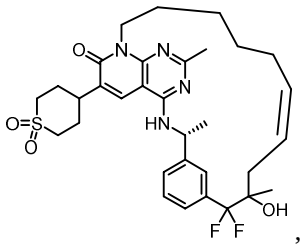
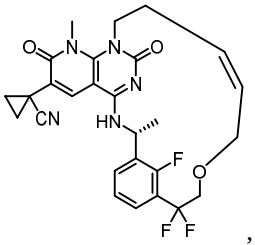
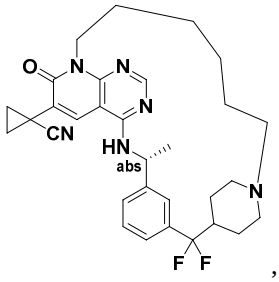
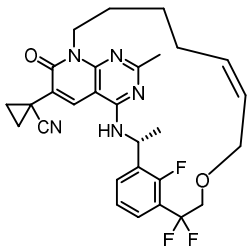
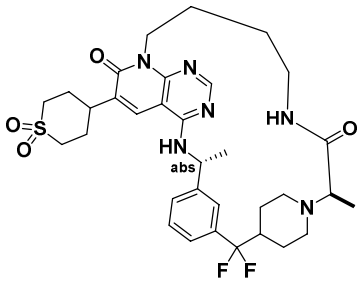
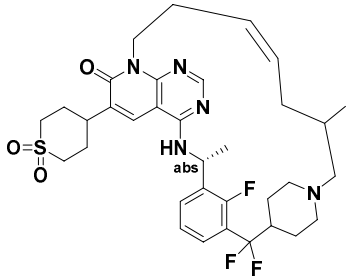
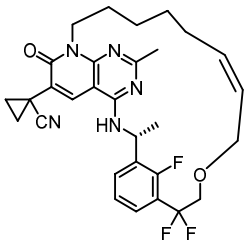
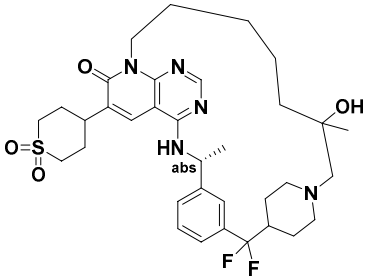
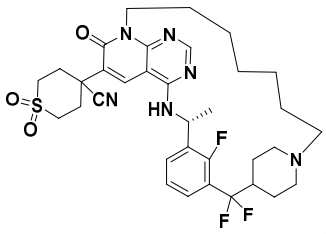
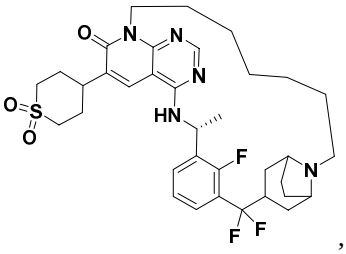
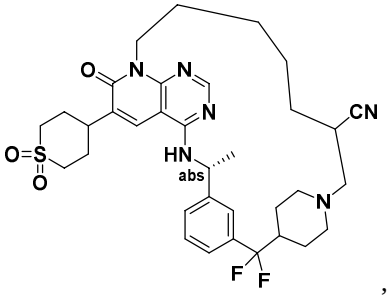
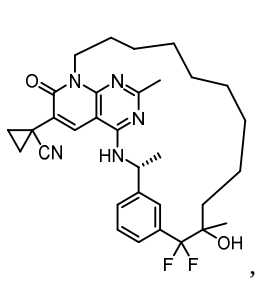
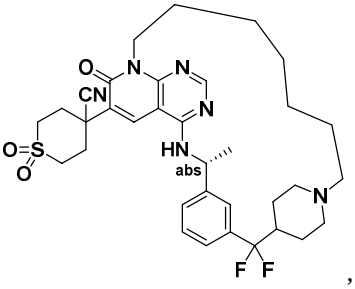
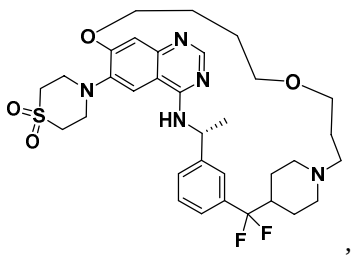
,

