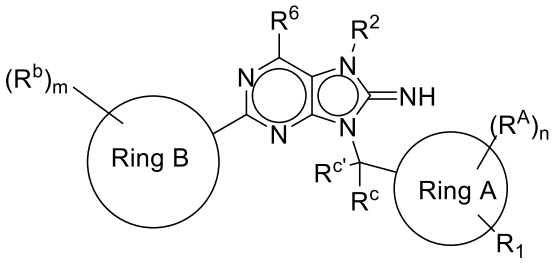
related USPs as well as dissimilar DUBs (i.e., UCHL-1 and UCHL-3). Another small molecule USP1-UAF1 inhibitor (ML323) has been more recently disclosed (Dexheimer et al, J. Med. Chem. 2014, 57, 8099-8110; Liang et al, Nature Chem. Bio. 2015, 10, 298-304; US 9802904 B2). Additional USP1 inhibitors have also been described in WO2017087837, WO2020132269, WO2020139988, and WO2021163530.

[0007] The foregoing shows that there exists an unmet need for new selective inhibitors of USP1, and in addition, that inhibition of USP1 with small molecule inhibitors has the potential to be a treatment for cancers and other disorders. For these reasons, there remains a considerable need for potent small molecule inhibitors of USP1.

Summary

[0007a] In an aspect of the present disclosure, there is provided a compound of Formula (I) or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof;

wherein:



Formula (I)

Ring B is a 5-6 member monocyclic aryl or heteroaryl;

Ring A is selected from C_6–C_{10} aryl, 5-10 membered heteroaryl, –C_3–C_{10} cycloalkyl, and 3-10 membered heterocyclyl;

R^1 is an optionally substituted 5-10 membered heteroaryl or an optionally substituted 3-10 membered heterocyclyl;

R^2 is selected from H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 hydroxyalkyl, –C_3-C_{10} cycloalkyl and arylalkyl, wherein each hydrogen of the alkyl, haloalkyl, heteroalkyl, hydroxylalkyl and arylalkyl can be independently replaced with a deuterium atom;

R^6 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkynyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, 6-10 member heteroaryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a6}, –$N(R^{a6})_2$, –$C(=O)R^{a6}$, –$C(=O)OR^{a6}$, –$NR^{a6}C(=O)R^{a6}$, –

$NR^{a6}C(=O)OR^{a6}$, $–C(=O)N(R^{a6})_2$, and $–OC(=O)N(R^{a6})_2$, wherein each alkyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

each R^{a6} is independently selected from H, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $-C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^A is independently selected from –D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, $–OR^{A1}$, $–N(R^{A1})_2$;
each R^{A1} is independently selected from H, $–C_1–C_6$ alkyl, $–C_1–C_6$ haloalkyl and $C_3–C_9$ cycloalkyl;

each R^b is independently selected from D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1$-C_6 alkenyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, 3-10 membered heterocyclyl, $–C_6$-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{b1}$, $–N(R^{b1})_2$, $–C(=O)R^{b1}$, $–C(=O)OR^{b1}$, $–NR^{b1}C(=O)R^{b1}$, $–NR^{b1}C(=O)OR^{b1}$, $–C(=O)N(R^{b1})_2$, $–OC(=O)N(R^{b1})_2$, $–S(=O)R^{b1}$, $–S(=O)_2R^{b1}$, $–SR^{b1}$, $–S(=O)(=NR^{b1})R^{b1}$, $–NR^{b1}S(=O)_2R^{b1}$ and $–S(=O)_2N(R^{b1})_2$ or 2 R^b together with the atoms to which they are attached form a 4-7 member carbocyclyl or a 4-7 member heterocyclyl, wherein each alkyl, carbocylyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of R^b is optionally substituted at any available position;

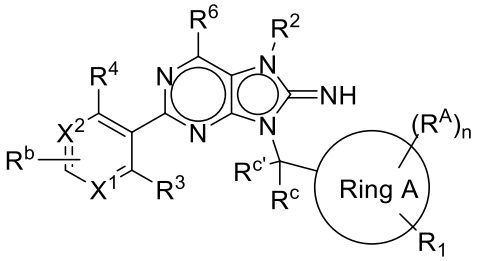
each R^{b1} is independently selected from H, $–C_1–C_6$ alkyl (wherein each hydrogen can be independently replaced by deuterium), $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $-C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^c and $R^{c'}$ is independently selected from H, –D, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl and $–C_1–C_6$ haloalkyl or R^c and $R^{c'}$ can be taken together with the atom to which they are attached to form a $–C_3–C_9$ cycloalkyl or a carbonyl;

n is 0, 1, 2 or 3; and

m is 0, 1, 2 or 3.

[0007b] In another aspect of the present disclosure, there is provided a compound as disclosed herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the compound is of Formula (II)
wherein:



Formula (II)

X^1 is selected from CH and N;

X^2 is selected from CH and N;

R^3 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a3}, –$N(R^{a3})_2$, –$C(=O)R^{a3}$, –$C(=O)OR^{a3}$, –$NR^{a3}C(=O)R^{a3}$, –$NR^{a3}C(=O)OR^{a3}$, –$C(=O)N(R^{a3})_2$, –$OC(=O)N(R^{a3})_2$, -$S(=O)R^{a3}$, –$S(=O)_2R^{a3}$, –SR^{a3}, –$S(=O)(=NR^{a3})R^{a3}$, –$NR^{a3}S(=O)_2R^{a3}$ and –$S(=O)_2N(R^{a3})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

R^4 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a4}, –$N(R^{a4})_2$, –$C(=O)R^{a4}$, –$C(=O)OR^{a4}$, –$NR^{a4}C(=O)R^{a4}$, –$NR^{a4}C(=O)OR^{a4}$, –$C(=O)N(R^{a4})_2$, –$OC(=O)N(R^{a4})_2$, -$S(=O)R^{a4}$, –$S(=O)_2R^{a4}$, –SR^{a4}, –$S(=O)(=NR^{a4})R^{a4}$, –$NR^{a4}S(=O)_2R^{a4}$ and –$S(=O)_2N(R^{a4})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position; and

each R^{a3} and R^{a4} is independently selected from H, –C_1–C_6 alkyl (wherein each hydrogen can be replaced by deuterium), –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, -C_3–C_9 cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl.

[0007c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as disclosed herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof and a pharmaceutically acceptable carrier.

[0007d] In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein in the manufacture of a medicament for treating cancer in a patient in need

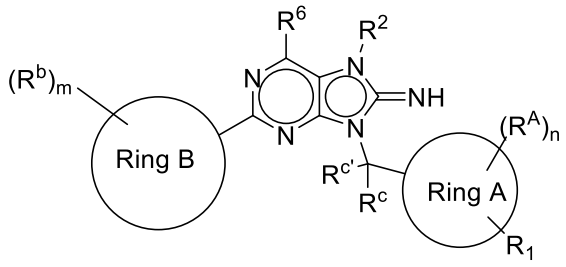
thereof, wherein the compound or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof is to be administered to the patient.

[0007e] In a further aspect of the present disclosure, there is provided a use of a composition as disclosed herein in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the composition is to be administered to the patient.

[0007f] In another aspect of the present disclosure, there is provided a compound as disclosed herein, or a pharmaceutical composition as disclosed herein, for use in therapy.

[0008] In one example, provided is a compound of Formula (I) or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof

wherein:



Formula (I)

Ring B is a 5-6 member monocyclic aryl or heteroaryl;

Ring A is selected from C_6–C_{10} aryl, 5-10 membered heteroaryl, –C_3–C_{10} cycloalkyl, and 3-10 membered heterocyclyl;

R^1 is an optionally substituted 5-10 membered heteroaryl or an optionally substituted 3-10 membered heterocyclyl;

R^2 is selected from H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 hydroxyalkyl, –C_3-C_{10} cycloalkyl and arylalkyl, wherein each hydrogen of the alkyl, haloalkyl, heteroalkyl, hydroxylalkyl and arylalkyl can be independently replaced with a deuterium atom;

R^6 is selected from H, –D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkynyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, 6-10 member heteroaryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a6}, –$N(R^{a6})_2$, –$C(=O)R^{a6}$, –$C(=O)OR^{a6}$, –$NR^{a6}C(=O)R^{a6}$, –$NR^{a6}C(=O)OR^{a6}$, –$C(=O)N(R^{a6})_2$, and –$OC(=O)N(R^{a6})_2$, wherein each alkyl, alkynyl,

cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

each R^{a6} is independently selected from H, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^A is independently selected from –D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, $–OR^{A1}$, $–N(R^{A1})_2$;

each R^{A1} is independently selected from H, $–C_1–C_6$ alkyl, $–C_1–C_6$ haloalkyl and $C_3–C_9$ cycloalkyl;

each R^b is independently selected from –D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1$-C_6 alkenyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, 3-10 membered heterocyclyl, $–C_6$-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{b1}$, $–N(R^{b1})_2$, $–C(=O)R^{b1}$, $–C(=O)OR^{b1}$, $–NR^{b1}C(=O)R^{b1}$, $–NR^{b1}C(=O)OR^{b1}$, $–C(=O)N(R^{b1})_2$, $–OC(=O)N(R^{b1})_2$, $–S(=O)R^{b1}$, $–S(=O)_2R^{b1}$, $–SR^{b1}$, $–S(=O)(=NR^{b1})R^{b1}$, $–NR^{b1}S(=O)_2R^{b1}$ and $–S(=O)_2N(R^{b1})_2$ or 2 R^b together with the atoms to which they are attached form a 4-7 member carbocyclyl or a 4-7 member heterocyclyl, wherein each alkyl, carbocylyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of R^b is optionally substituted at any available position;

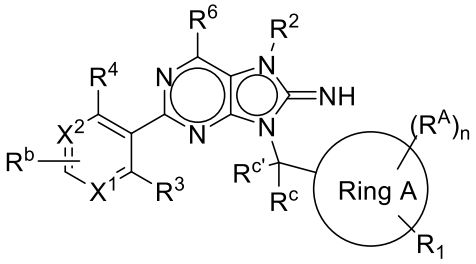
each R^{b1} is independently selected from H, $–C_1–C_6$ alkyl (wherein each hydrogen can be independently replaced by deuterium), $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^c and $R^{c'}$ is independently selected from H, –D, $–C_1–C_6$ alkyl (*e.g.*, –Me), $–C_1–C_6$ heteroalkyl and $–C_1–C_6$ haloalkyl or R^c and $R^{c'}$ can be taken together with the atom to which they are attached to form a $–C_3–C_9$ cycloalkyl (*e.g.*, cyclopropyl) or a carbonyl;

n is 0, 1, 2 or 3; and

m is 0, 1, 2 or 3.

[0009] In some examples, provided is a compound is of Formula (II)
wherein:



Formula (II)

X^1 is selected from CH and N;

X^2 is selected from CH and N;

R^3 is selected from H, –D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a3}, –$N(R^{a3})_2$, –$C(=O)R^{a3}$, –$C(=O)OR^{a3}$, –$NR^{a3}C(=O)R^{a3}$, –$NR^{a3}C(=O)OR^{a3}$, –$C(=O)N(R^{a3})_2$, –$OC(=O)N(R^{a3})_2$, –$S(=O)R^{a3}$, –$S(=O)_2R^{a3}$, –SR^{a3}, –$S(=O)(=NR^{a3})R^{a3}$, –$NR^{a3}S(=O)_2R^{a3}$ and –$S(=O)_2N(R^{a3})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

R^4 is selected from H, –D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a4}, –$N(R^{a4})_2$, –$C(=O)R^{a4}$, –$C(=O)OR^{a4}$, –$NR^{a4}C(=O)R^{a4}$, –$NR^{a4}C(=O)OR^{a4}$, –$C(=O)N(R^{a4})_2$, –$OC(=O)N(R^{a4})_2$, –$S(=O)R^{a4}$, –$S(=O)_2R^{a4}$, –SR^{a4}, –$S(=O)(=NR^{a4})R^{a4}$, –$NR^{a4}S(=O)_2R^{a4}$ and –$S(=O)_2N(R^{a4})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position; and

each R^{a3} and R^{a4} is independently selected from H, –C_1–C_6 alkyl (wherein each hydrogen can be replaced by deuterium), –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_3–C_9 cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl.

[0010] In some examples, provided are compounds selected from the compounds of Table 1, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0011] In some examples, provided is a pharmaceutical composition comprising a compound as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof and a pharmaceutically acceptable carrier.

[0012] In some examples, the pharmaceutical composition comprises a second therapeutic agent.

[0013] In some examples, provided is a method for treating or preventing a disease or disorder associated with the inhibition of USP1 comprising administering to a patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0014] In some examples, provided is a method of treating a disease or disorder associated with the inhibition of USP1 comprising administering to a patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0015] In some examples, provided is a method for inhibiting USP1 comprising administering to a patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0016] In some examples, provided is a method for treating or preventing cancer in a patient in need thereof comprising administering to the patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0017] In some examples, provided is a method for treating cancer in a patient in need thereof comprising administering to the patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0018] In some examples, provided is a method for treating or preventing a disease or disorder associated with DNA damage comprising administering to a patient in need of a treatment for diseases or disorders associated with DNA damage an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof. In some examples the disease is cancer.

[0019] In some examples, provided is a method for treating a disease or disorder associated with DNA damage comprising administering to a patient in need of a treatment for diseases or disorders associated with DNA damage an effective amount (*e.g.*, a therapeutically effective amount) of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0020] In some examples, provided is a method of inhibiting, modulating or reducing DNA repair activity exercised by USP1 comprising administering to a patient in need thereof an effective amount of a compound of Formula (I) as described herein or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

Detailed Description

[0021] The disclosure herein sets forth exemplary methods, parameters and the like. It should be recognized, however, that such description is not intended as a limitation on the scope of the present disclosure but is instead provided as a description of exemplary embodiments.

Definitions

[0022] As used in the present disclosure, the following words and phrases are generally intended to have the meanings as set forth below unless expressly indicated otherwise or the context in which they are used indicates otherwise.

