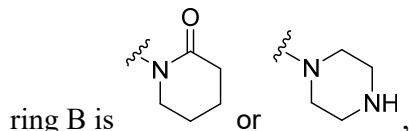
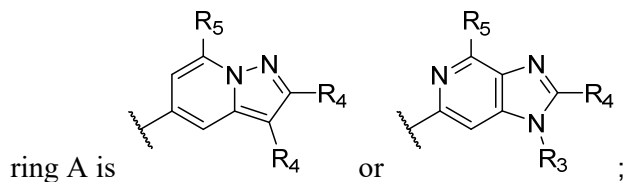


or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein



each of which is optionally substituted with one or two R₂ groups;

Linker L is a bond;

R₁ is H;

each instance of R₂ is H, deuterium, halogen, -OH, CN, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₈ alkoxy, -(CH₂)_nOR₆, -(CH₂)_nSR₆, -(CH₂)_nC(O)R₆, -(CH₂)_nC(O)OR₆, -(CH₂)_nS(O)_mR₆, -(CH₂)_nNR₇R₈, -(CH₂)_nC(O)NR₇R₈, -(CH₂)_nNR₇C(O)R₆, -(CH₂)_nNR₇S(O)_mR₆, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl represented by R₂ is each optionally substituted with one or more groups selected from deuterium, halogen, CN, -OH, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ alkoxy, and NR₇R₈;

each instance of R₃ is H, deuterium, C₁₋₄ alkyl optionally substituted with -OH, or C₃₋₆ cycloalkyl optionally substituted with -OH;

each instance of R₄ is H, deuterium, halogen, C₁₋₄ alkyl optionally substituted with fluoro, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl optionally substituted with methyl, or 3-6 membered heterocyclyl; or two R₄ groups attached to the same ring atom of ring A form C₃₋₆ cycloalkyl or 3-6 membered heterocyclyl, each of which is optionally

substituted with one or more groups selected from halogen, CN, -OH, C₁₋₂ alkyl, C₁₋₂ alkoxy, and NR₇R₈;

each instance of R₅ is H, deuterium, halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ alkoxy, or C₁₋₄ haloalkoxy;

each instance of R₆ is independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl, wherein the C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl represented by R₆ is each optionally substituted with one or more groups selected from halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, and NR₇R₈;

each instance of R₇ and R₈ is independently H, C₁₋₄ alkyl or cyclopropyl;

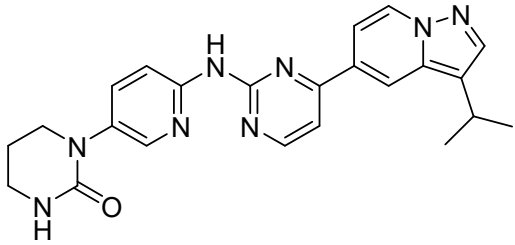
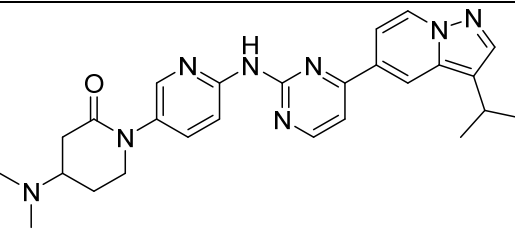
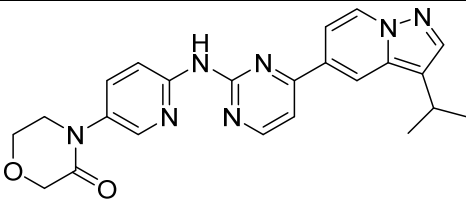
each instance of R₁₂ is H, F, Cl, CH₃, or CF₃;

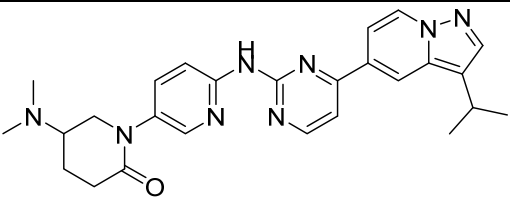
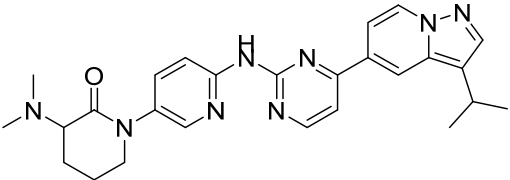
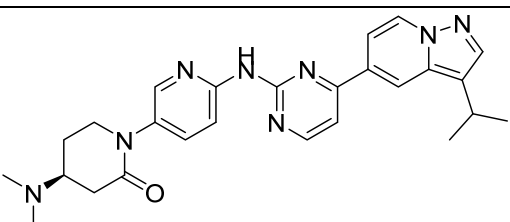
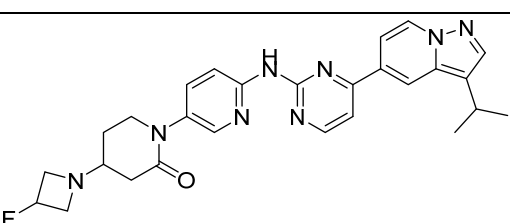
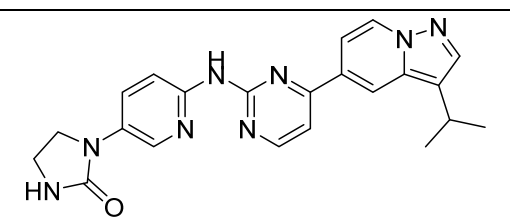
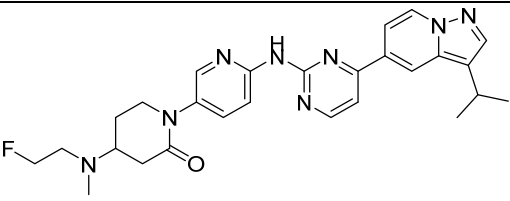
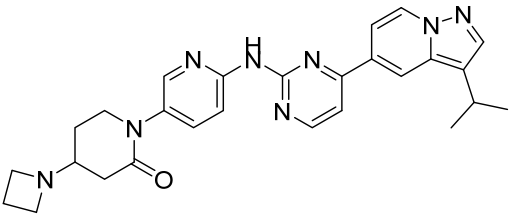
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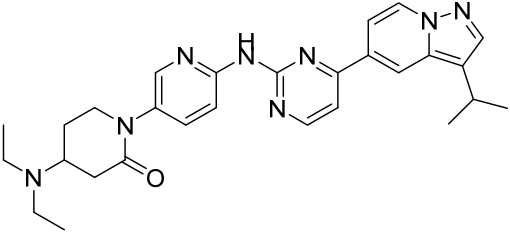
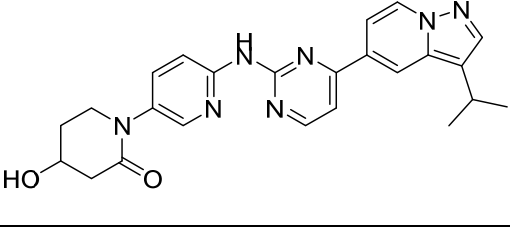
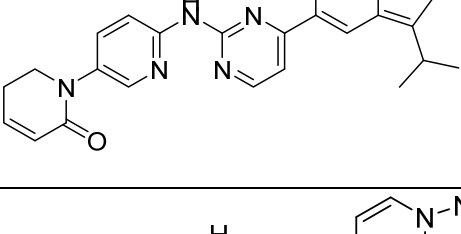
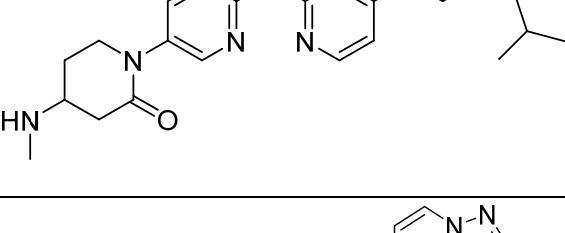
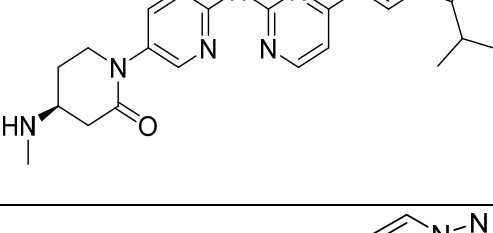
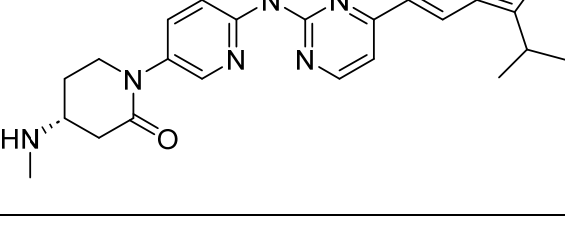
n is 0, 1, 2, 3, 4, or 5; and