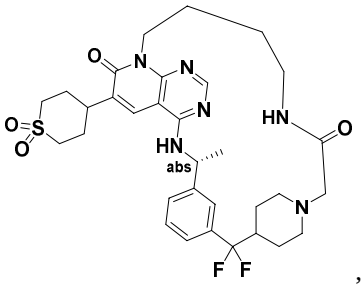
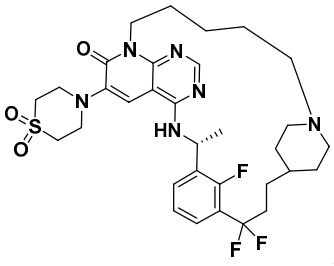
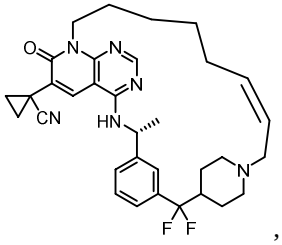
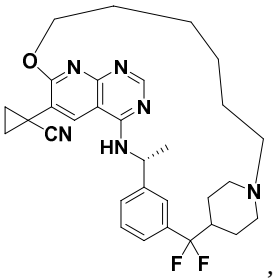
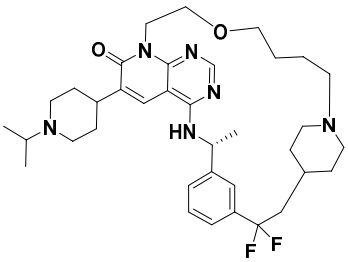
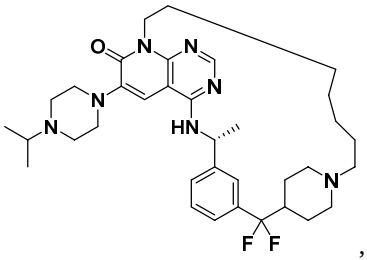
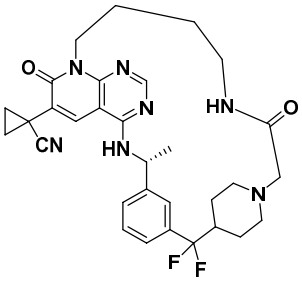
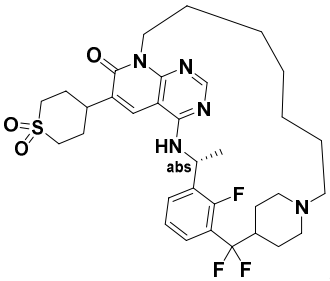
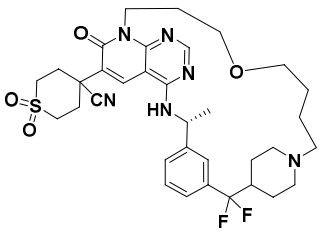
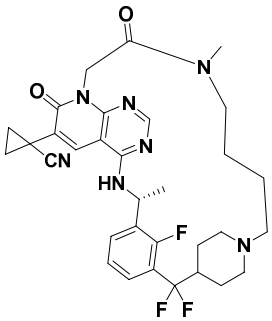
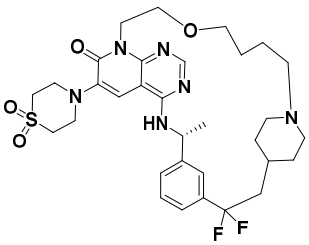
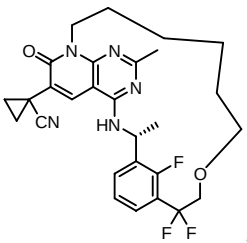
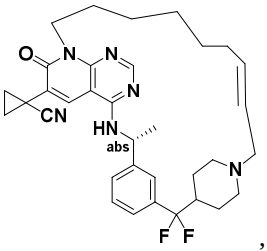
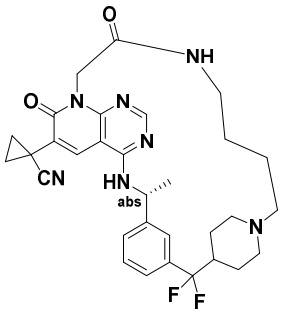
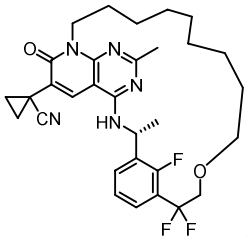
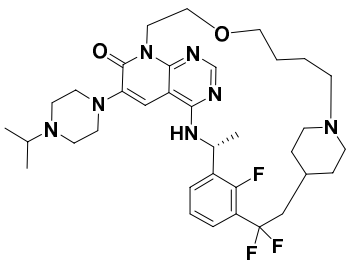
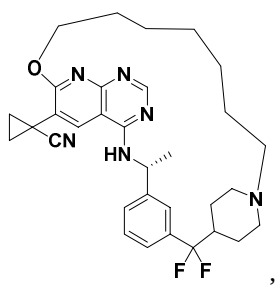
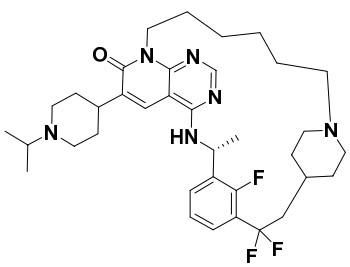
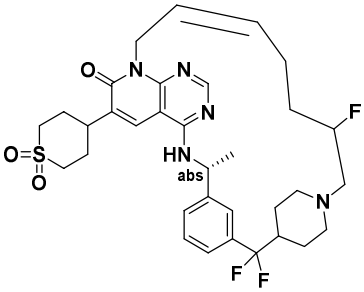
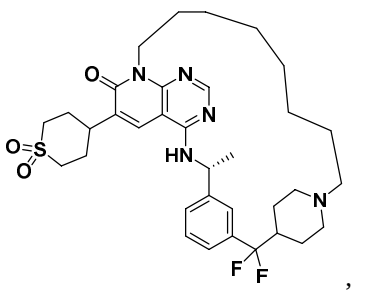