Chemical Definitions

[0023] Definitions of specific functional groups and chemical terms are described in more detail below. The chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, *Handbook of Chemistry and Physics*, 75th Ed., inside cover, and specific functional groups are generally defined as described therein. Additionally, general principles of organic chemistry, as well as specific functional moieties and reactivity, are described in Thomas Sorrell, *Organic Chemistry*, University Science Books, Sausalito, 1999; Smith and March, *March's Advanced Organic Chemistry*, 5th Edition, John Wiley & Sons, Inc., New York, 2001; Larock, *Comprehensive Organic Transformations*, VCH Publishers, Inc., New York, 1989; and Carruthers, *Some Modern Methods of Organic Synthesis*, 3rd Edition, Cambridge University Press, Cambridge, 1987.

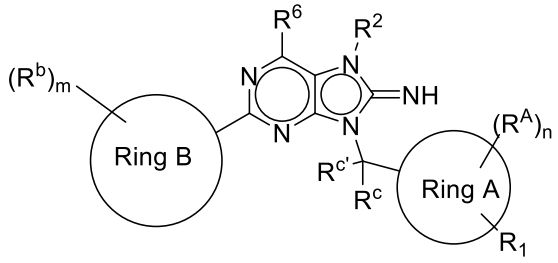
[0024] Compounds described herein can comprise one or more asymmetric centers, and thus can exist in various isomeric forms, *e.g.*, enantiomers and/or diastereomers. For example, the compounds described herein can be in the form of an individual enantiomer, diastereomer or geometric isomer, or can be in the form of a mixture of stereoisomers, including racemic mixtures and mixtures enriched in one or more stereoisomer. Isomers can be isolated from mixtures by methods known to those skilled in the art, including chiral high-pressure liquid chromatography (HPLC) and the formation and crystallization of chiral salts; or preferred isomers can be prepared by asymmetric syntheses. See, for example, Jacques *et al.*, *Enantiomers, Racemates and Resolutions* (Wiley Interscience, New York, 1981); Wilen *et al.*,

Claims

What is claimed is:

1. A compound of Formula (I) or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof;

wherein:



Formula (I)

Ring B is a 5-6 member monocyclic aryl or heteroaryl;

Ring A is selected from C_6–C_{10} aryl, 5-10 membered heteroaryl, –C_3–C_{10} cycloalkyl, and 3-10 membered heterocyclyl;

R^1 is an optionally substituted 5-10 membered heteroaryl or an optionally substituted 3-10 membered heterocyclyl;

R^2 is selected from H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 hydroxyalkyl, –C_3-C_{10} cycloalkyl and arylalkyl, wherein each hydrogen of the alkyl, haloalkyl, heteroalkyl, hydroxylalkyl and arylalkyl can be independently replaced with a deuterium atom;

R^6 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkynyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, 6-10 member heteroaryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a6}, –$N(R^{a6})_2$, –$C(=O)R^{a6}$, –$C(=O)OR^{a6}$, –$NR^{a6}C(=O)R^{a6}$, –$NR^{a6}C(=O)OR^{a6}$, –$C(=O)N(R^{a6})_2$, and –$OC(=O)N(R^{a6})_2$, wherein each alkyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

each R^{a6} is independently selected from H, –C_1–C_6 alkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, -C_3–C_9 cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^A is independently selected from –D, halo, –CN, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, –OR^{A1}, –$N(R^{A1})_2$;

each R^{A1} is independently selected from H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl and C_3–C_9 cycloalkyl;

each R^b is independently selected from D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{b1}, –$N(R^{b1})_2$, –$C(=O)R^{b1}$, –$C(=O)OR^{b1}$, –$NR^{b1}C(=O)R^{b1}$, –$NR^{b1}C(=O)OR^{b1}$, –$C(=O)N(R^{b1})_2$, –$OC(=O)N(R^{b1})_2$, –$S(=O)R^{b1}$, –$S(=O)_2R^{b1}$, –SR^{b1}, –$S(=O)(=NR^{b1})R^{b1}$, –$NR^{b1}S(=O)_2R^{b1}$ and –$S(=O)_2N(R^{b1})_2$ or 2 R^b together with the atoms to which they are attached form a 4-7 member carbocyclyl or a 4-7 member heterocyclyl, wherein each alkyl, carbocylyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of R^b is optionally substituted at any available position;

each R^{b1} is independently selected from H, –C_1–C_6 alkyl (wherein each hydrogen can be independently replaced by deuterium), –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, -C_3–C_9 cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl;

each R^c and $R^{c'}$ is independently selected from H, –D, –C_1–C_6 alkyl, –C_1–C_6 heteroalkyl and –C_1–C_6 haloalkyl or R^c and $R^{c'}$ can be taken together with the atom to which they are attached to form a –C_3–C_9 cycloalkyl or a carbonyl;

n is 0, 1, 2 or 3; and

m is 0, 1, 2 or 3.

2. The compound of claim 1 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein m is 1 or 2.

3. The compound of claim 1 or 2 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^b is independently selected from halo, –CN, –C_1-C_6, –C_1–C_6 alkyl, –C_6-C_{10} aryl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –OR^{b1} and –$N(R^{b1})_2$, or 2 R^b together with the atoms to which they are attached form a 4-7 member carbocyclyl or a 4-7 member heterocyclyl, wherein each aryl, alkyl, carbocyclyl, cycloalkyl and heterocyclyl is substituted with 0, 1, 2 or 3 instances of halo or –Me, and wherein each R^{b1} is independently selected from H, –C_1–C_6 alkyl (wherein each hydrogen can be independently replaced by deuterium), –C_1–C_6 haloalkyl and -C_3–C_9 cycloalkyl.

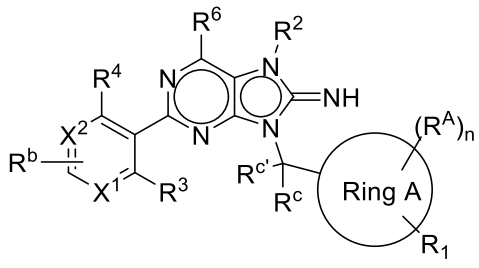
4. The compound of any one of claims 1 to 3 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^b is

independently selected from –CN, –C(=CH_2)CH_3, –F, –^{i}Pr, –CF_3, cyclopropyl (substituted with 0, 1 or 2 instances of –F, –Me, –CN), –OCF_3, –$OCHF_2$, and –OMe.

5. The compound of any one of claims 1 to 4 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein Ring B is a 6 membered heteroaryl containing 1-3 nitrogen atoms.

6. The compound of any one of claims 1 to 4 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein Ring B is selected from phenyl, pyridinyl and pyrimidinyl.

7. A compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the compound is of Formula (II) wherein:



Formula (II)

X^1 is selected from CH and N;

X^2 is selected from CH and N;

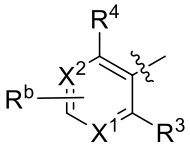
R^3 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a3}, –$N(R^{a3})_2$, –$C(=O)R^{a3}$, –$C(=O)OR^{a3}$, –$NR^{a3}C(=O)R^{a3}$, –$NR^{a3}C(=O)OR^{a3}$, –$C(=O)N(R^{a3})_2$, –$OC(=O)N(R^{a3})_2$, -$S(=O)R^{a3}$, –$S(=O)_2R^{a3}$, –SR^{a3}, –$S(=O)(=NR^{a3})R^{a3}$, –$NR^{a3}S(=O)_2R^{a3}$ and –$S(=O)_2N(R^{a3})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position;

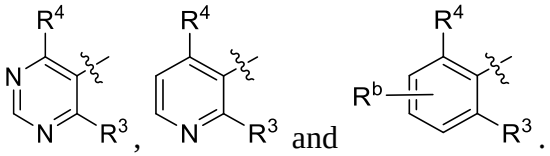
R^4 is selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a4}, –$N(R^{a4})_2$, –$C(=O)R^{a4}$, –$C(=O)OR^{a4}$, –$NR^{a4}C(=O)R^{a4}$, –$NR^{a4}C(=O)OR^{a4}$, –$C(=O)N(R^{a4})_2$, –$OC(=O)N(R^{a4})_2$, -$S(=O)R^{a4}$, –$S(=O)_2R^{a4}$, –SR^{a4}, –$S(=O)(=NR^{a4})R^{a4}$, –$NR^{a4}S(=O)_2R^{a4}$ and –$S(=O)_2N(R^{a4})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl,

heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position; and

each R^{a3} and R^{a4} is independently selected from H, $–C_1–C_6$ alkyl (wherein each hydrogen can be replaced by deuterium), $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $-C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl.

8. The compound of claim 7 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the moiety represented by

 is selected from:

.

9. The compound of claim 7 or 8 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^3 is independently selected from H, -D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1$-C_6 alkenyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, 3-10 membered heterocyclyl, $–C_6$-C_{10} aryl, $–OR^{a3}$ and $–N(R^{a3})_2$, wherein each aryl, alkyl, cycloalkyl and heterocyclyl is substituted with 0, 1, 2 or 3 instances of halo, and wherein each R^{a3} is independently selected from H, $–C_1–C_6$ alkyl (wherein each hydrogen can be replaced by deuterium), $–C_1–C_6$ haloalkyl and $-C_3–C_9$ cycloalkyl.

10. The compound of any claim 7 or 8 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^3 is independently selected from H, -D, –CN, $–C(=CH_2)CH_3$, $-C(CH_3)CH_2CH_3$, –Cl, –F, –Me, $–^i$Pr, $–CH_2N(CH_3)CH_2CF_3$, $–CF_3$, $–CH_2CF_3$, cyclopropyl (substituted with 0 or 1 instance of –CN), azetidinyl (substituted with 0 or 1 instances of –F), phenyl (substituted with 0 or 1 instances of halo), $–OCF_3$, $–OCH_2CF_3$, $–OCHF_2$, $–OCH_2F$, $–O^i$Pr, –OMe, –OEt, $–OCD_3$, $–OCH_2CH(CH_3)_3$, $–N(Me)_2$, –NHMe and $–NH^i$Pr.

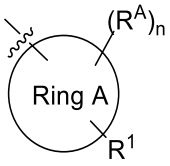
11. The compound of any one of claims 7 to 10 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^4 is

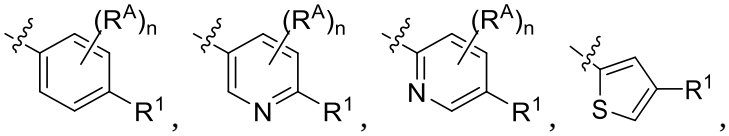
independently selected from H, -D, halo, –CN, –C_1–C_6 alkyl, –C_1-C_6 alkenyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_1–C_6 hydroxyalkyl, –C_3–C_{10} cycloalkyl, 3-10 membered heterocyclyl, –C_6-C_{10} aryl, –OR^{a4} and –$N(R^{a4})_2$, wherein each aryl, alkyl, cycloalkyl and heterocyclyl is substituted with 0, 1, 2 or 3 instances of halo or –Me, and wherein each R^{a4} is independently selected from H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl and -C_3–C_9 cycloalkyl.

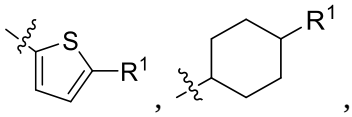
12. The compound of any one of claims 7 to 10 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^4 is independently selected from H, -D, –CN, –$C(=CH_2)CH_3$, -$C(CH_3)CH_2CH_3$, –Cl, –F, –Me, –^{i}Pr, –$CH_2N(CH_3)CH_2CF_3$, –CF_3, –CH_2CF_3, cyclopropyl (substituted with 0, 1 or 2 instances of –CN, –F, or –Me), azetidinyl (substituted with 0 or 1 instances of –F), phenyl (substituted with 0 or 1 instances of halo), –OCF_3, –OCH_2CF_3, –$OCHF_2$, –O^{i}Pr, –OMe, –$OCH_2CH(CH_3)_3$, –$N(Me)_2$ and –NHMe and –NH^{i}Pr.

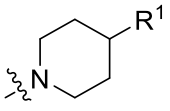
13. The compound of any one of claims 7 to 10 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^4 is selected from H and –OMe.

14. The compound any one of claims 1 to 13 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^c and $R^{c'}$ are each independently selected from H and –Me or are taken together to form a cyclopropyl group.

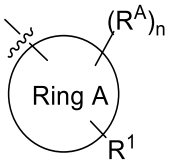
15. The compound of any one of claims 1 to 14 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the moiety represented by 

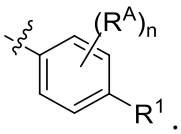
is selected from 

, 

and 

.

16. The compound of any one of claims 1 to 14 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the moiety represented by 

is 

.

17. The compound of any one of 1 to 16 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^A is independently selected from –D, halo, $–C_1–C_6$ alkyl, –OH and $–O–C_1–C_6$ alkyl.

18. The compound of claim 17 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein each R^A is independently selected from –F, –Cl, –Me, –OH and –OMe.