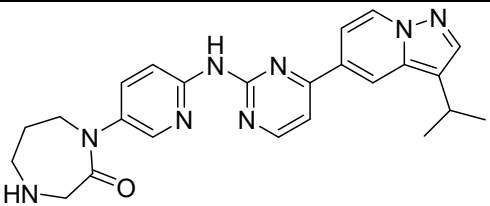
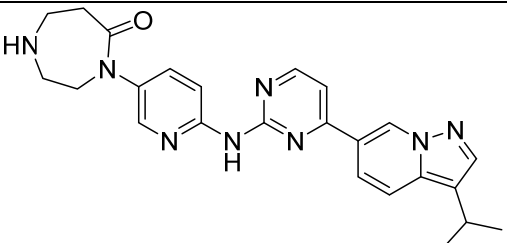
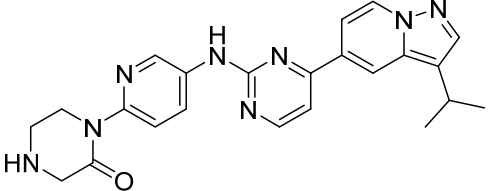
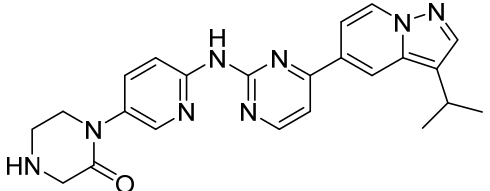
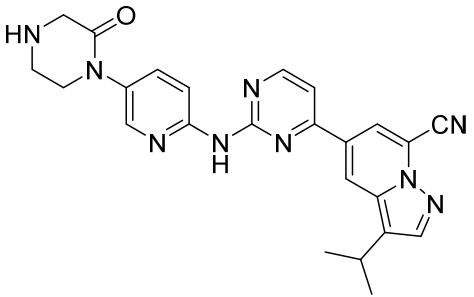
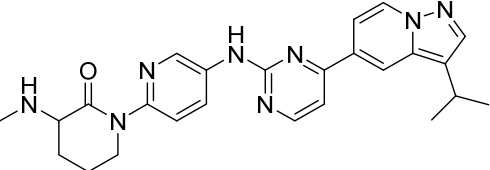
m is 0, 1, or 2.

In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein the compound is:

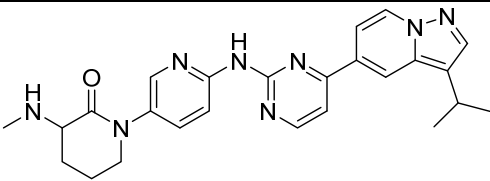
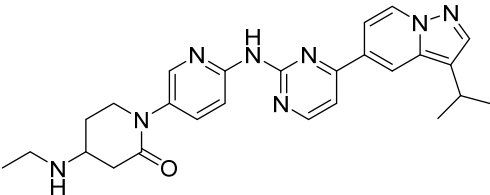
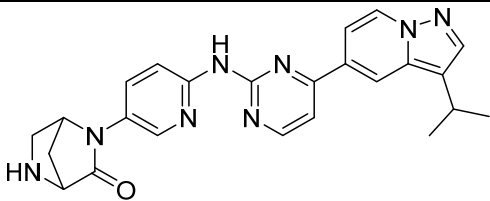
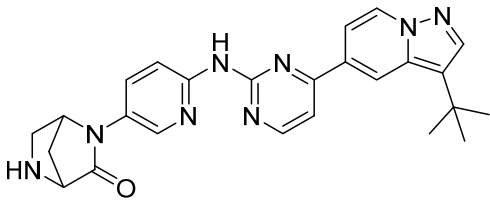
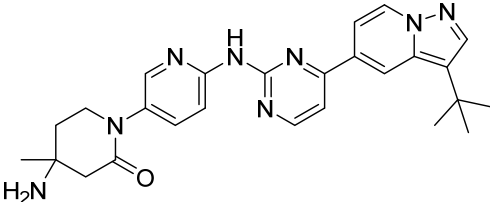
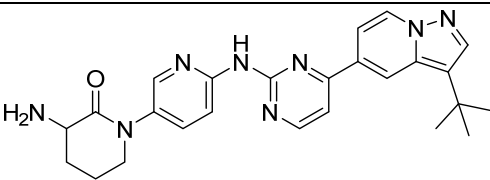
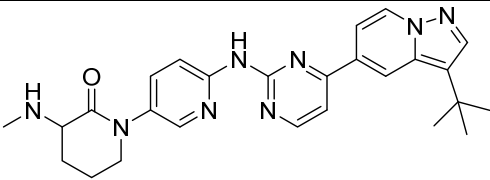
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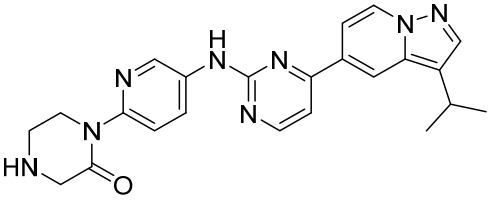
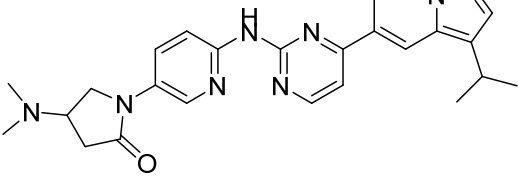
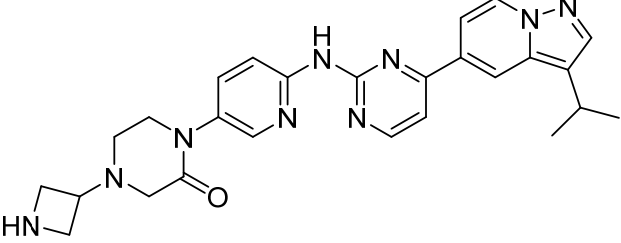
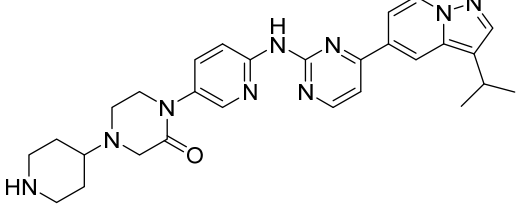
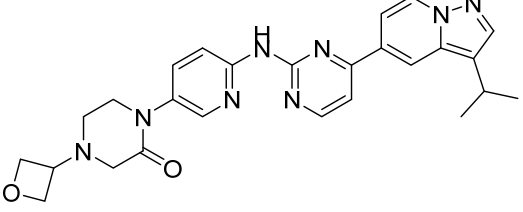
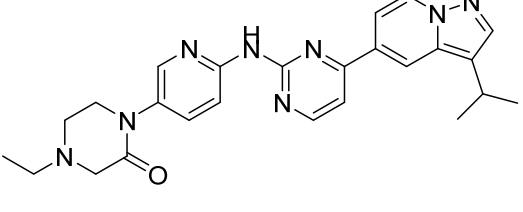
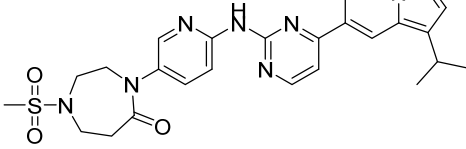
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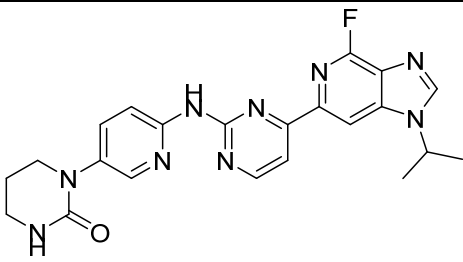
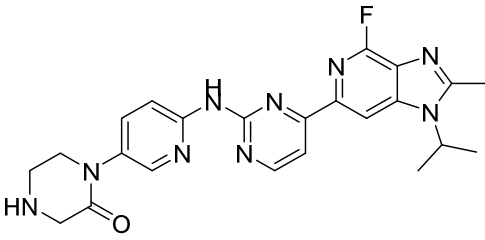
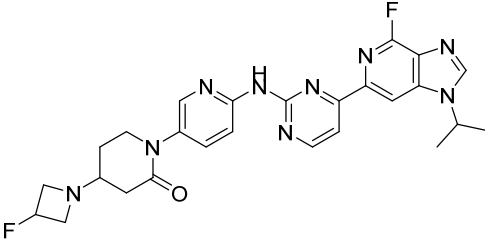
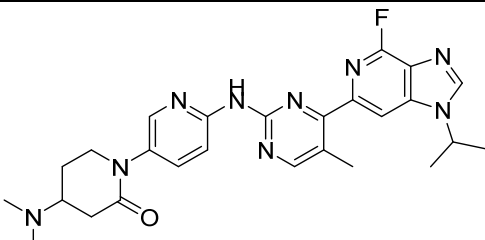
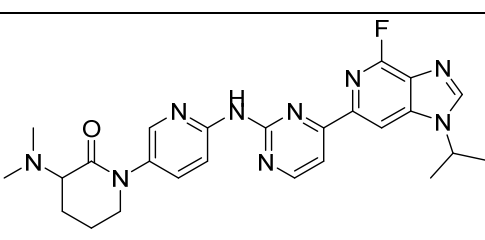
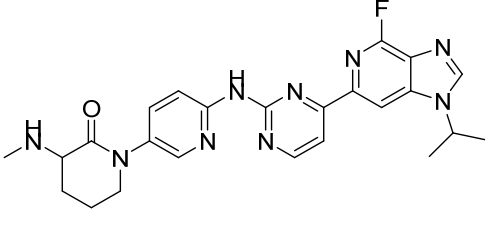
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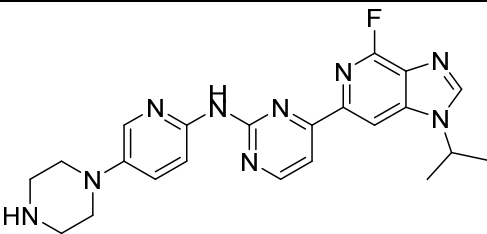
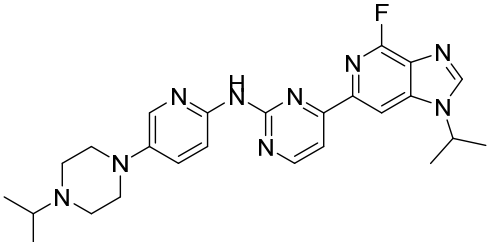
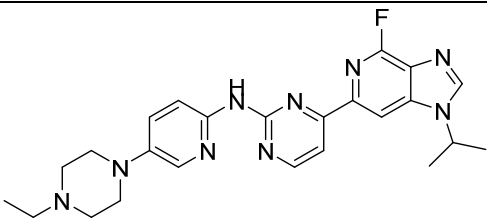
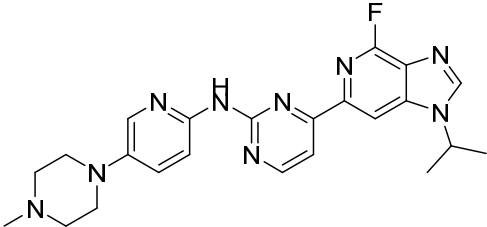
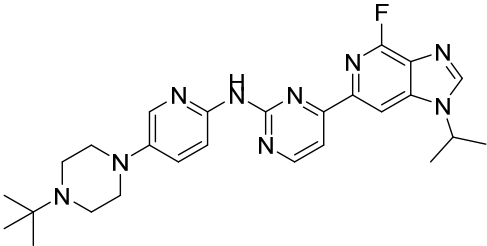
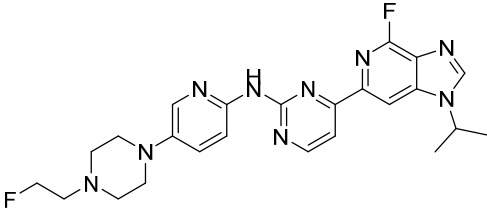
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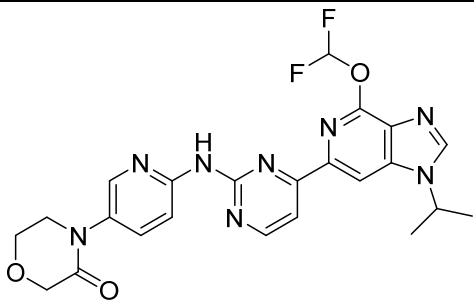
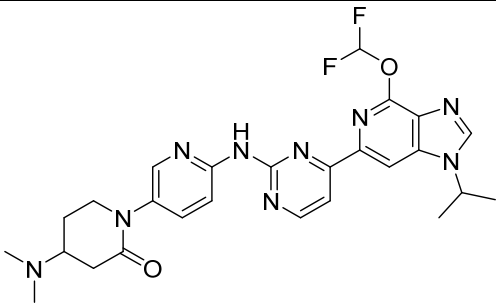
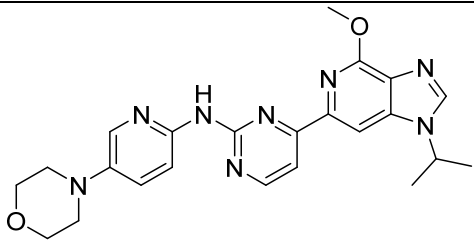
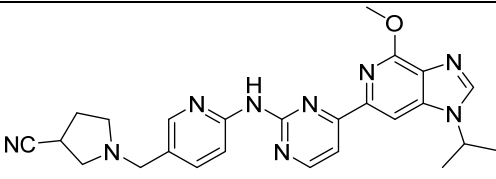
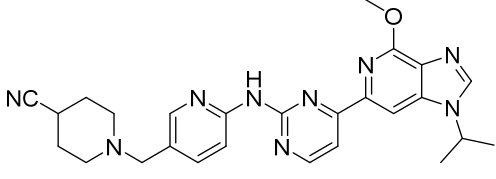
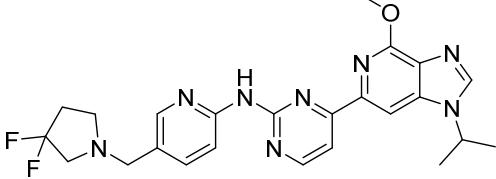
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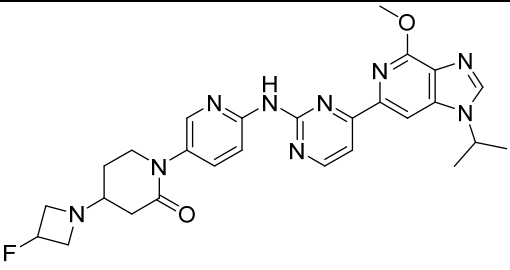
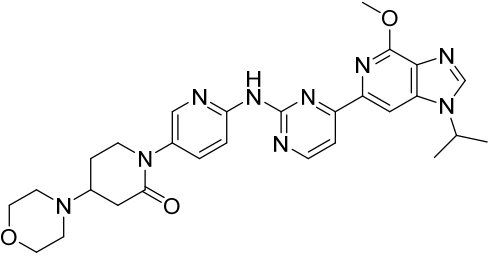
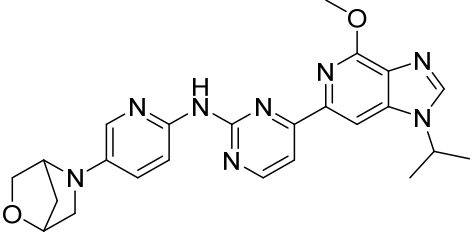
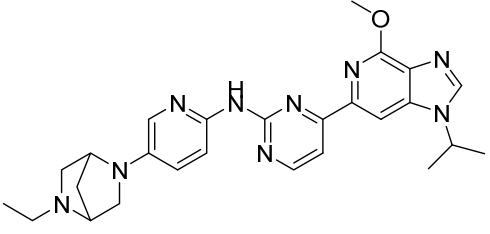
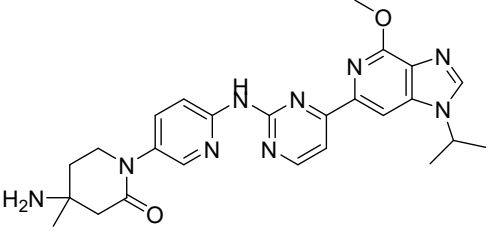
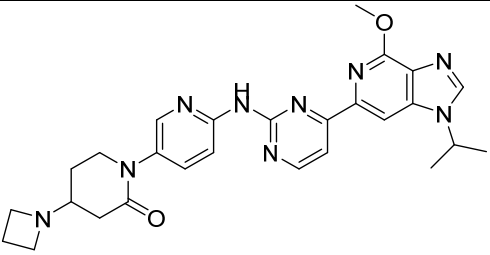
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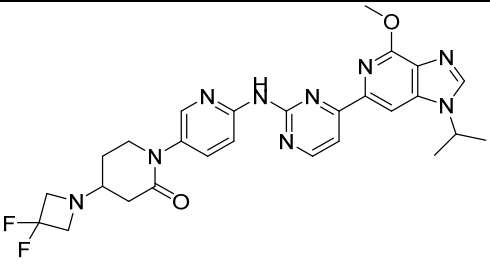
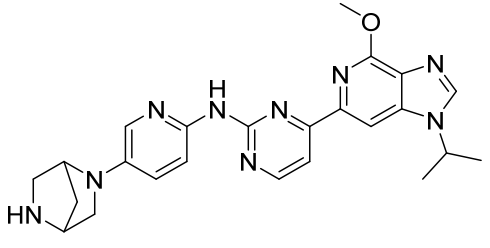
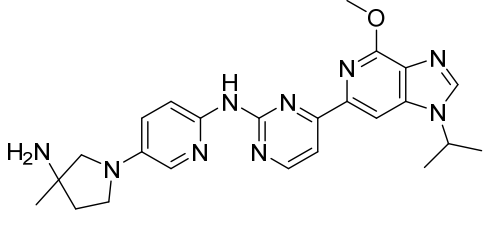
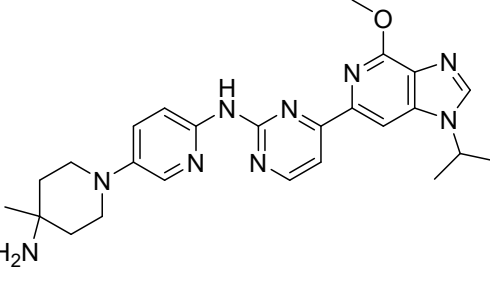
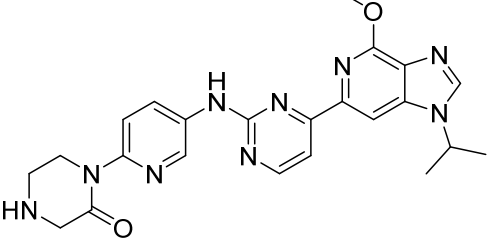
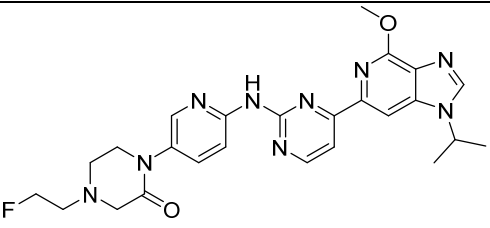
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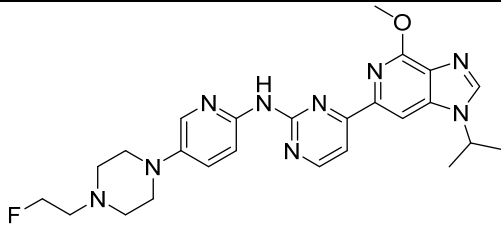
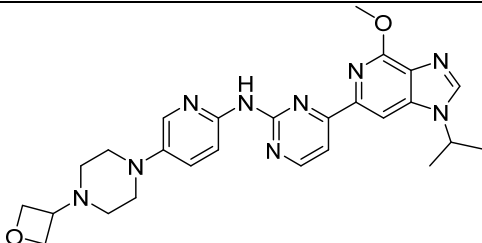
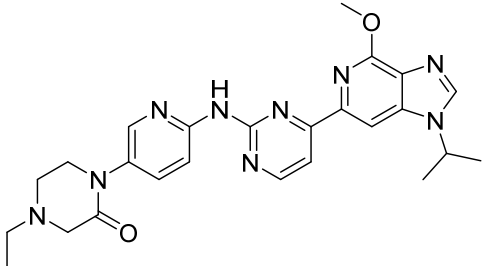
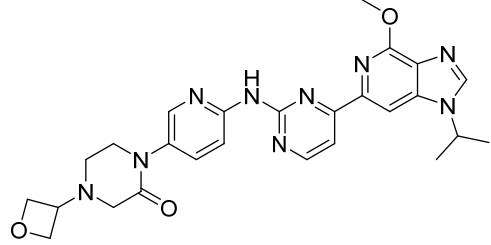
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In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising an effective amount of the compound disclosed herein or a pharmaceutically acceptable salt, or a stereoisomer thereof, and a pharmaceutically acceptable carrier.