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

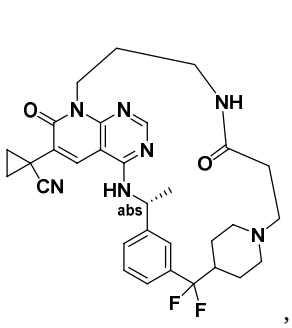
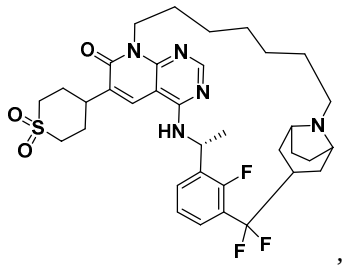
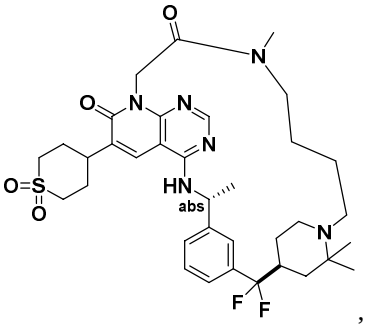
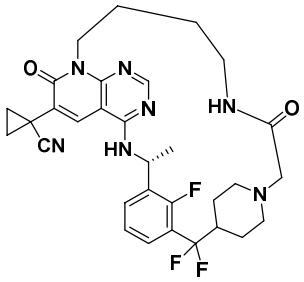
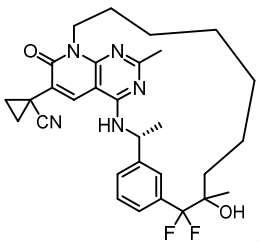
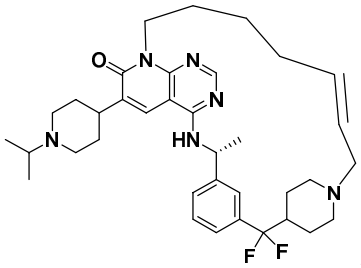
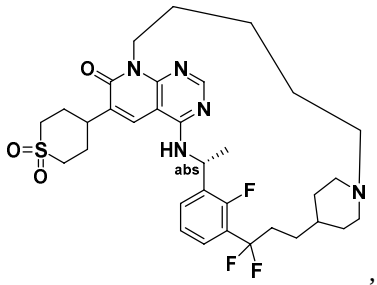
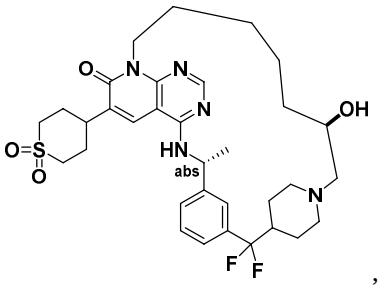
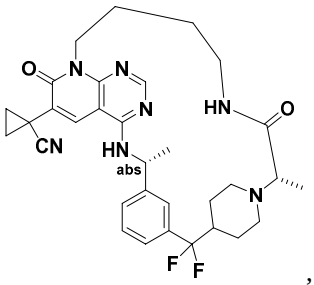