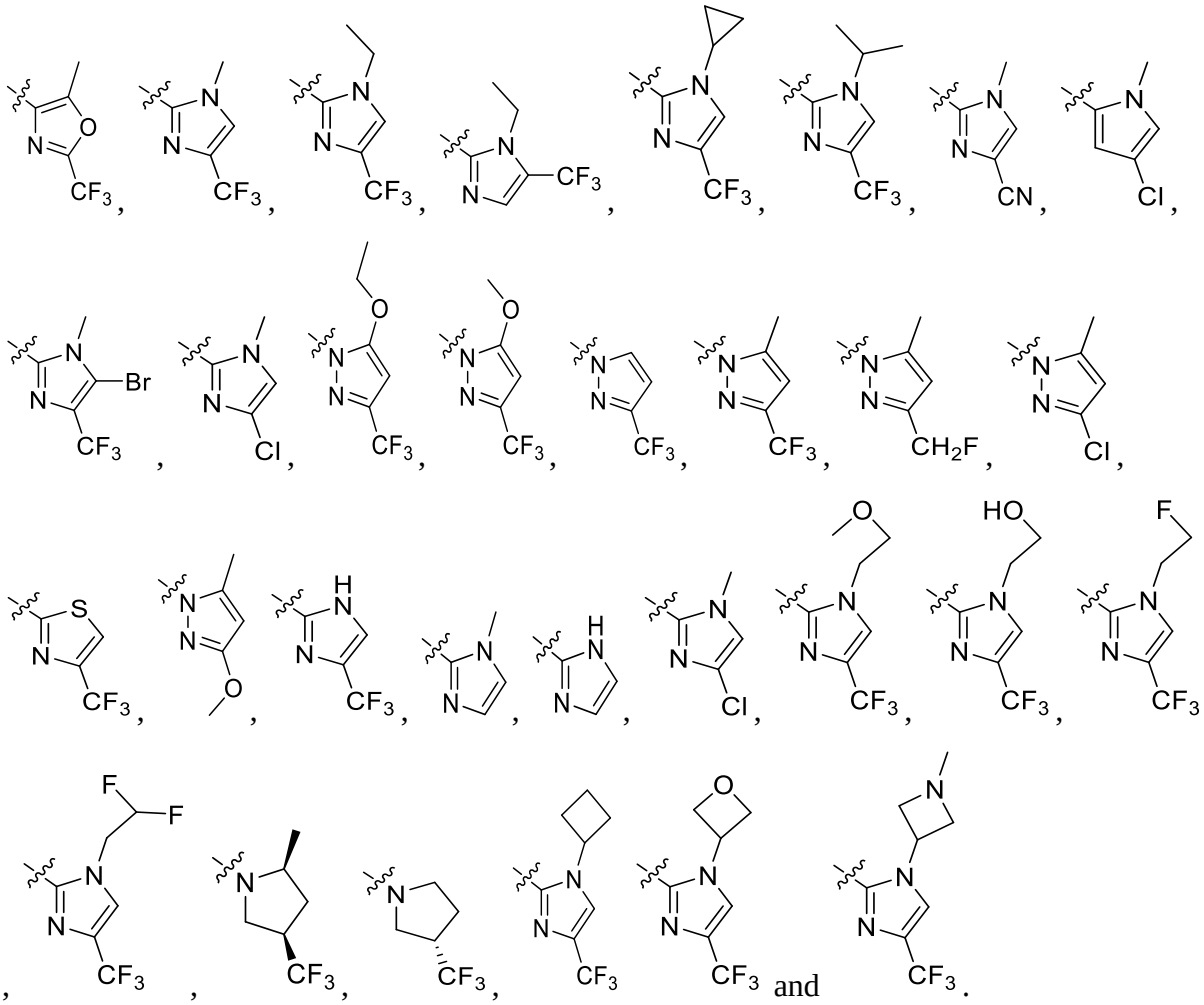
19. The compound of any one of claims 1 to 18 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^1 is a 5-10 memberer heteroaryl or a 3-10 memberer heterocyclyl, each substituted with 0, 1, 2 or 3 instances of R^5, wherein each R^5 is independently selected from halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_1–C_6$ hydroxyalkyl, $–C_3–C_{10}$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a5}$, $–N(R^{a5})_2$, $–C(=O)R^{a5}$, $–C(=O)OR^{a5}$, $–NR^{a5}C(=O)R^{a5}$, $–NR^{a5}C(=O)OR^{a5}$, $–C(=O)N(R^{a5})_2$, $–OC(=O)N(R^{a5})_2$, $–S(=O)R^{a5}$, $–S(=O)_2R^{a5}$, $–SR^{a5}$, $–S(=O)(=NR^{a5})R^{a5}$, $–NR^{a5}S(=O)_2R^{a5}$ and $–S(=O)_2N(R^{a5})_2$ wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position and wherein each R^{a5} is independently selected from H, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl.

20. The compound of claim 19 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^1 is a 5 member monocyclic heteroaryl containing 1-3 heteroatoms selected from O, N and S.

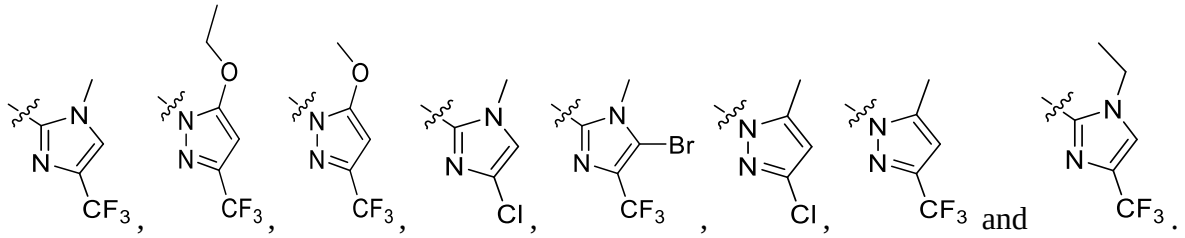
21. The compound of claim 20 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^1 is imidazolyl or pyrazolyl, each substituted with 0, 1, 2 or 3 instances of R^5.

22. The compound of any one of claims 19 to 21 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^5 is selected from –CN, –F, –Cl, –Br, –Me, –Et, $–^iPr$, $–CF_3$, $–CH_2CH_2F$, $–CH_2CHF_2$, –OMe, –OEt, $–CH_2CH_2OMe$, $–CH_2CH_2OH$, cyclopropyl, oxetanyl and azetidinyl.

23. The compound of any one of claims 1 to 22 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^1 is selected from:



24. The compound of any one of claims 1 to 22 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^1 is selected from:



25. The compound of any one of claims 1 to 24 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^2 is selected from –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –C_1–C_6 heteroalkyl, –C_3-C_{10} cycloalkyl wherein each hydrogen of the alkyl, haloalkyl and heteroalkyl can be independently replaced with a deuterium atom.

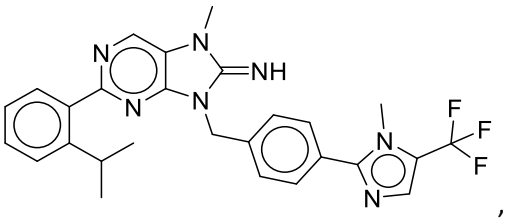
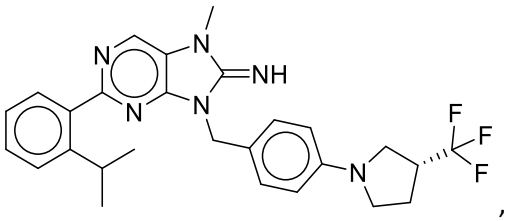
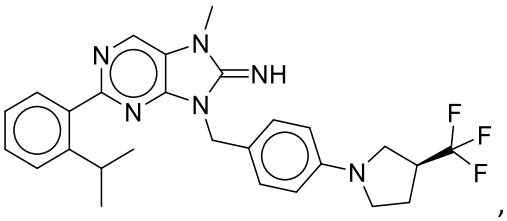
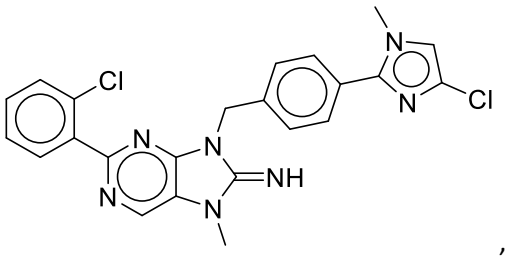
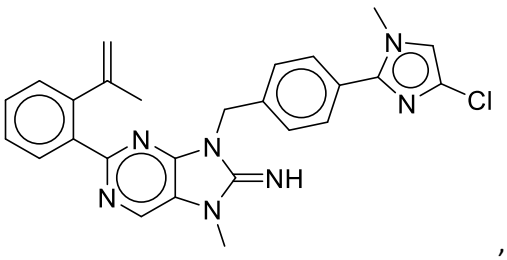
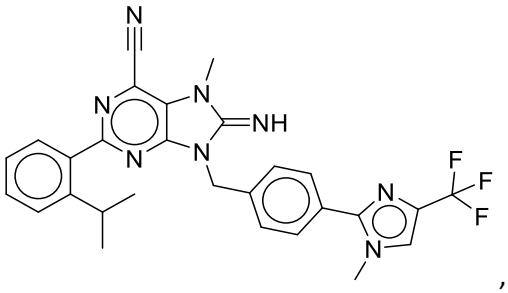
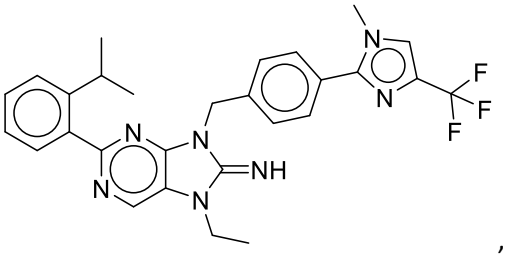
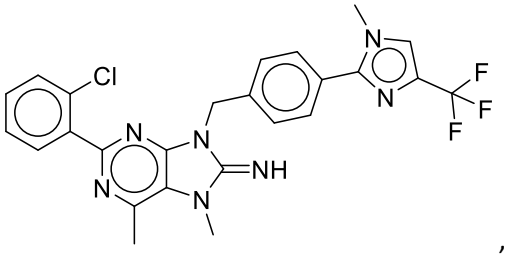
26. The compound of claim 25 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^2 is –CD_3.

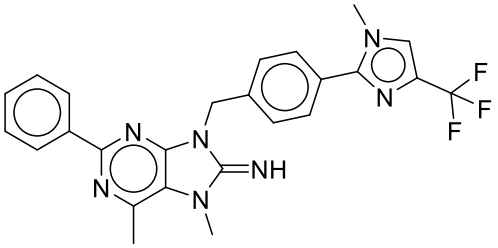
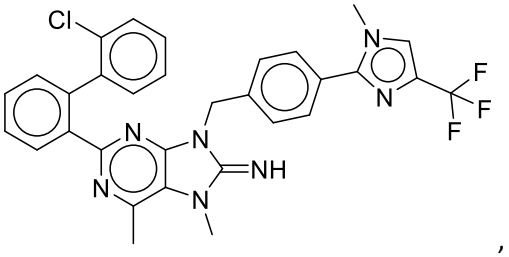
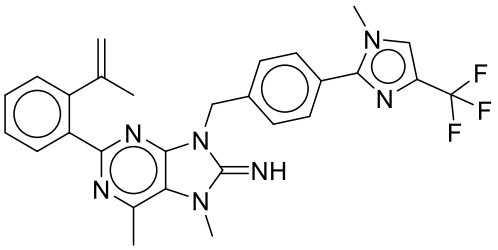
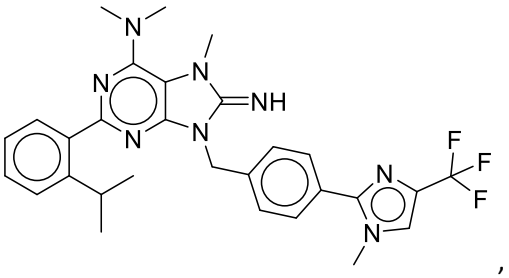
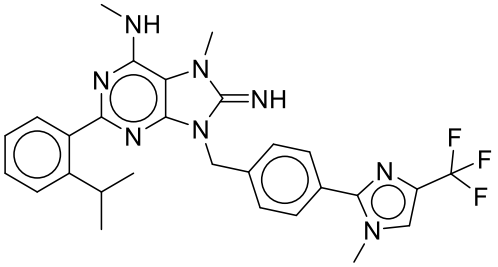
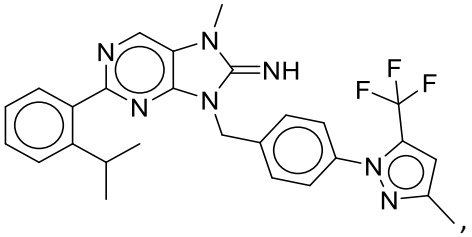
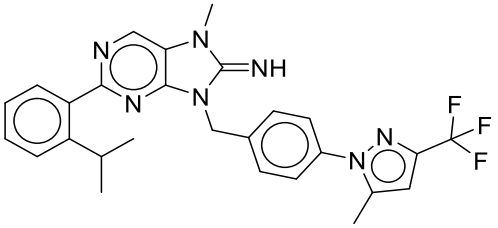
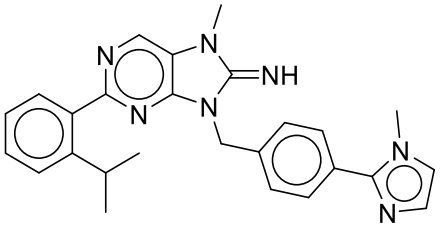
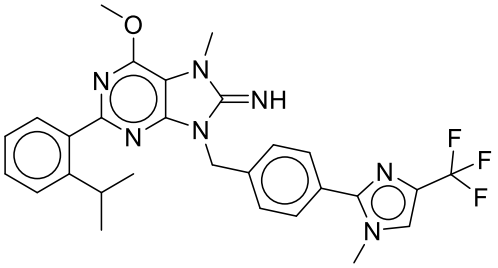
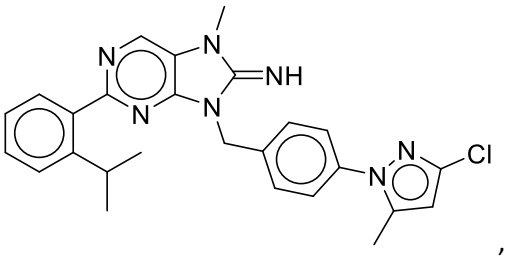
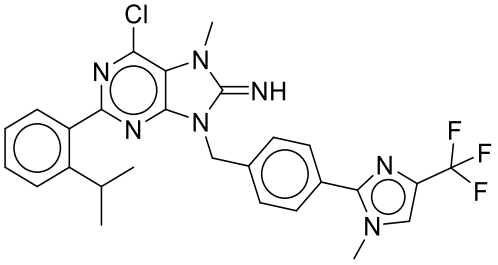
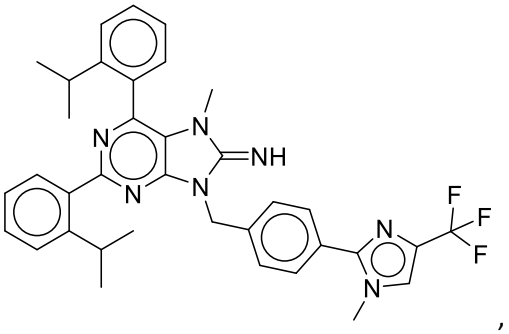
27. The compound of any one of claims 1 to 24 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^2 is –Me.