In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, or a stereoisomer thereof, in the manufacture of a medicament for treating cancer, wherein the cancer is selected from the group consisting of colorectal cancer, breast cancer, lung cancer, prostate cancer, glioblastoma,

In another aspect of the present disclosure, there is provided a use of a compound

disclosed herein, in the manufacture of a medicament for treating a cancer by inhibiting a cyclin-dependent kinase (CDK) wherein the cancer is carcinoma of the bladder, breast, colon, kidney, epidermis, liver, lung, oesophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, nose, head and neck, prostate, or skin; a hematopoietic tumor of lymphoid lineage; a hematopoietic tumor of myeloid lineage; thyroid follicular cancer; a tumor of mesenchymal origin; a tumor of the central or peripheral nervous system; melanoma; seminoma; teratocarcinoma; osteosarcoma; xeroderma pigmentosum; keratoacanthoma; or Kaposi's sarcoma.

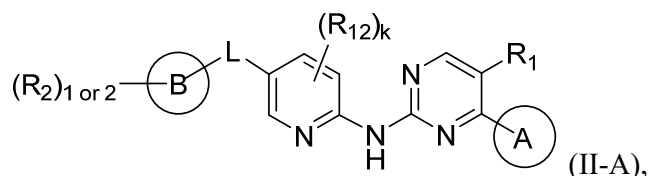
In a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt, or a stereoisomer thereof, for use in treating cancer, wherein the cancer is selected from the group consisting of colorectal cancer, breast cancer, lung cancer, prostate cancer, glioblastoma, mantle cell lymphoma, chronic myeloid leukemia and acute myeloid leukemia.

Described herein are compounds of Formulae (I), (II-A)-(II-J), and the compounds of the examples (collectively referred to herein as “the compounds of the invention” or “the compounds of the present disclosure”), that inhibit the activity of a cyclin-dependent kinase (CDK), *e.g.*, CDK2, CDK4, and/or CDK6, and pharmaceutically acceptable salts, or stereoisomers thereof.

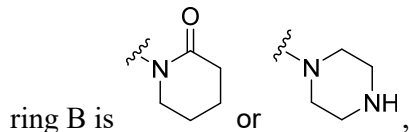
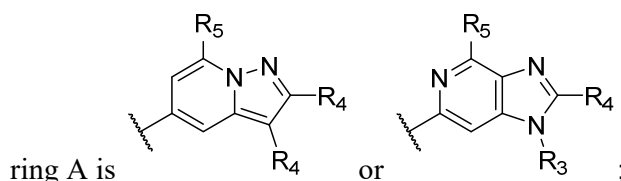
In one example, the present disclosure provides a compound of Formula (I) or a pharmaceutically acceptable salt, or a stereoisomer thereof:

CLAIMS

1. A compound represented by structural formula (IIA):



or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein



each of which is optionally substituted with one or two R₂ groups;

Linker L is a bond;