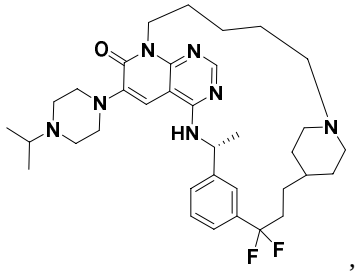
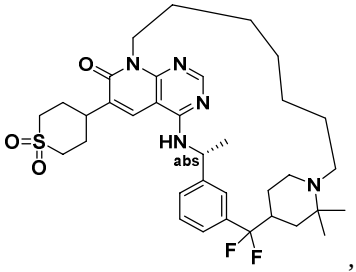
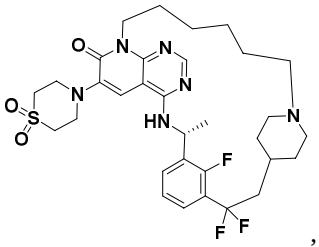
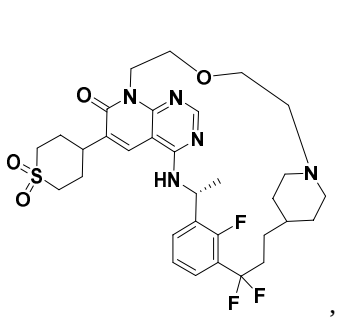
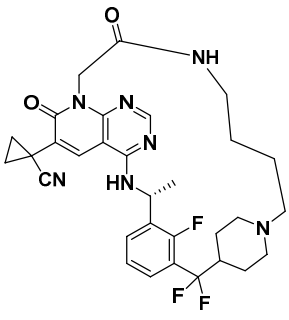
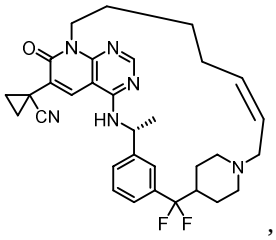
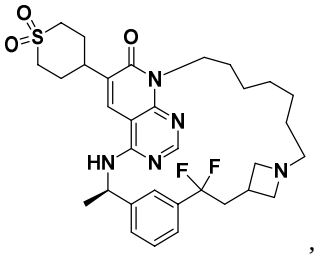
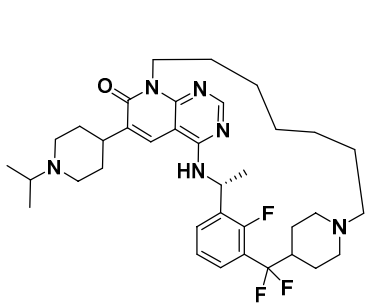
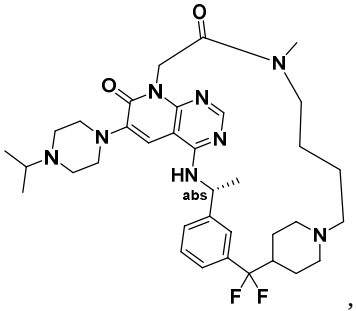
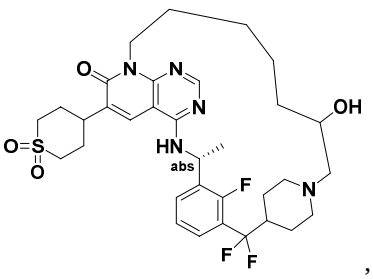
,