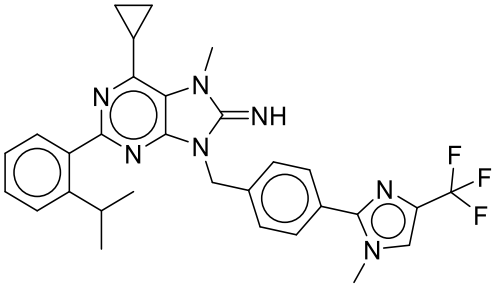
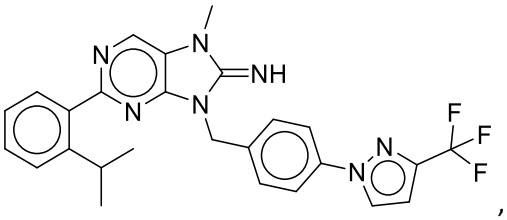
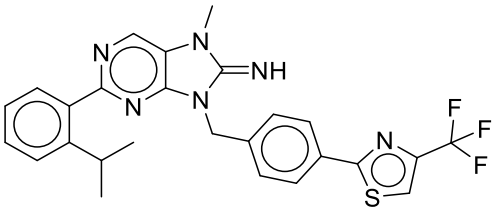
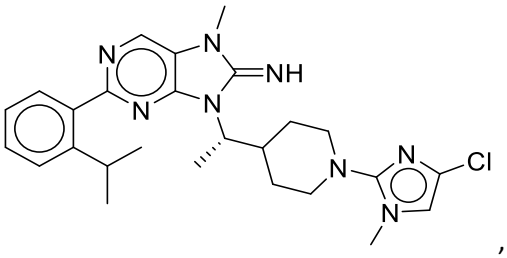
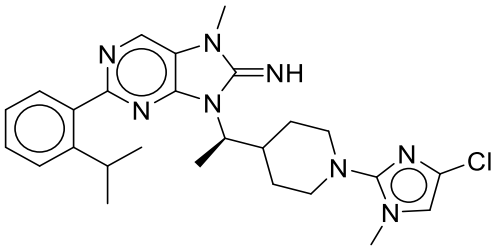
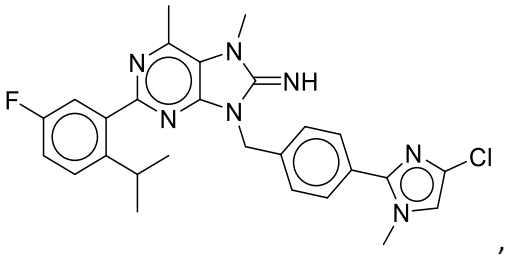
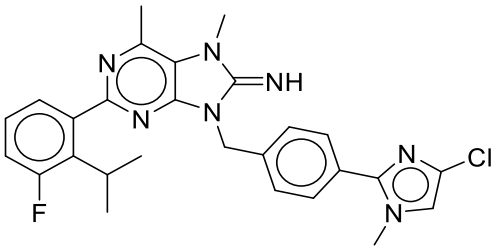
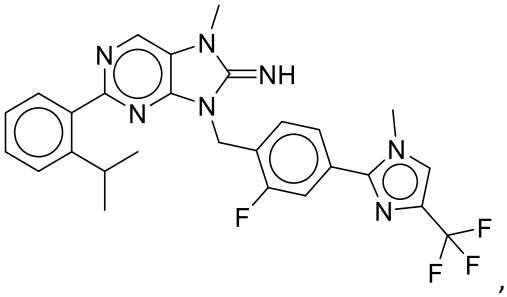
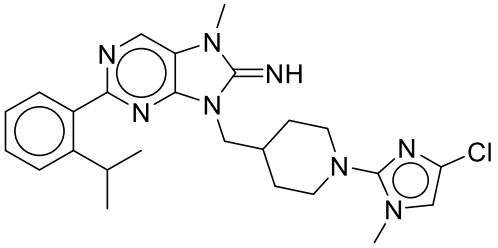
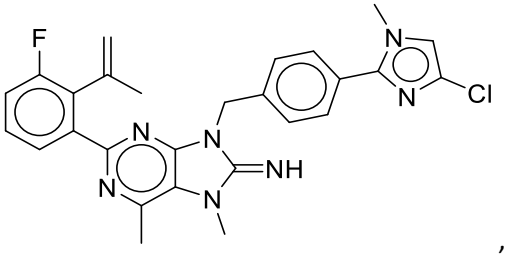
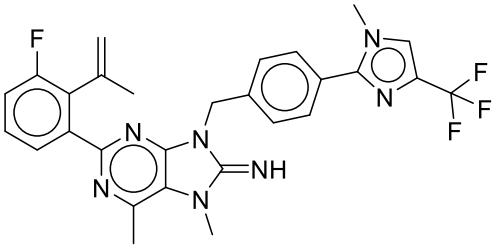
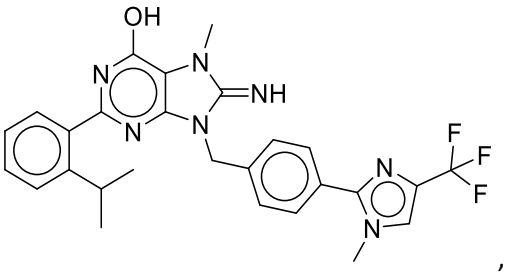
28. The compound of any one of claims 1 to 27 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^6 is selected from H, –D, –CN, –F, –Cl, –Me, –Et, –Pr, –^{i}Pr, –^{n}Bu, –^{t}Bu, –CF_3, –CHF_2, phenyl, –pyridinyl, –CC-CH_3, –CC-cyclopropyl, –C(=O)NMe_2, –C(=O)NHMe, –C(=O)NH_2, -NH_2, –NMe_2, –NHMe, –OH and –OMe.

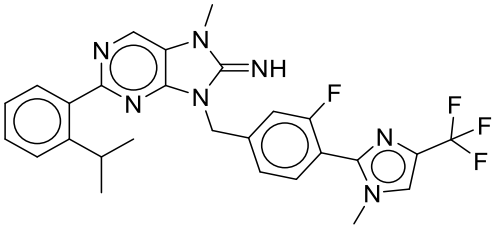
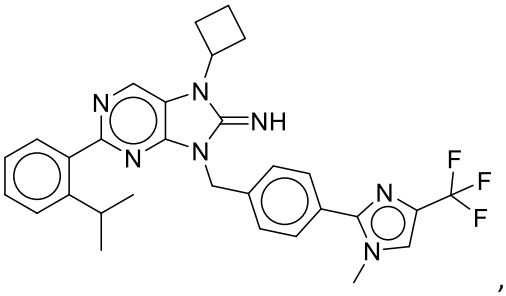
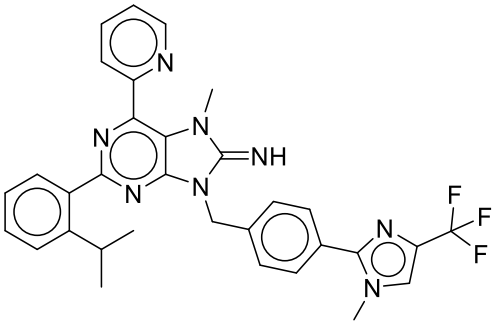
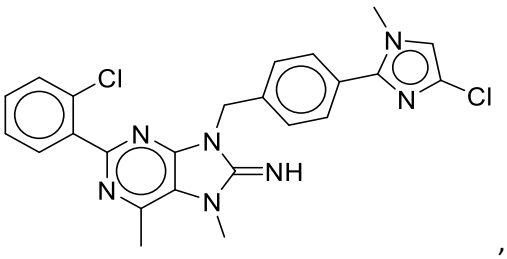
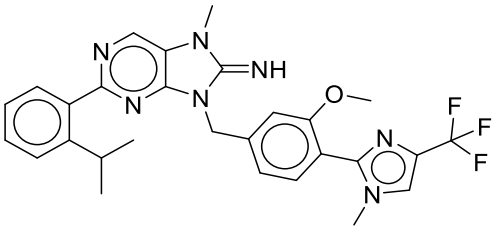
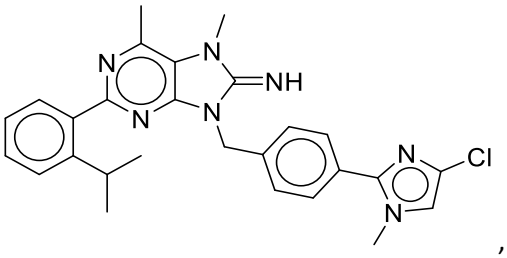
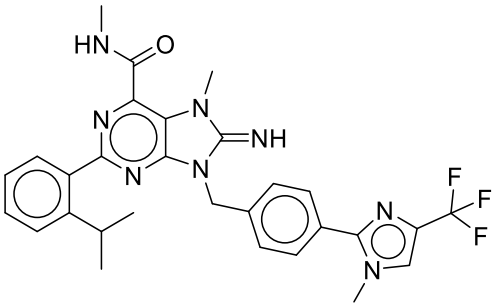
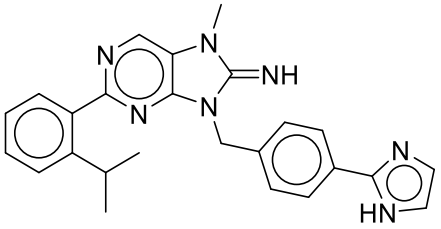
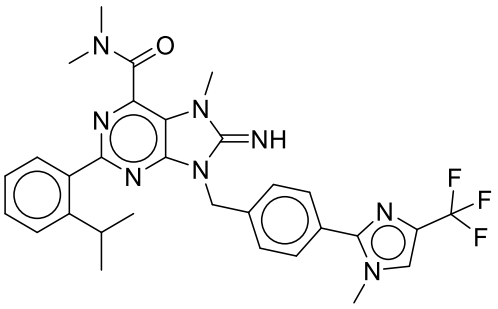
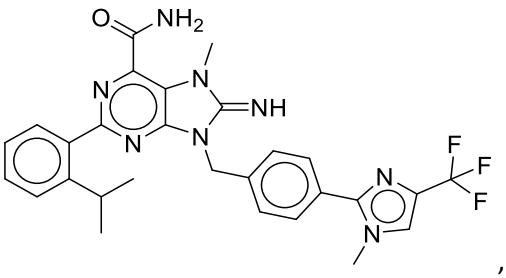
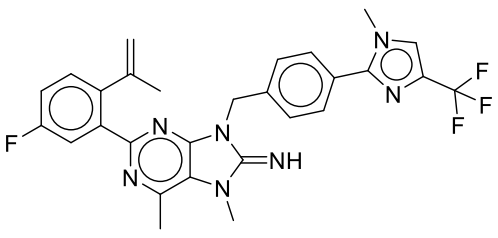
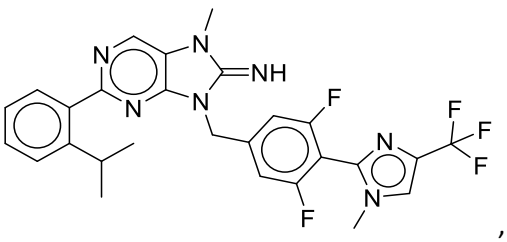
29. The compound of any one of claims 1 to 27 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein R^6 is H.

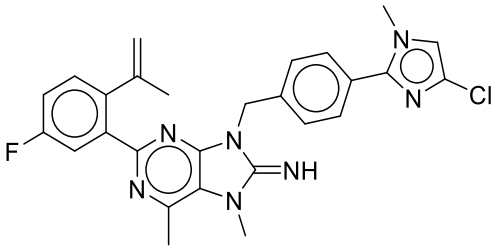
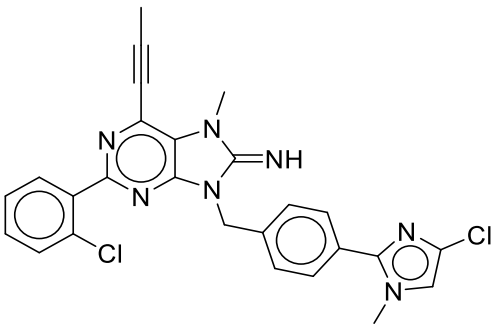
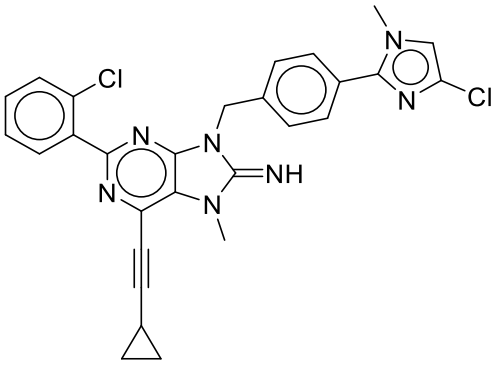
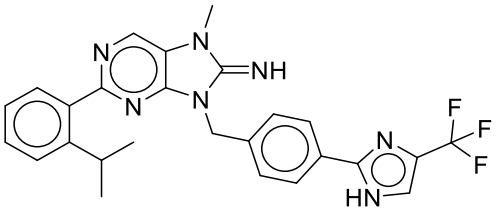
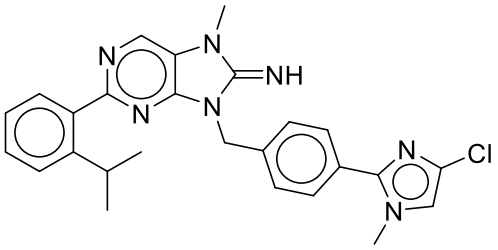
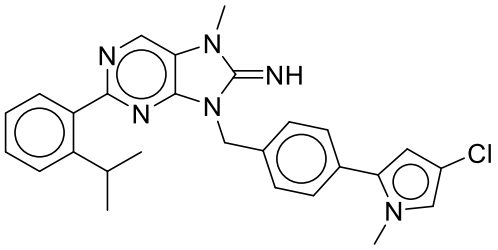
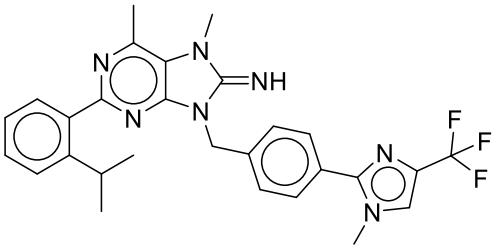
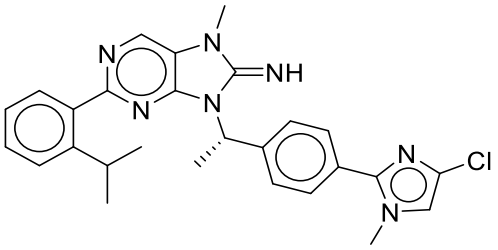
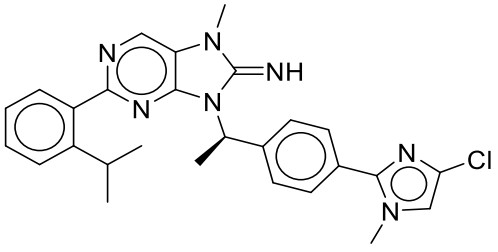
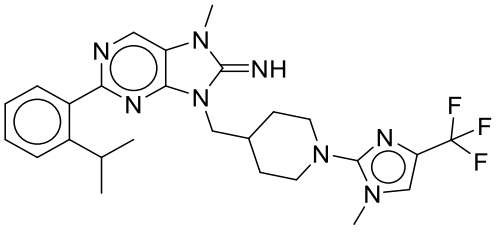
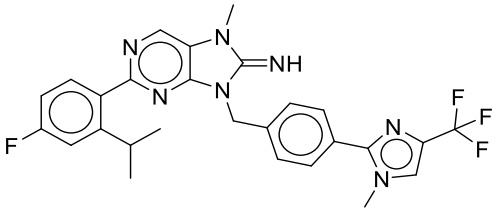
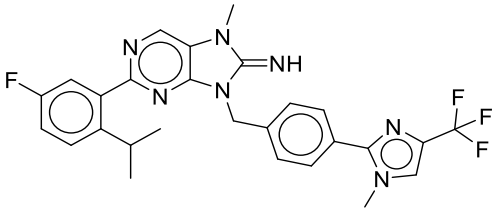
30. The compound of any one of claims 1 to 29 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein the compound is selected from