R₁ is H;

each instance of R₂ is H, deuterium, halogen, -OH, CN, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₈ alkoxy, -(CH₂)_nOR₆, -(CH₂)_nSR₆, -(CH₂)_nC(O)R₆, -(CH₂)_nC(O)OR₆, -(CH₂)_nS(O)_mR₆, -(CH₂)_nNR₇R₈, -(CH₂)_nC(O)NR₇R₈, -(CH₂)_nNR₇C(O)R₆, -(CH₂)_nNR₇S(O)_mR₆, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl represented by R₂ is each optionally substituted with one or more groups selected from deuterium, halogen, CN, -OH, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ alkoxy, and NR₇R₈;

each instance of R₃ is H, deuterium, C₁₋₄ alkyl optionally substituted with -OH, or C₃₋₆ cycloalkyl optionally substituted with -OH;

each instance of R₄ is H, deuterium, halogen, C₁₋₄ alkyl optionally substituted with fluoro, C₂₋₄ alkenyl, C₃₋₆ cycloalkyl optionally substituted with methyl, or 3-6 membered heterocyclyl; or two R₄ groups attached to the same ring atom of ring A form C₃₋₆ cycloalkyl or 3-6 membered heterocyclyl, each of which is optionally substituted with one or more groups selected from halogen, CN, -OH, C₁₋₂ alkyl, C₁₋₂ alkoxy, and NR₇R₈;

each instance of R₅ is H, deuterium, halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ alkoxy, or C₁₋₄ haloalkoxy;

each instance of R₆ is independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl, wherein the C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, 3-10 membered heterocyclyl, 6-14 membered aryl, 5-14 membered heteroaryl represented by R₆ is each optionally substituted with one or more groups selected from halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, and NR₇R₈;

each instance of R₇ and R₈ is independently H, C₁₋₄ alkyl or cyclopropyl;

each instance of R₁₂ is H, F, Cl, CH₃, or CF₃;

k is 0;

n is 0, 1, 2, 3, 4, or 5; and

m is 0, 1, or 2.

2. The compound of claim 1 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein

each instance of R₂ is H, halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, -(CH₂)_nOR₆, -(CH₂)_nC(O)R₆, -(CH₂)_nC(O)OR₆, -(CH₂)_nS(O)₂R₆, -(CH₂)_nNR₇R₈, -(CH₂)_nC(O)NR₇R₈, -(CH₂)_nC(O)NHR₇, -(CH₂)_nNR₇C(O)R₆, -(CH₂)_nNR₇S(O)₂R₆, C₃₋₈ cycloalkyl, 3-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl;

each instance of R₆ is independently H, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, 3-7 membered heterocyclyl, phenyl, 5-6 membered heteroaryl, wherein the C₁₋₄ alkyl, C₃₋₆ cycloalkyl, 3-7 membered heterocyclyl, phenyl, 5-6 membered heteroaryl represented by R₆ is each optionally substituted with halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, or NR₇R₈; and

n is 0, 1, or 2.

3. The compound of claim 1 or 2 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein

each instance of R₂ is H, halogen, CN, -OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, -(CH₂)_nS(O)₂C₁₋₄ alkyl, -(CH₂)_nNR₇R₈, C₃₋₄ cycloalkyl, or 3-6 membered heterocyclyl; and n is 0, 1, or 2.

4. The compound of any one of claims 1-3 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein

each instance of R₃ is H, C₁₋₃ alkyl optionally substituted with -OH, or C₃₋₆ cycloalkyl optionally substituted with -OH;

each instance of R₄ is H, halogen, C₁₋₃ alkyl, C₂₋₄ alkenyl, cyclopentyl, tetrahydro-2H-pyranyl, 3,6-dihydro-2H-pyranyl; and

each instance of R₅ is H, F, CN, methoxy, OCHF₂.

5. The compound of any one of claims 1-4 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein

each instance of R₂ is H, halogen, CN, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ hydroxyalkyl, NH₂, N(CH₃)₂, NHcyclopropyl, -(CH₂)_nS(O)₂C₁₋₃ alkyl, cyclopropyl, azetidiny optionally substituted with F, oxetanyl, morpholinyl, piperidinyl, tetrahydro-2H-pyranyl, and

n is 0, 1, or 2.

6. The compound of any one of claims 1-5 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein

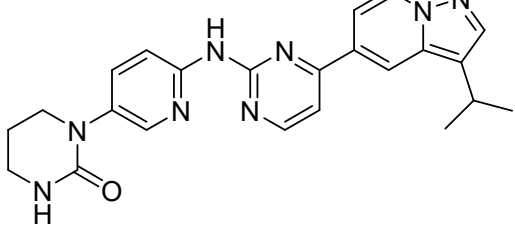
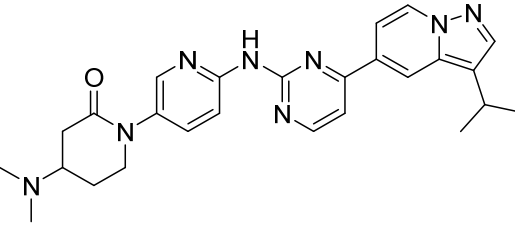
each instance of R₃ is H or C₁₋₃ alkyl;

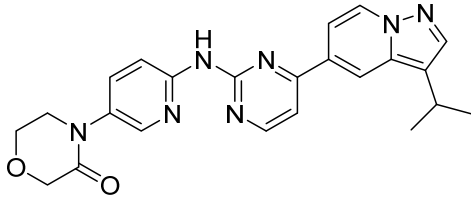
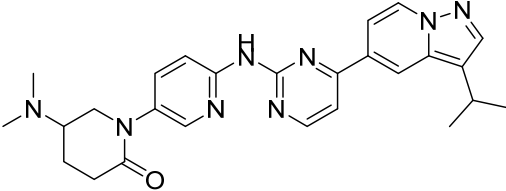
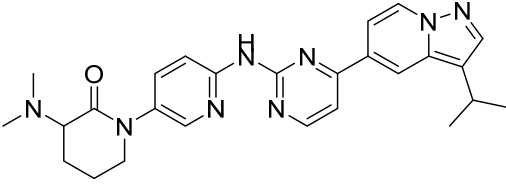
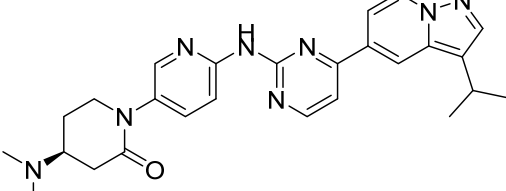
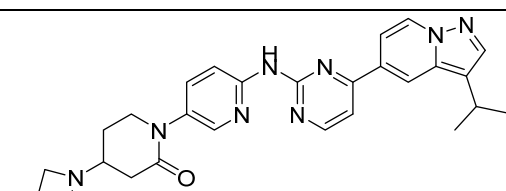
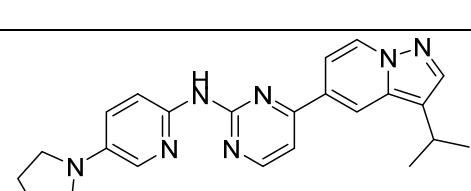
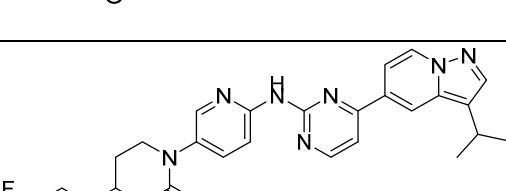
each instance of R₄ is H or C₁₋₃ alkyl; and

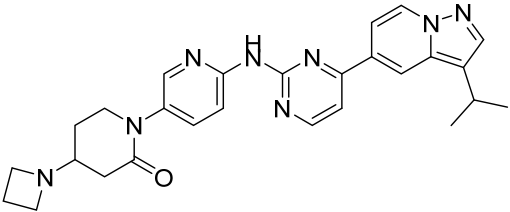
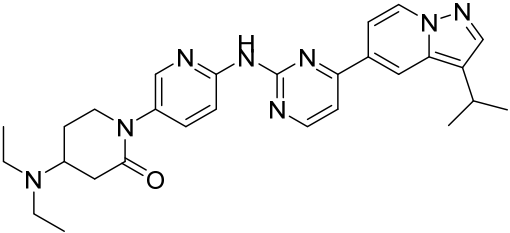
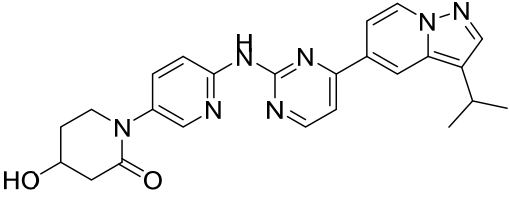
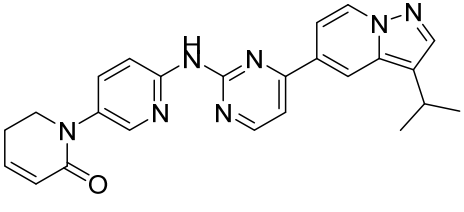
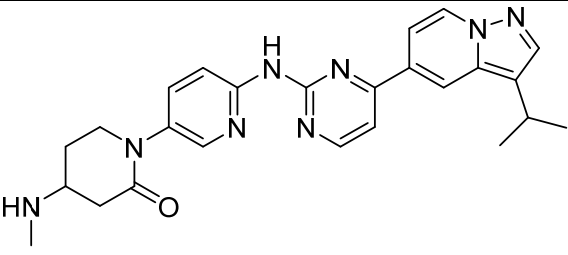
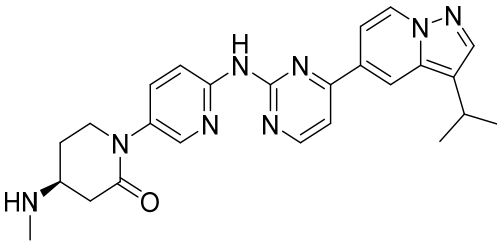
each instance of R₅ is H, F, or OMe.