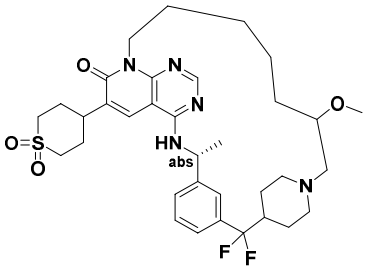
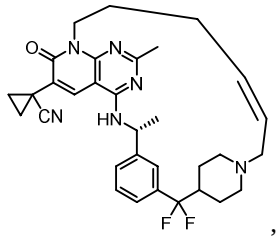
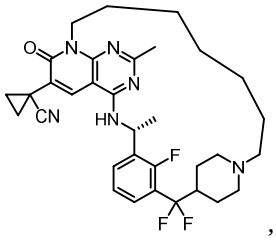
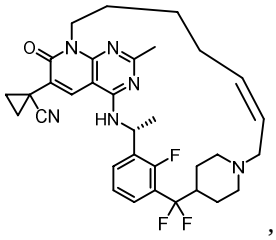
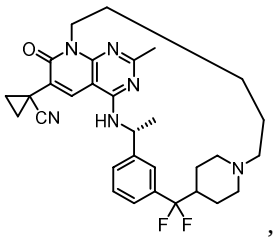
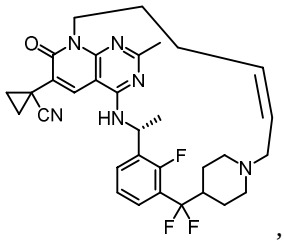
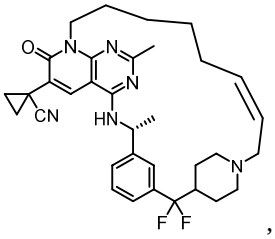
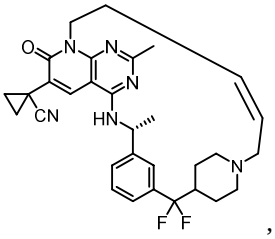
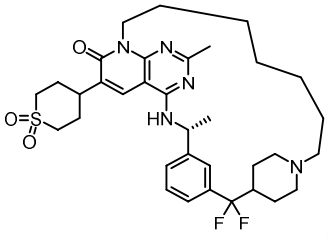
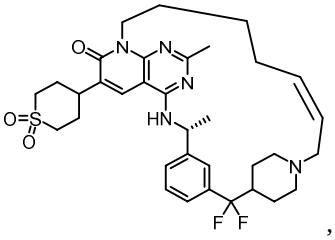
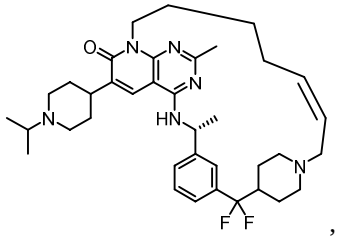
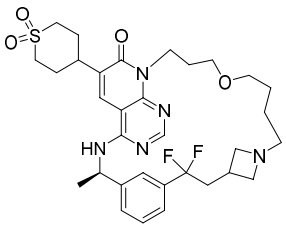
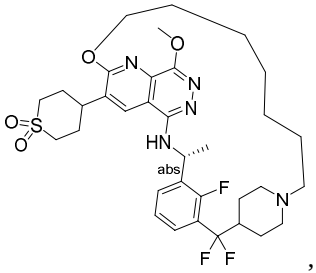