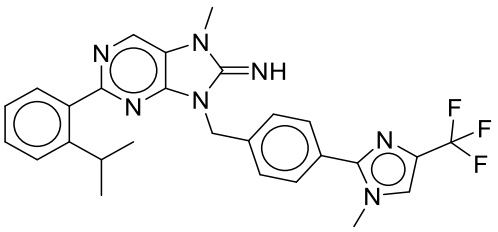
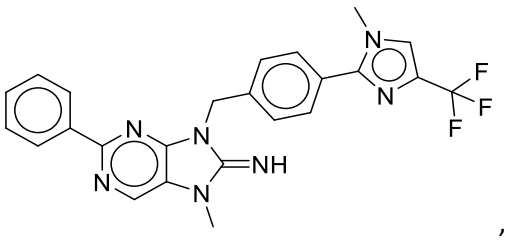
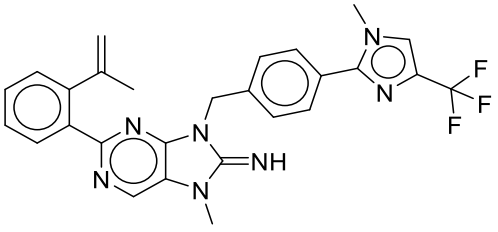
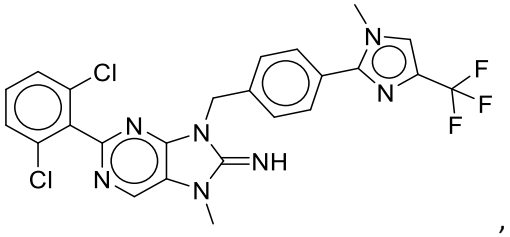
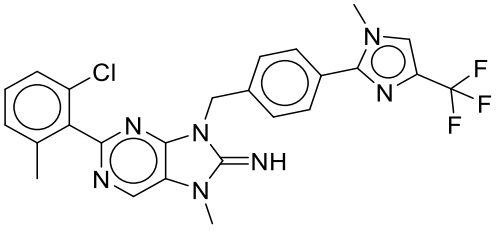
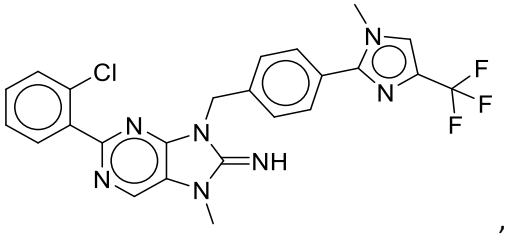
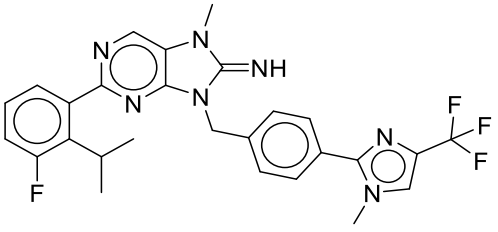
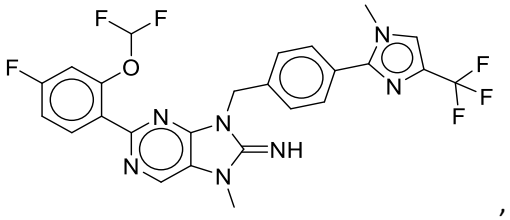
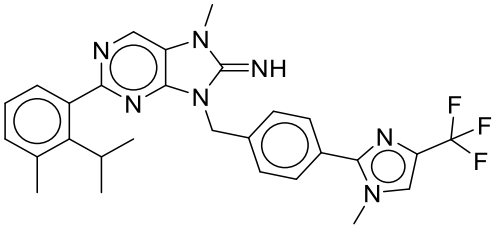
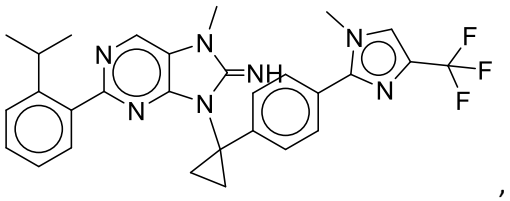
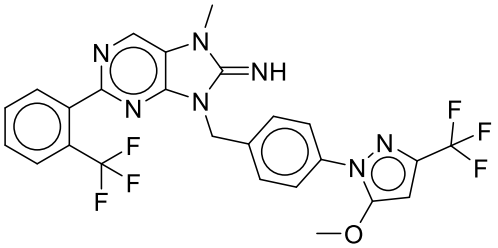
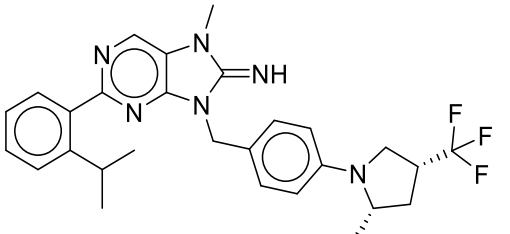
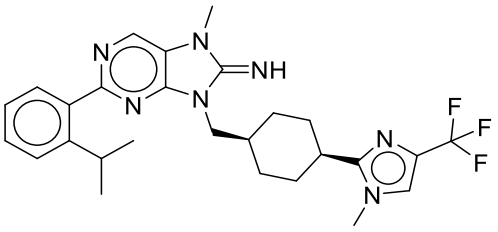
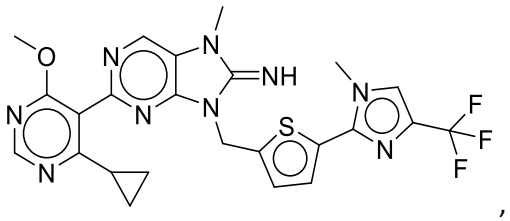

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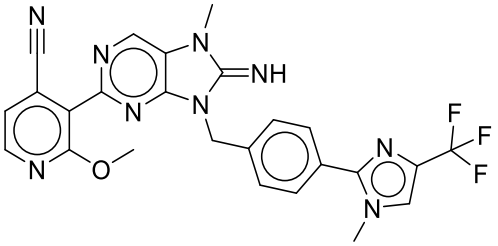
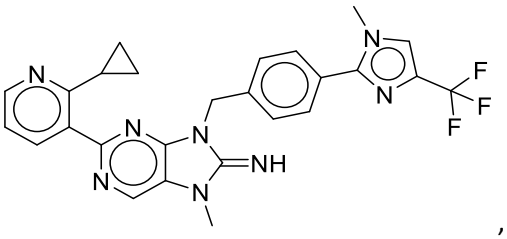
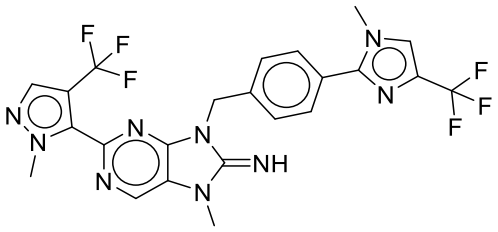
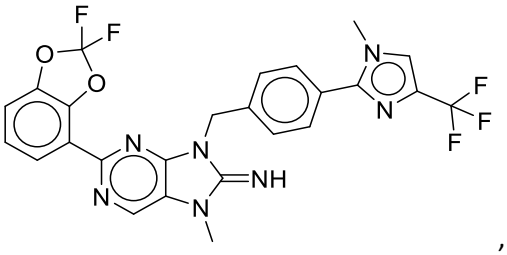
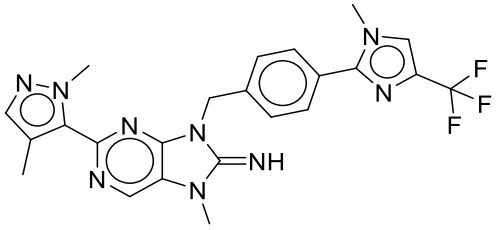
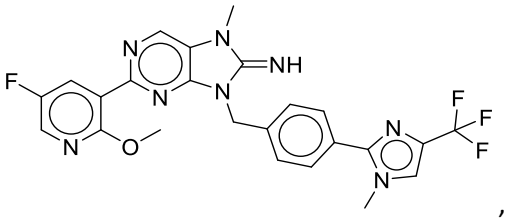
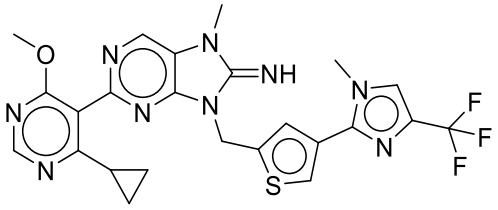
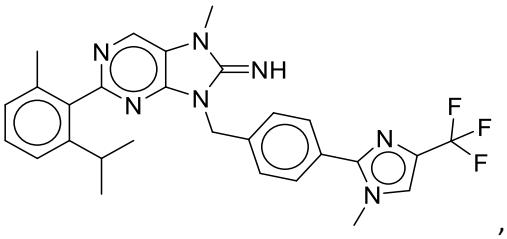
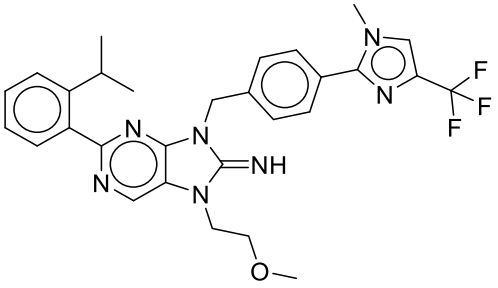
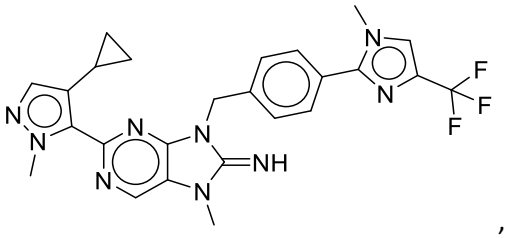
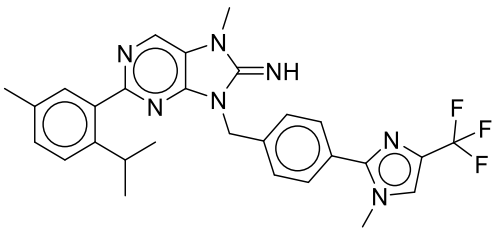

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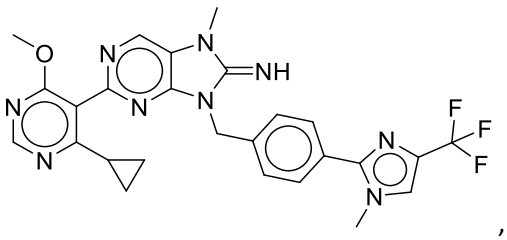