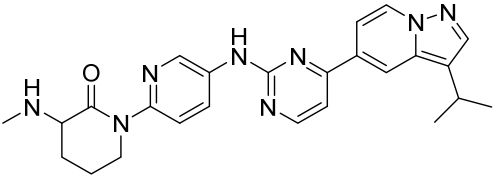
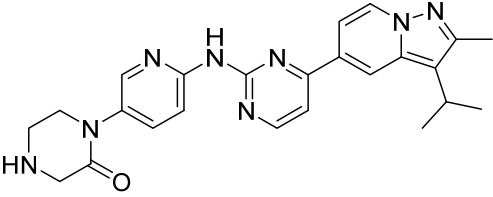
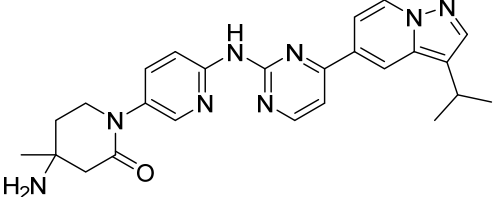
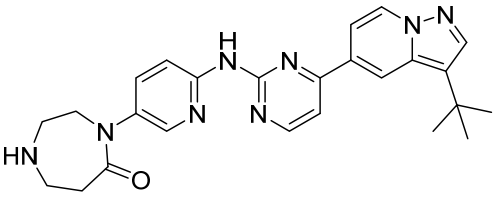
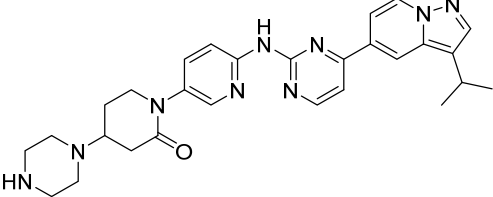
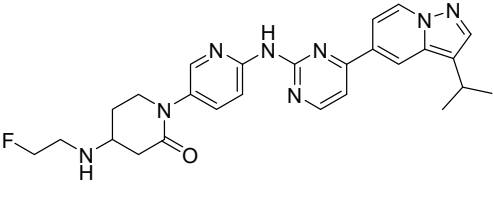
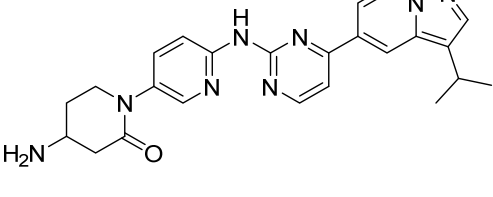
7. The compound of any one of claims 1-6 or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein each instance of R₂ is H, halogen, CN, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ hydroxyalkyl, NH₂, N(CH₃)₂, or NHcyclopropyl.