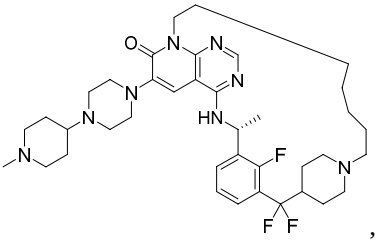
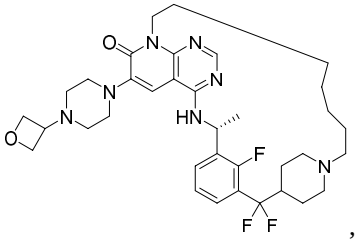
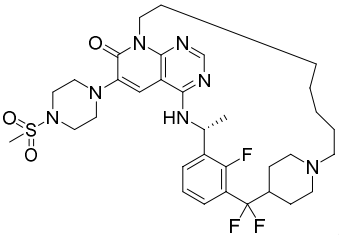
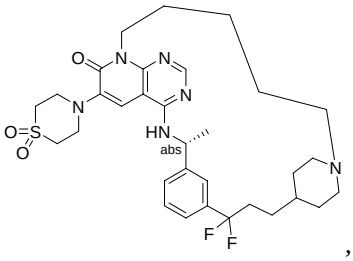
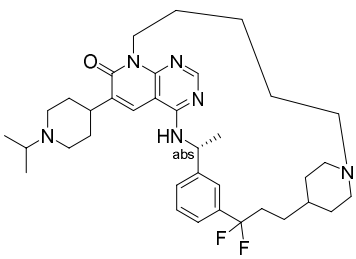
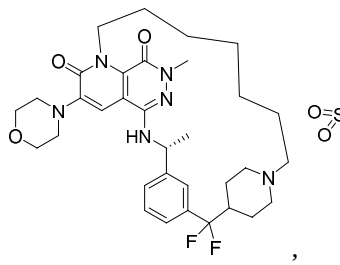
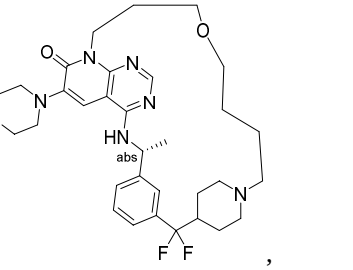
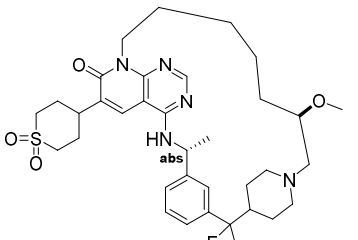
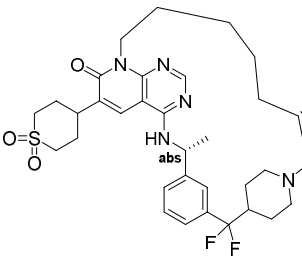
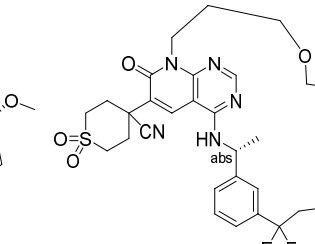
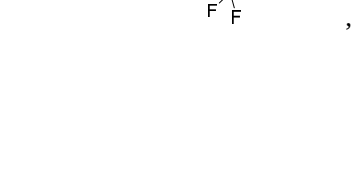
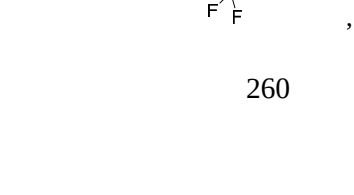
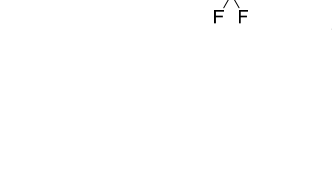
,