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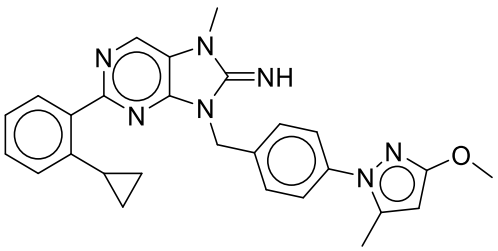
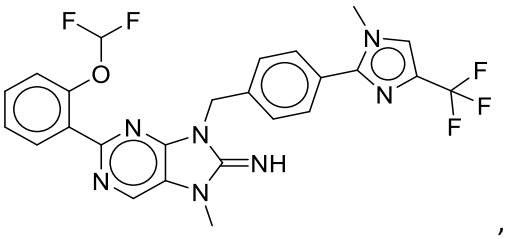
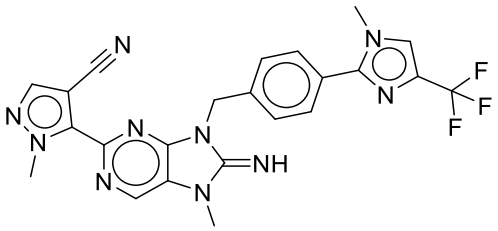
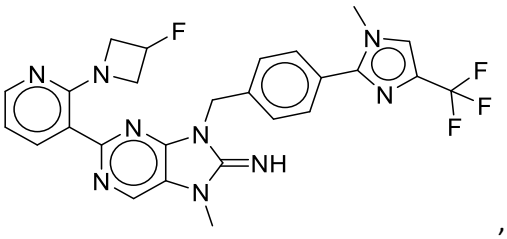
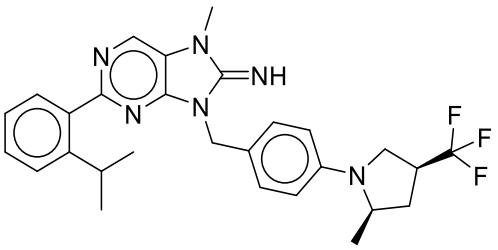
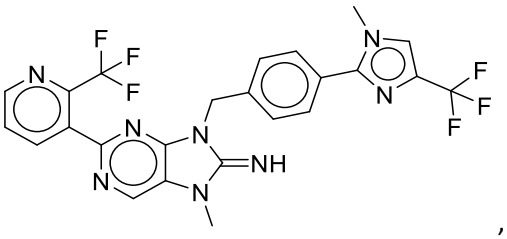
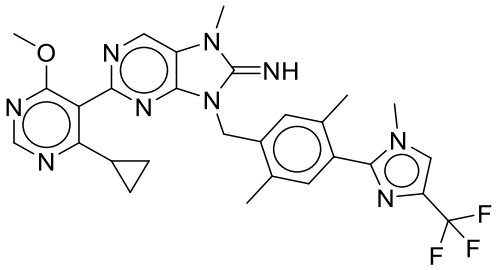
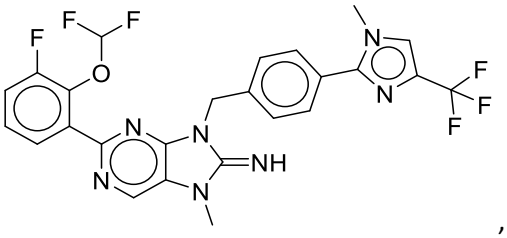
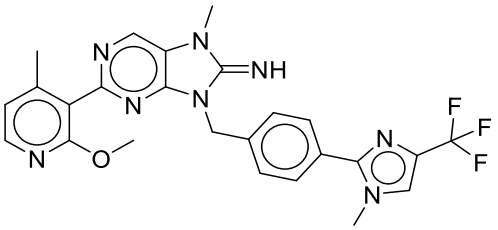
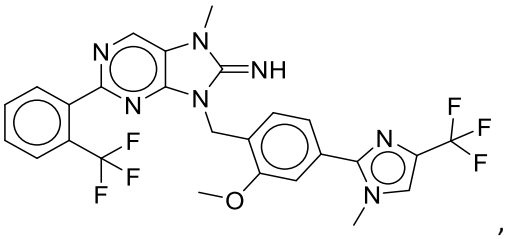
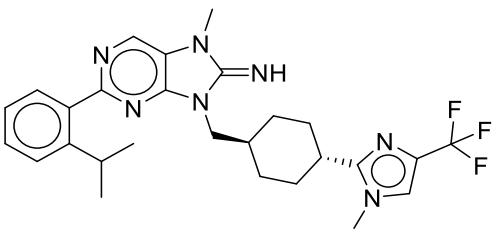
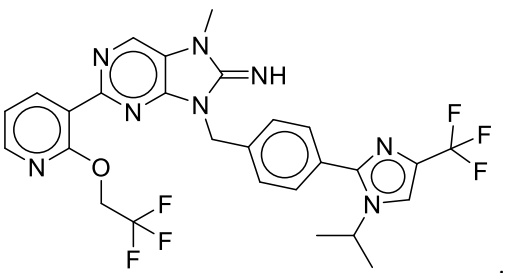

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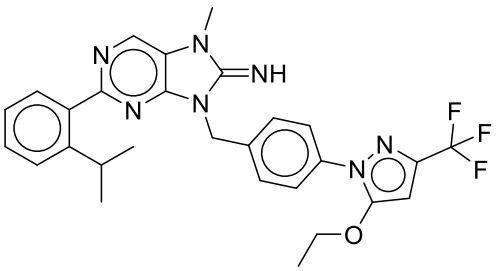
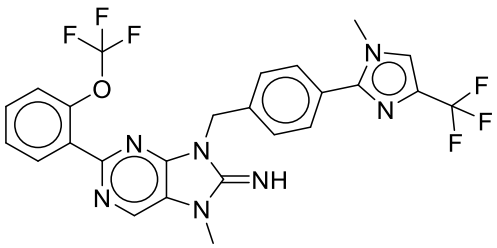
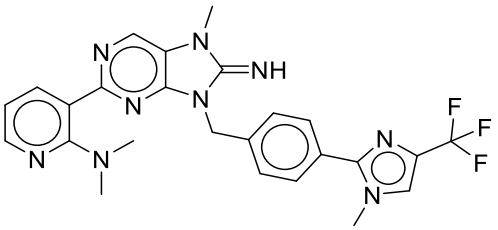
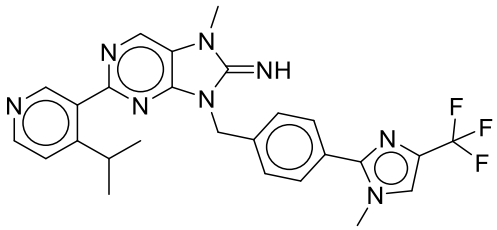
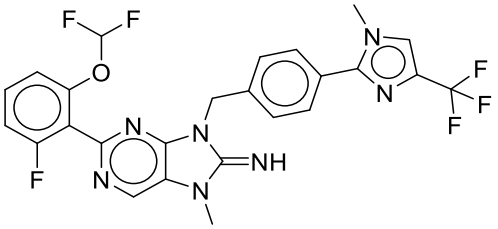
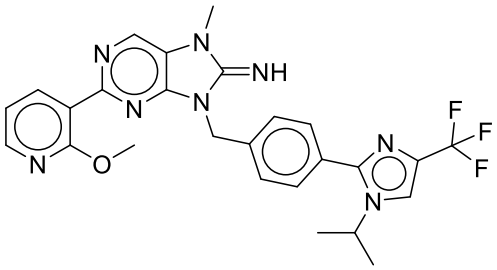
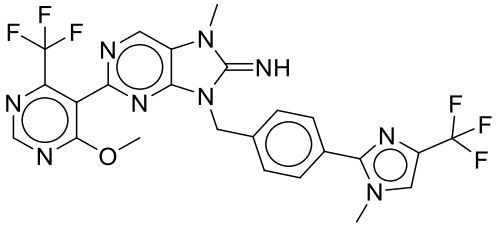
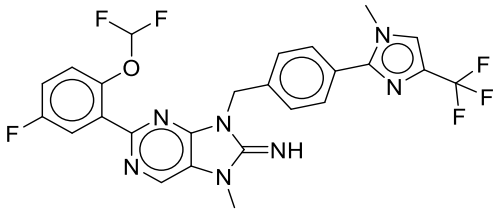
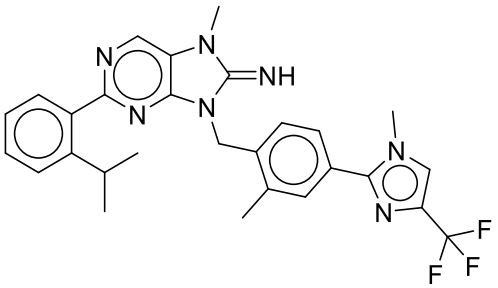
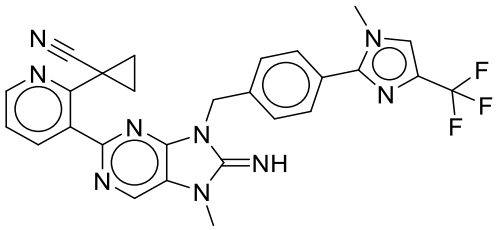
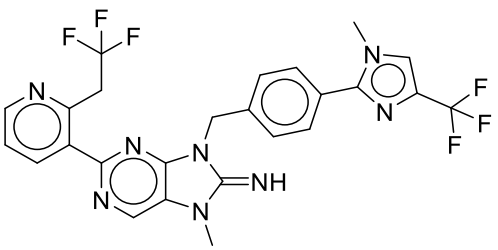
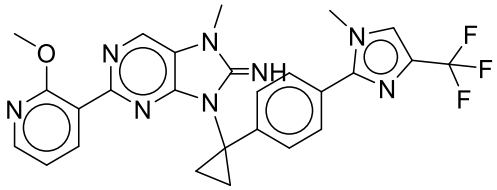

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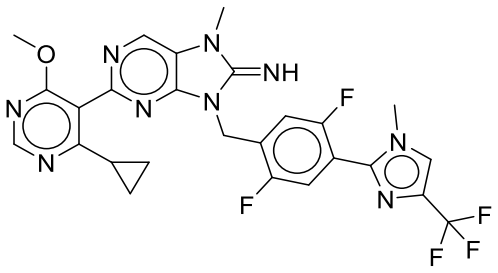
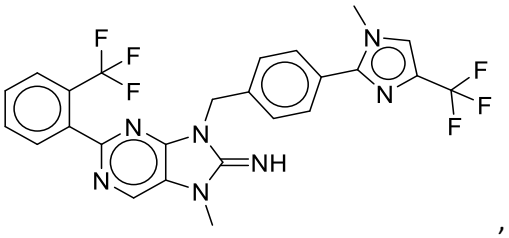
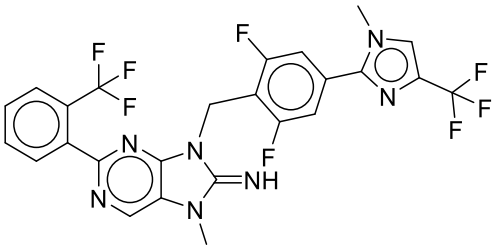
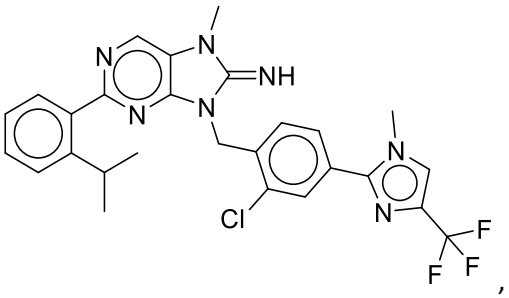
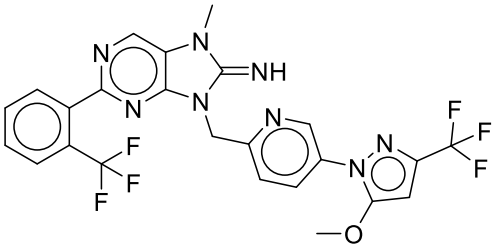
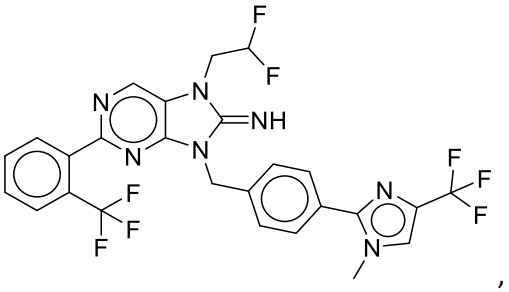
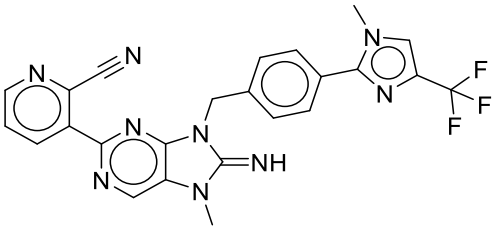
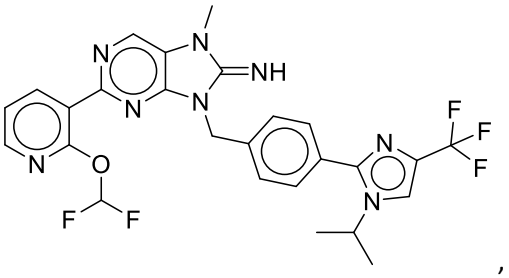
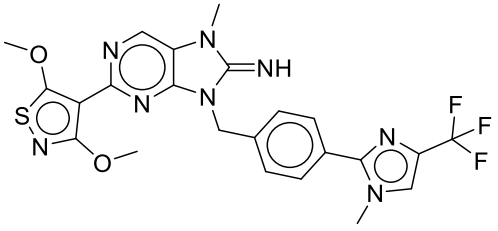
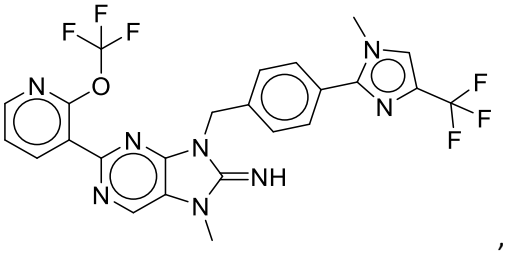
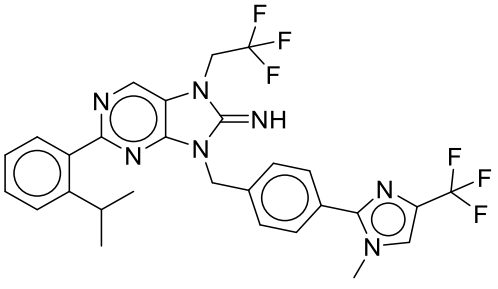
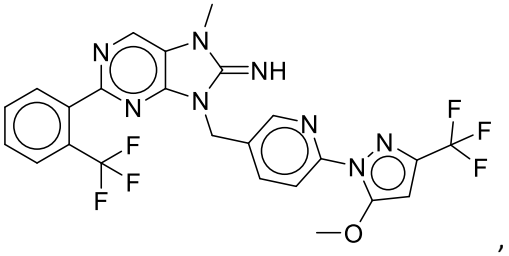