8. A compound, or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein the compound is:

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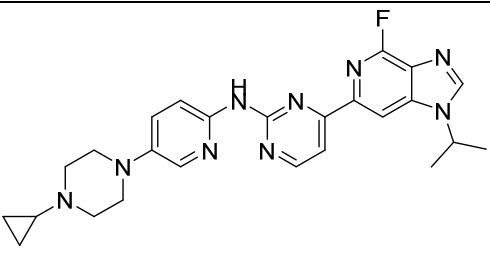
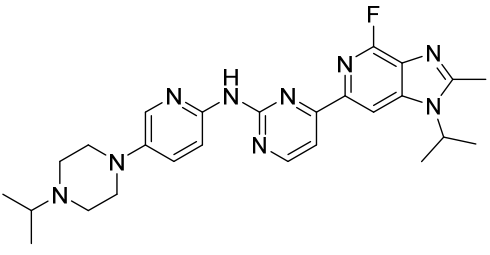
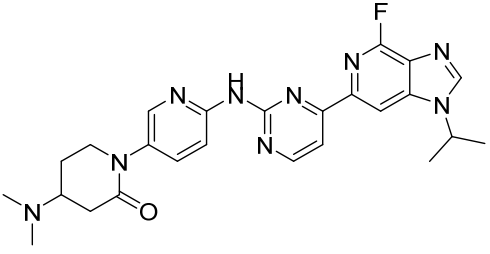
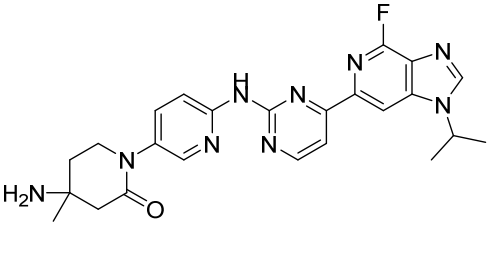
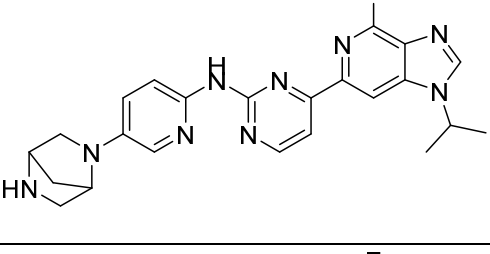
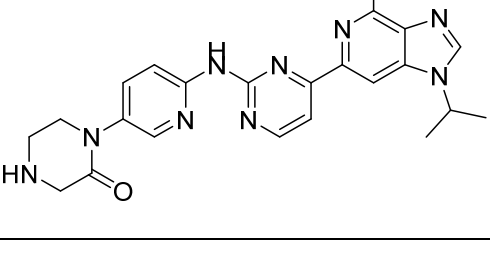
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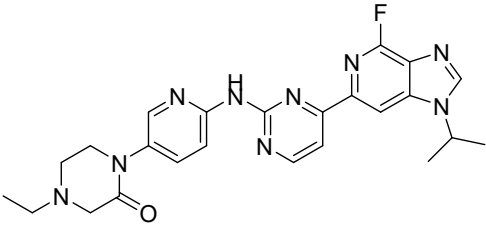
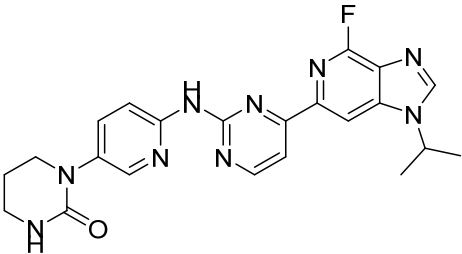
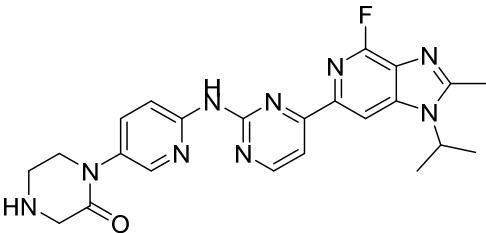
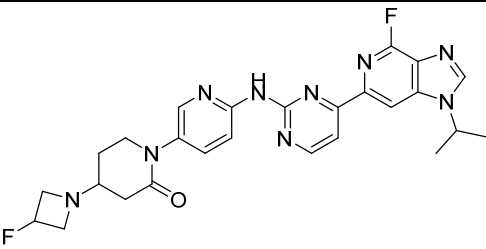
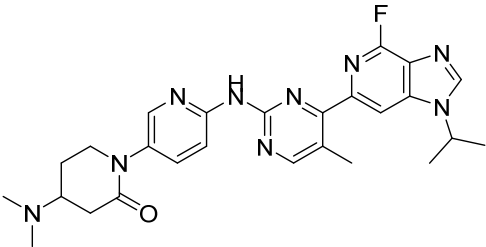
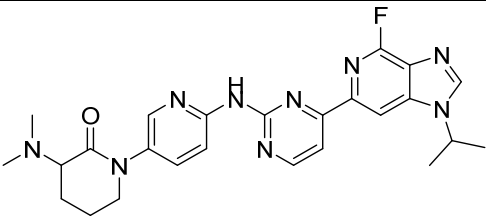
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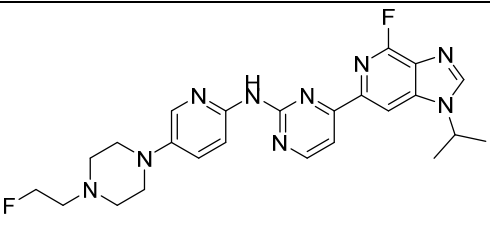
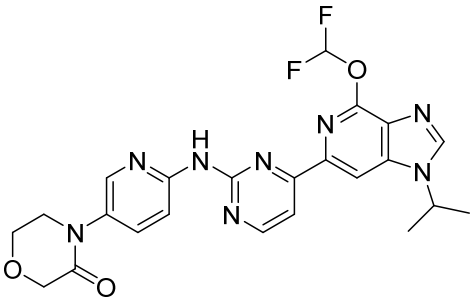
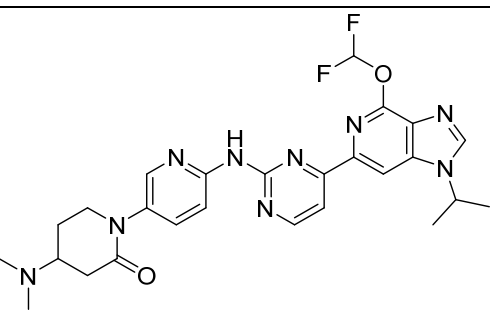
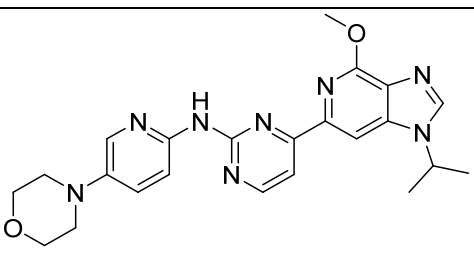
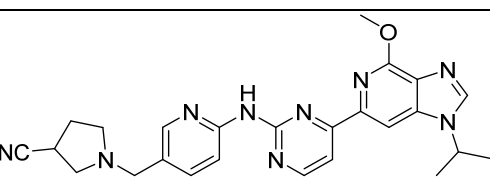
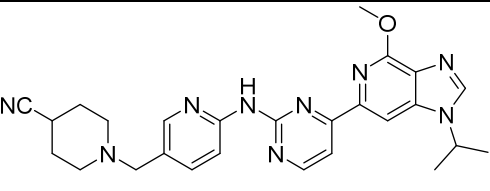
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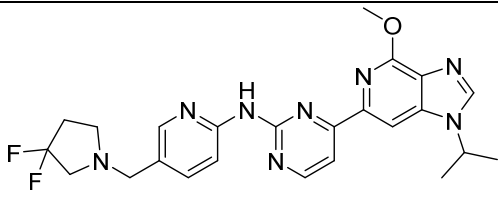
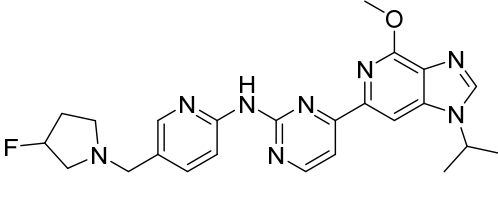
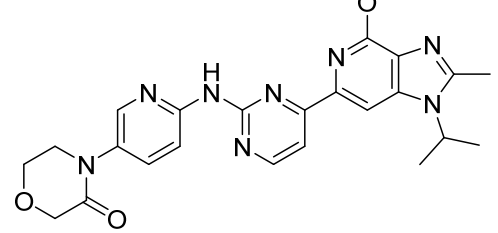
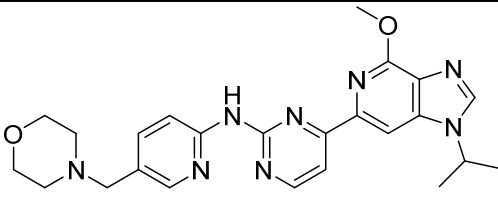
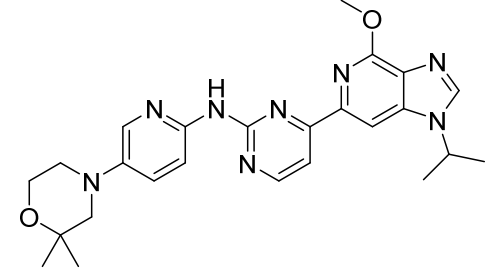
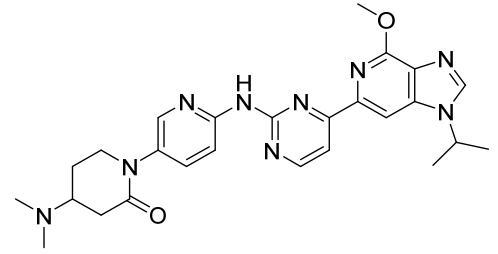
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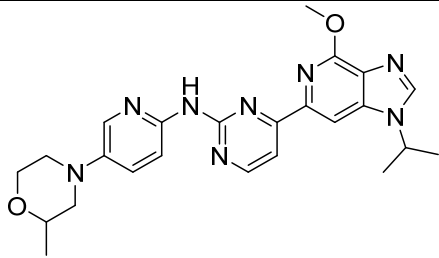
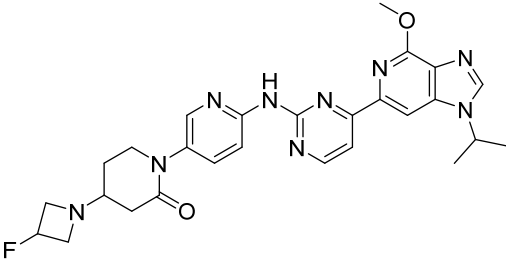
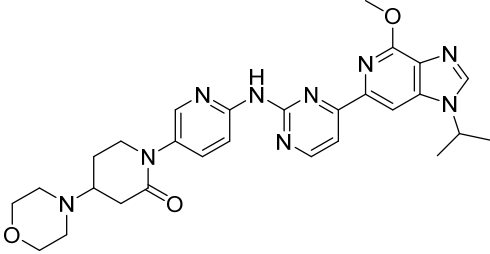
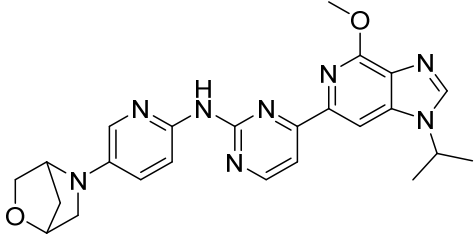
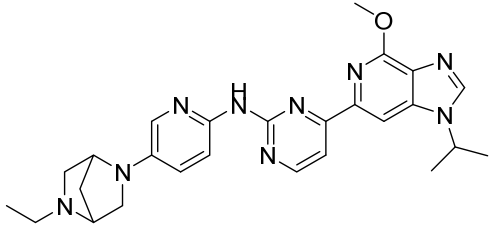
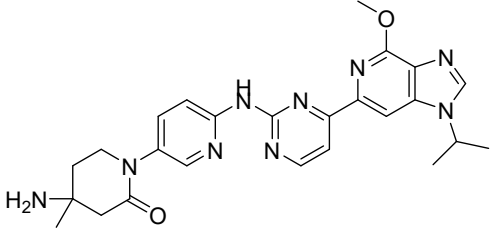
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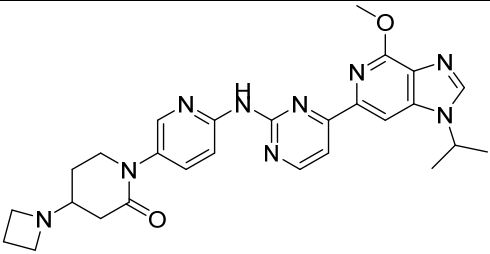
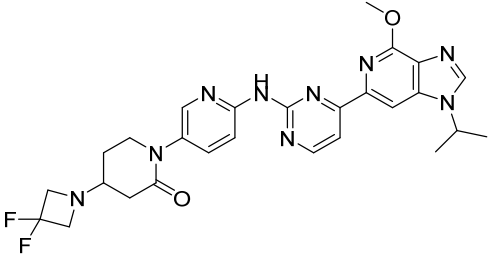
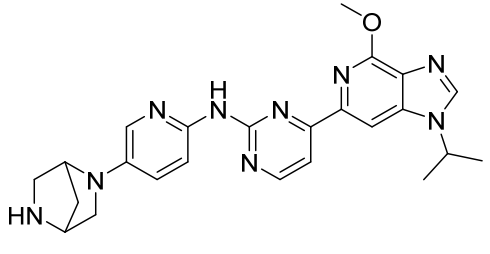
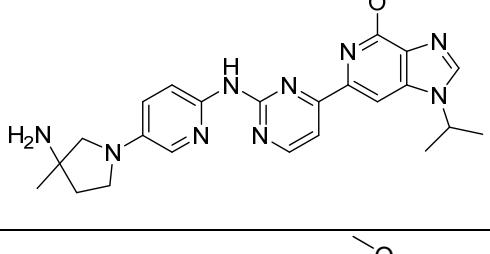
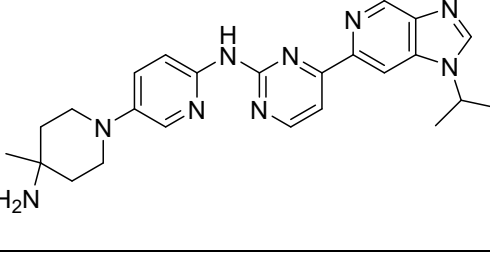
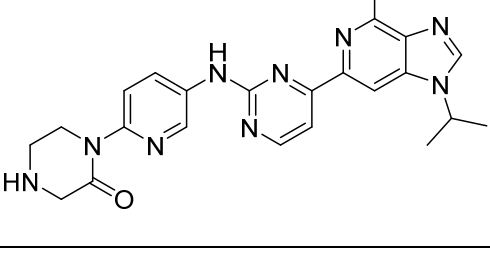
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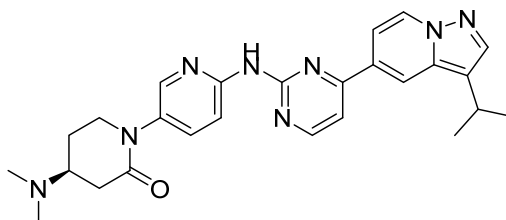
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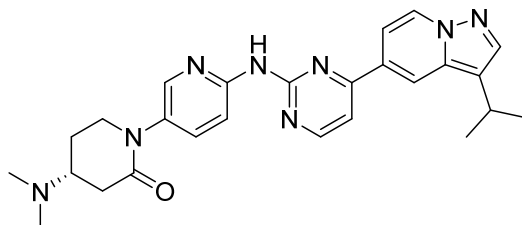
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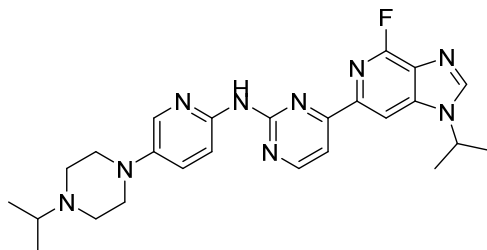
9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is