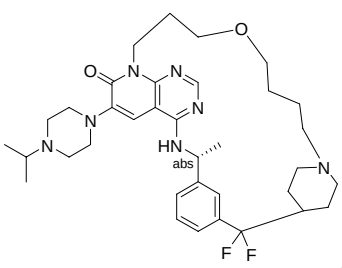
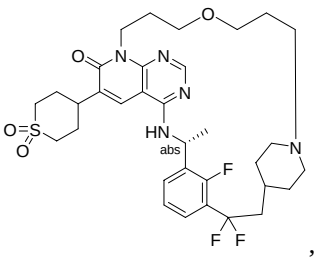
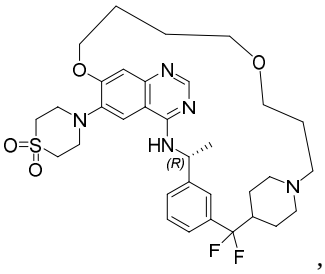
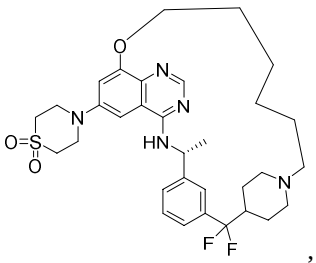
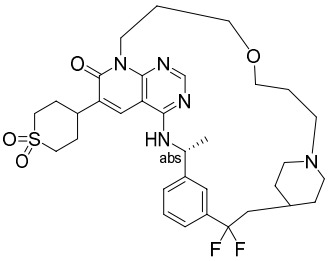
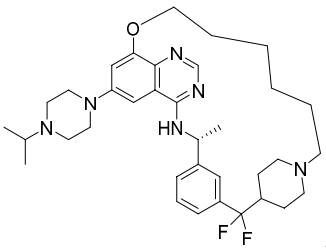
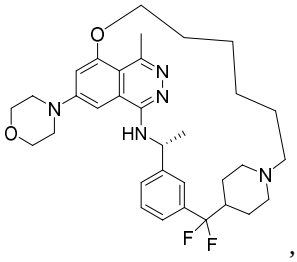
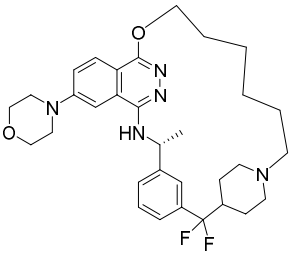
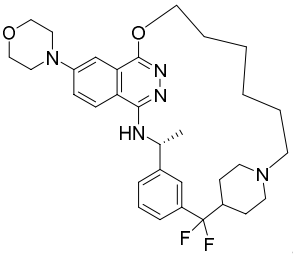
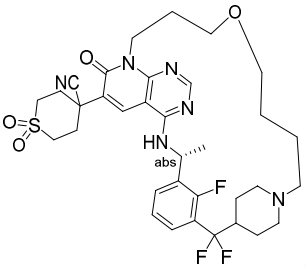
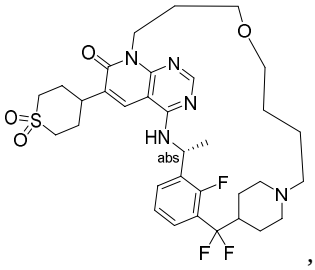
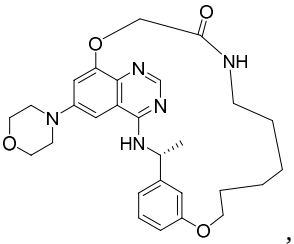
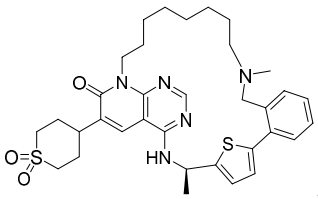
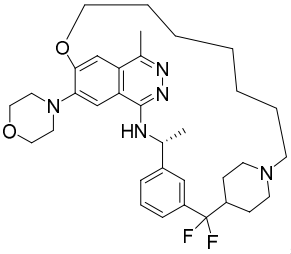
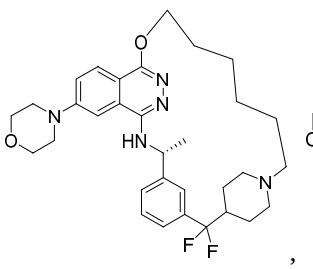
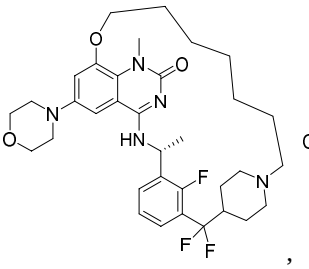
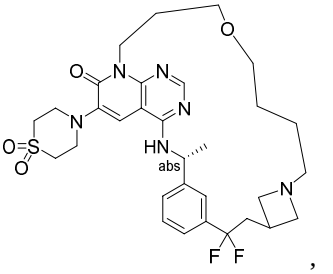
,