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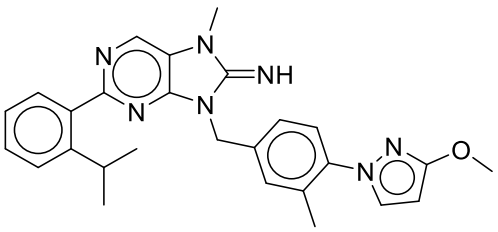
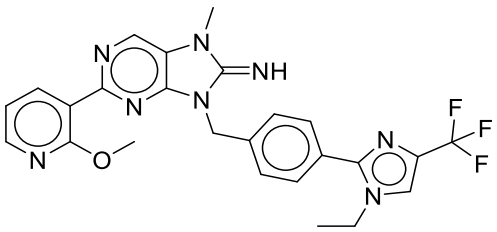
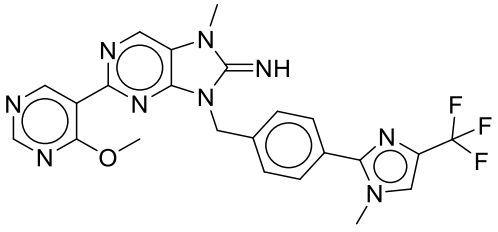
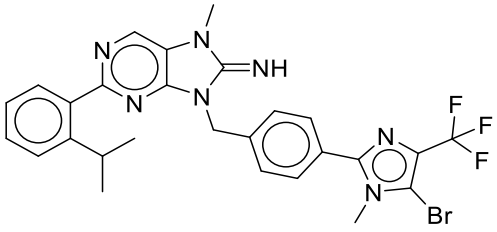
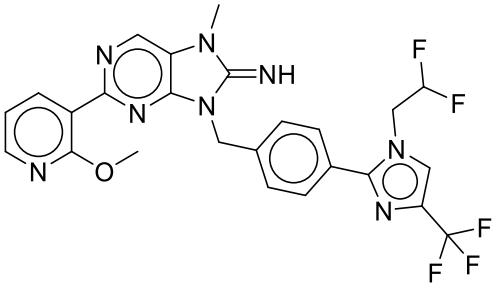
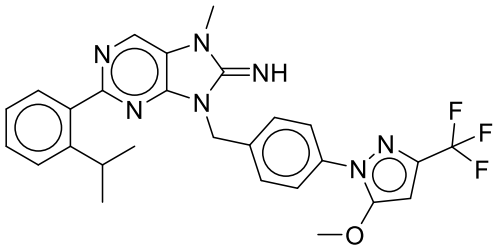
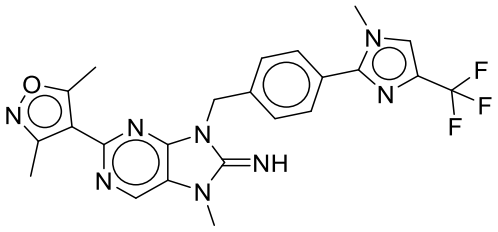
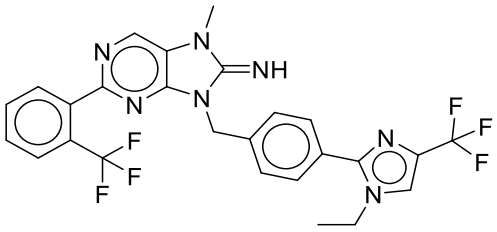
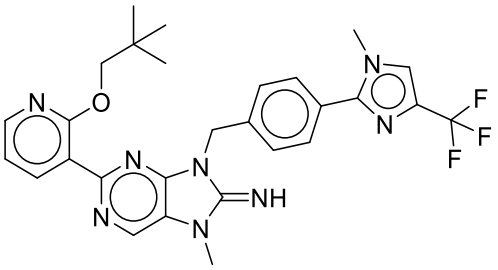
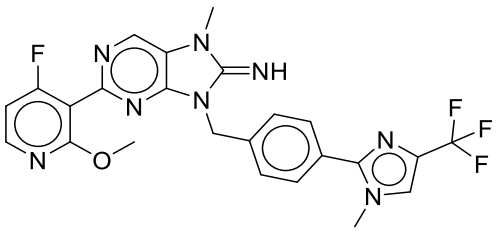
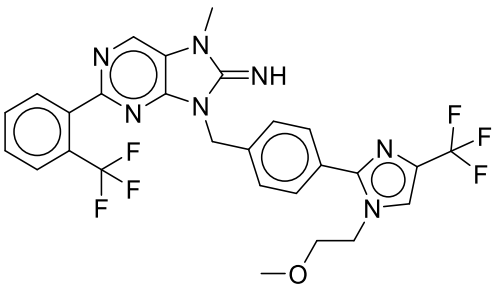
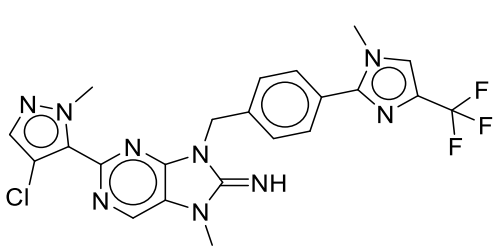
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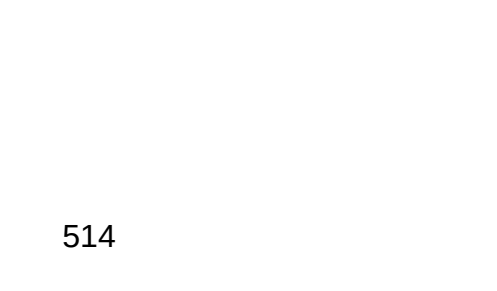
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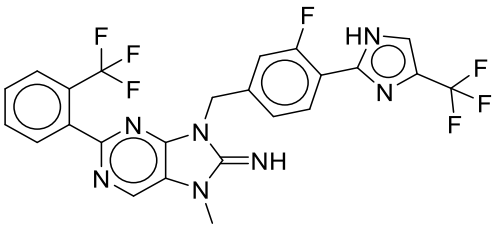
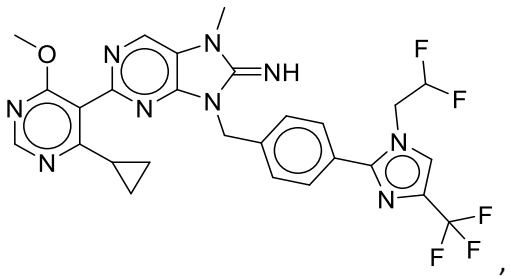
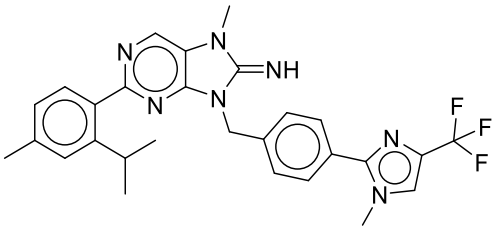
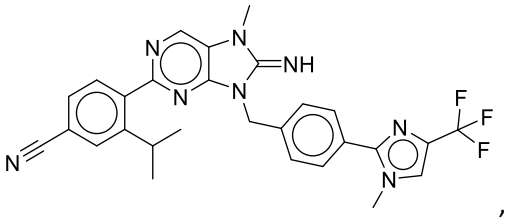
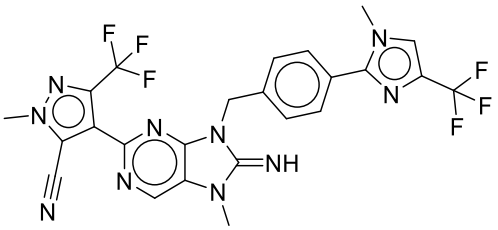
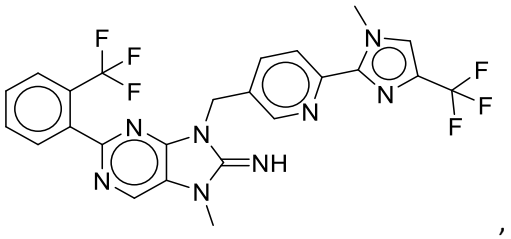
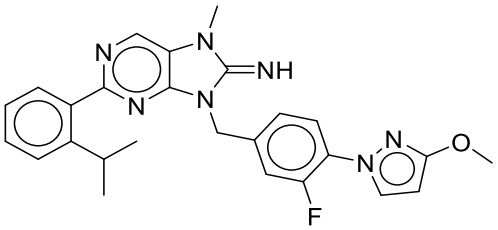
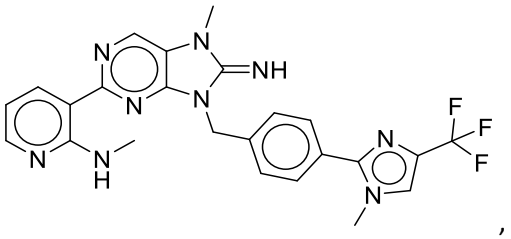
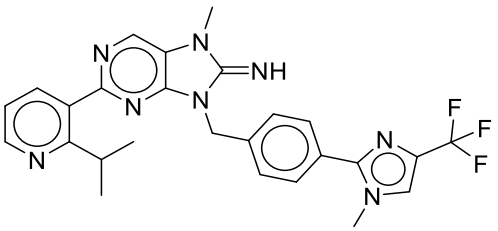
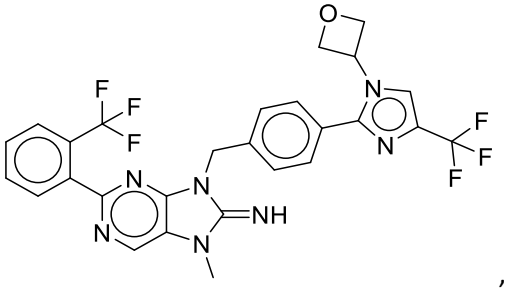
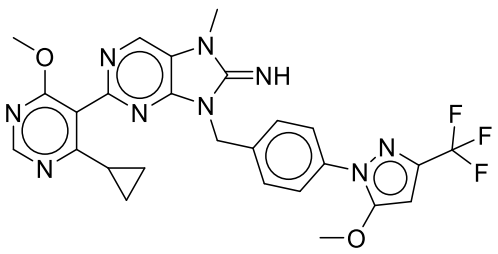
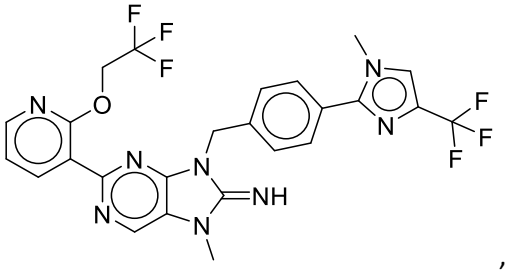
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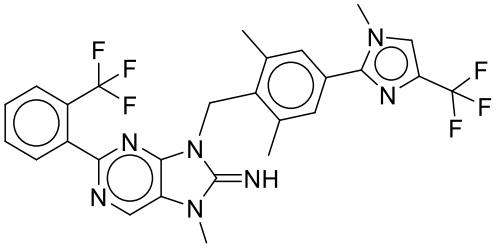
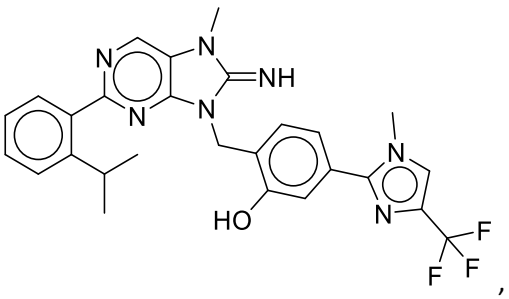
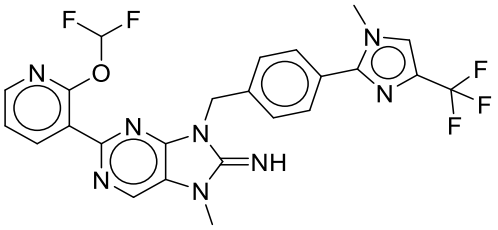
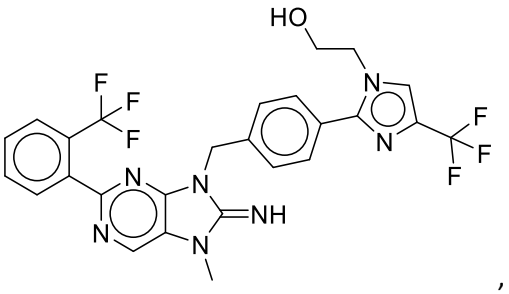
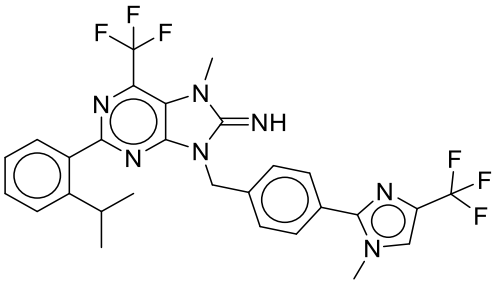
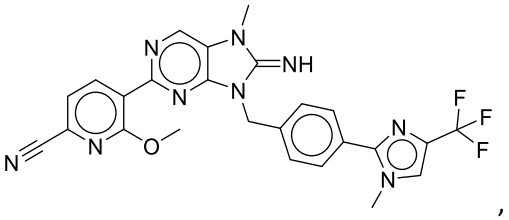
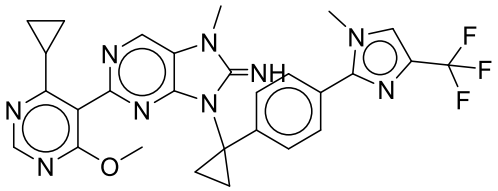
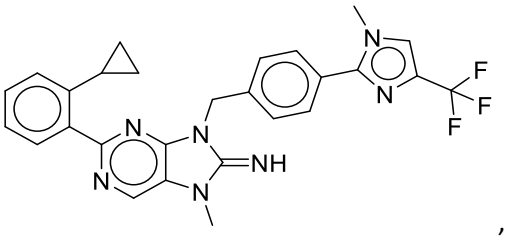
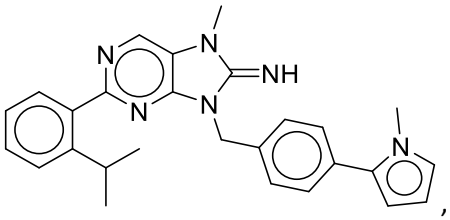
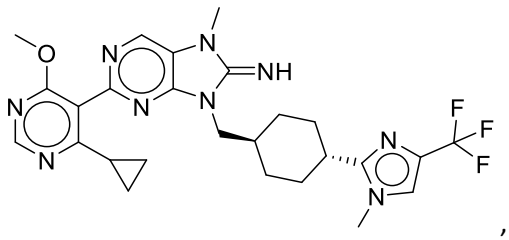
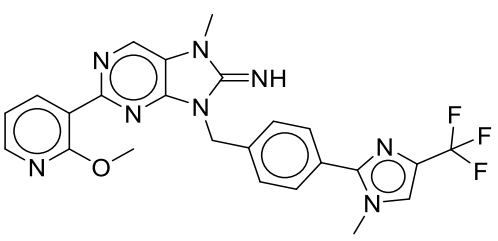
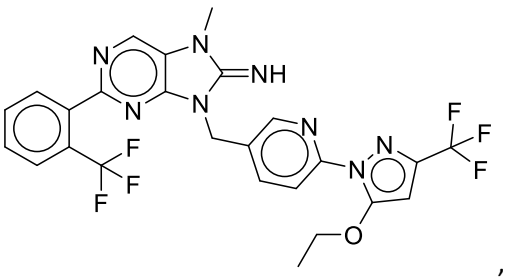
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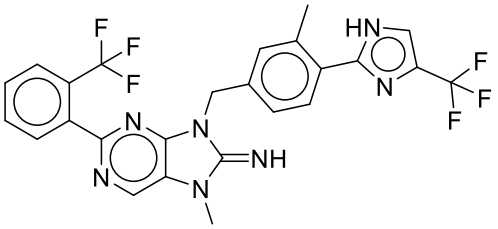
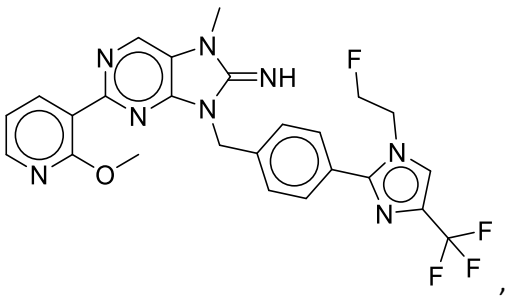
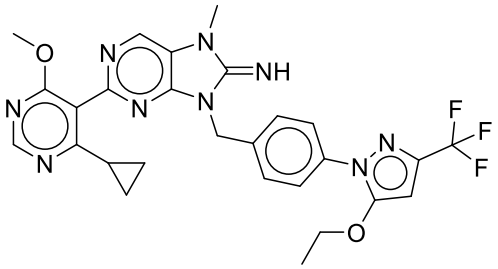
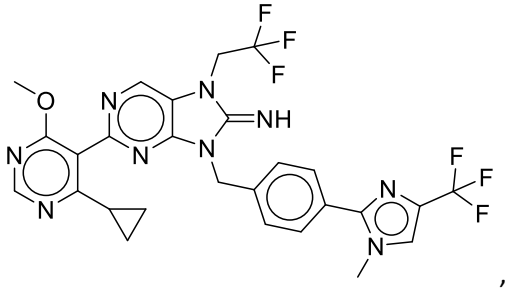
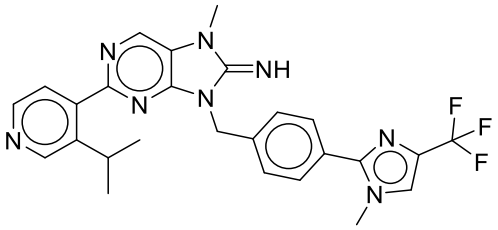
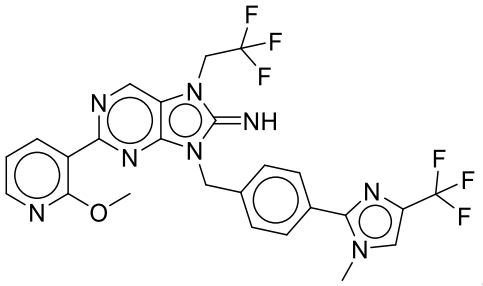
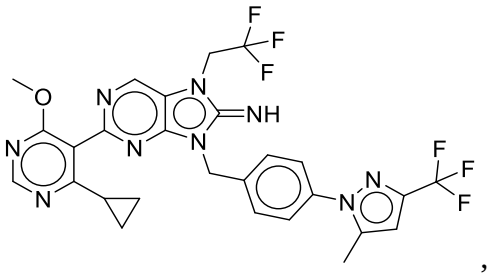
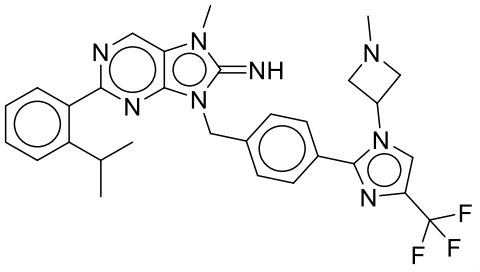
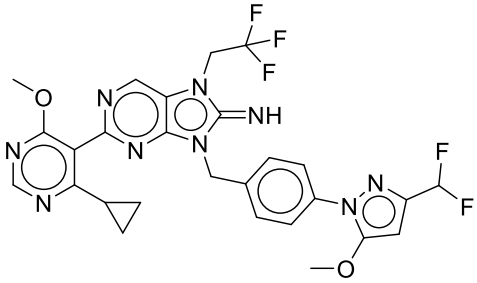
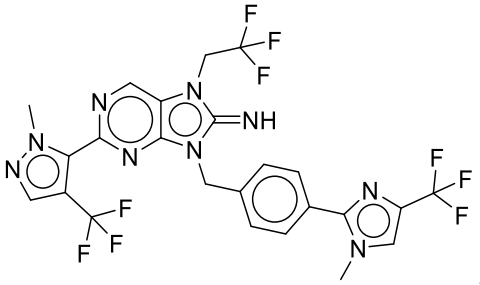
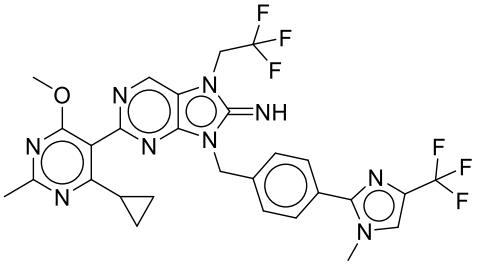
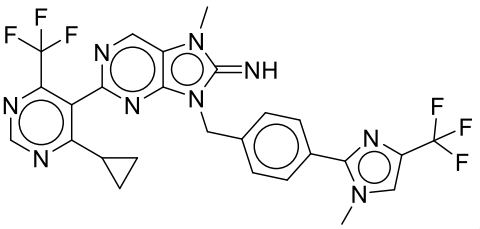