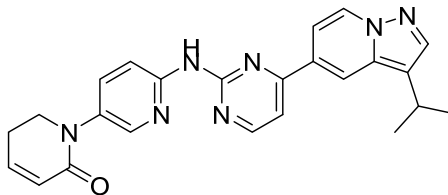
10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is



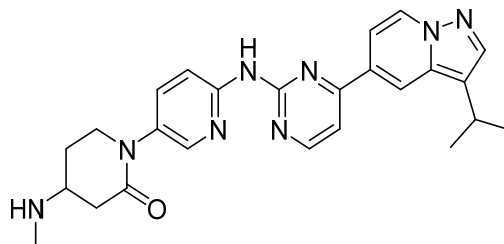
11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is



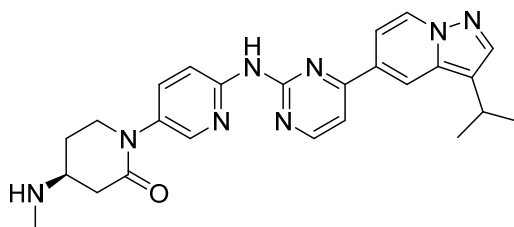
12. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is:



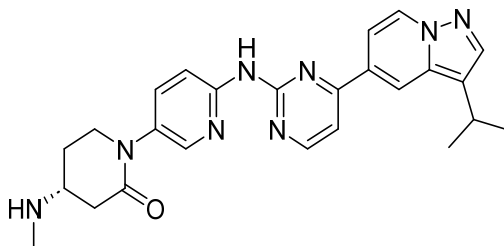
13. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is:



14. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is:



15. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is:



16. A pharmaceutical composition comprising an effective amount of the compound of any one of claims 1-15 or a pharmaceutically acceptable salt, or a stereoisomer thereof, and a pharmaceutically acceptable carrier.
17. Use of a compound of any one of claims 1-15, or a pharmaceutically acceptable salt, or a stereoisomer thereof, in the manufacture of a medicament for treating cancer, wherein the cancer is selected from the group consisting of colorectal cancer, breast cancer, lung cancer, prostate cancer, glioblastoma, mantel cell lymphoma, chronic myeloid leukemia and acute myeloid leukemia.
18. Use of a compound of any one of claims 1-15, in the manufacture of a medicament for treating a cancer by inhibiting a cyclin-dependent kinase (CDK), wherein the cancer is carcinoma of the bladder, breast, colon, kidney, epidermis, liver, lung, oesophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, nose, head and neck, prostate, or skin; a hematopoietic tumor of lymphoid lineage; a hematopoietic tumor of myeloid lineage; thyroid follicular cancer; a tumor of mesenchymal origin; a tumor of the central or peripheral nervous system; melanoma; seminoma; teratocarcinoma; osteosarcoma; xeroderma pigmentosum; keratoacanthoma; or Kaposi's sarcoma.
19. The use of claim 18, wherein the hematopoietic tumor of lymphoid lineage is leukemia, acute lymphocytic leukemia, chronic lymphocytic leukemia, B-cell

lymphoma, T-cell lymphoma, multiple myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma, or Burkett's lymphoma.

20. The use according to claim 18, wherein the cancer is pRb⁺ breast cancer, or hormone receptor (HR)-positive (*e.g.*, estrogen receptor positive (ER⁺), progesterone receptor positive (PR⁺), or ER⁺PR⁺), HER2/neu-negative cancer.
21. The use of claim 20, wherein the cancer is advanced or metastatic or recurrent breast cancer.
22. The use of claim 21, wherein the breast cancer is in an adult woman, or a postmenopausal woman.
23. The use of any of claims 20-22, wherein a second agent selected from: an aromatase inhibitor, a Selective Estrogen Receptor Modulator (SERM), a pure antiestrogen with no estrogen agonist activity, a compound that temporarily suppresses ovarian function (*e.g.*, estrogen and/or progesterone production) such as a gonadotropin-releasing hormone (GnRH) agonist or a luteinizing hormone-releasing hormone (LH-RH) agonist, a compound that inhibits CYP3A4, or a monoclonal antibody or an antigen-binding fragment thereof against IGF-1/IGF-2 is to be further administered.
24. The use of any of claims 17-23, wherein an immune checkpoint inhibitor (such as a PD-1 inhibitor, a PD-L1 inhibitor, or a CTLA-4 inhibitor), a receptor Tyr kinase inhibitor, and/or an antagonist of hormone receptor (such as estrogen receptor) is to be further administered.
25. A compound of any one of claims 1-15, or a pharmaceutically acceptable salt, or a stereoisomer thereof, for use in treating cancer, wherein the cancer is selected from the group consisting of colorectal cancer, breast cancer, lung cancer, prostate cancer, glioblastoma, mantel cell lymphoma, chronic myeloid leukemia and acute myeloid leukemia.