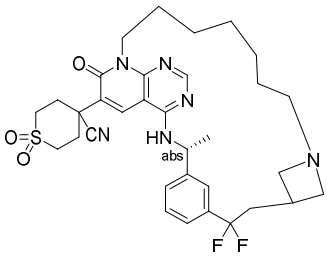
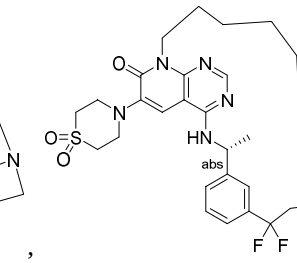
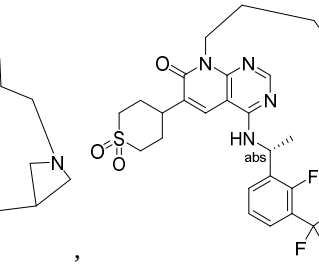

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

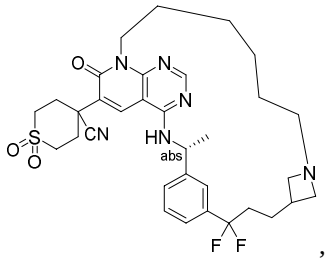

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

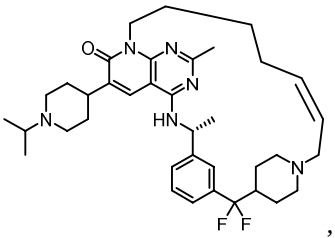
,

,

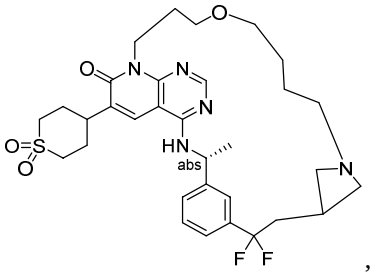
, and



, or a pharmaceutically acceptable salt or solvate thereof.

25. The compound of claim 1 having the structure 

, or a pharmaceutically acceptable salt or solvate thereof.

26. The compound of claim 1 having the structure 

, or a pharmaceutically acceptable salt or solvate thereof.

27. A pharmaceutical composition comprising a compound of any one of claims 1 to 26, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.

28. Use of a compound of any one of claims 1 to 26, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of cancer.

29. The use of claim 28, wherein the treatment further comprises an additional agent or therapy.

30. A compound of any one of claims 1 to 26, or a pharmaceutically acceptable salt or solvate thereof, for use in inhibiting cell growth in a cell that expresses SOS1.