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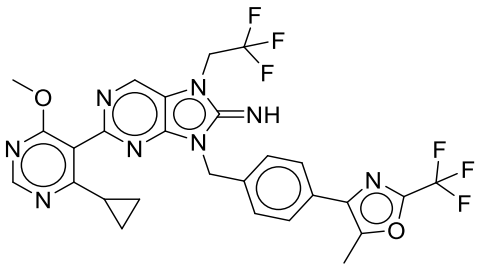
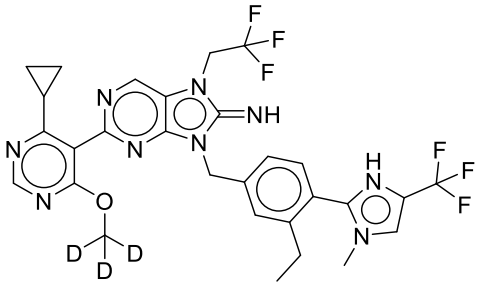
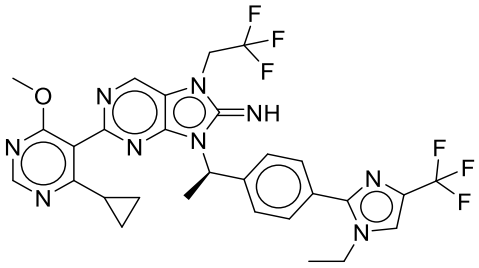
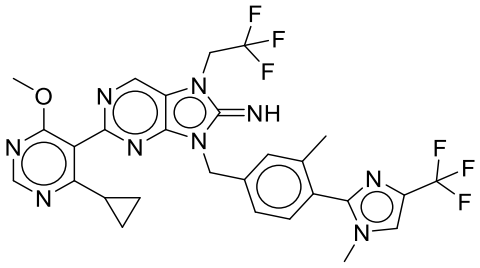
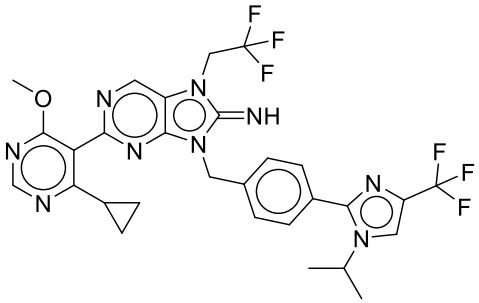
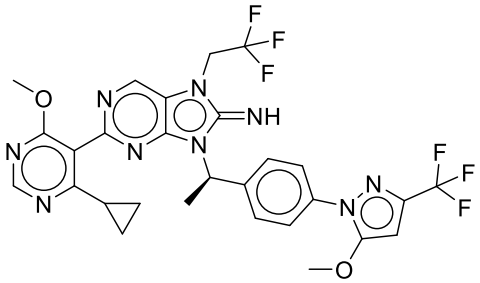
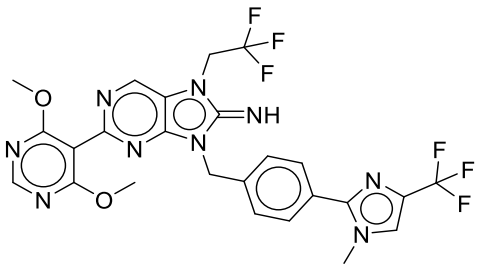
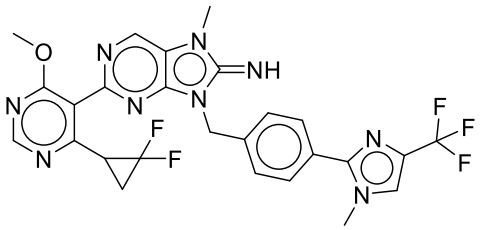
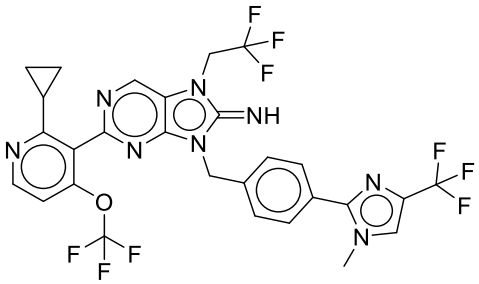
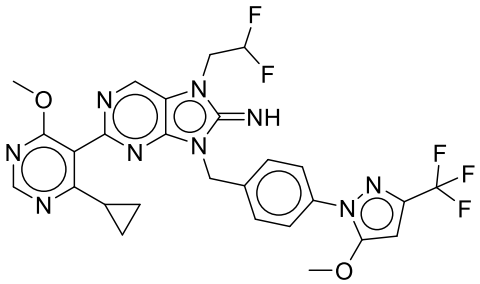

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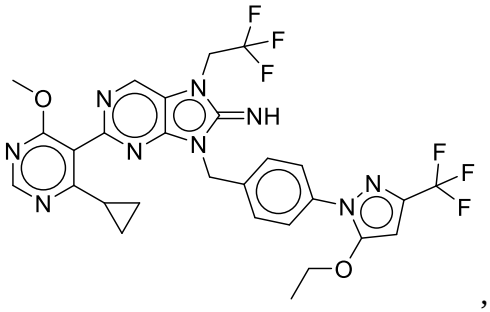
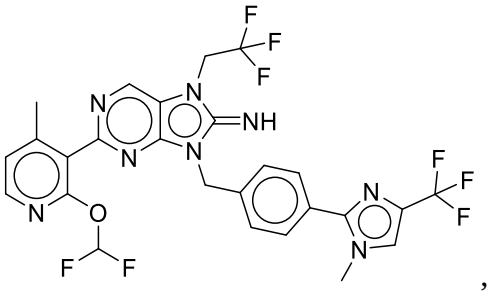
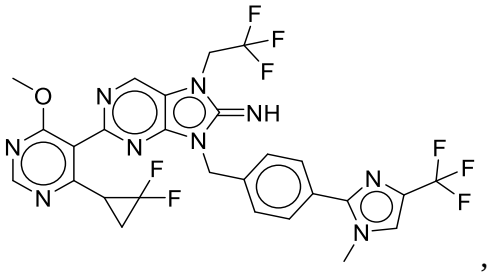
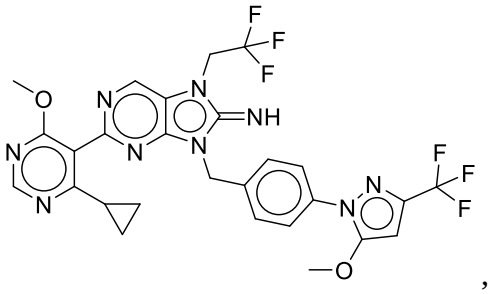
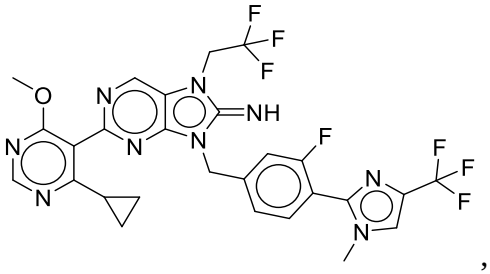
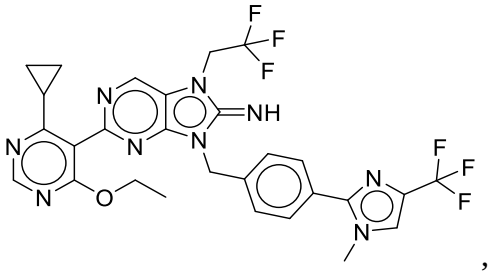
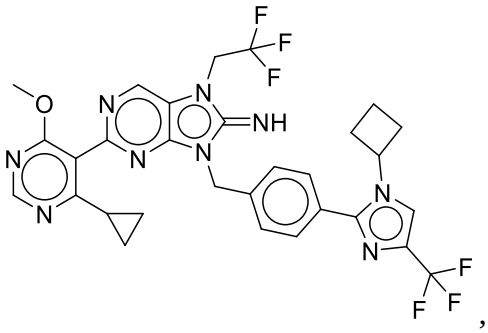
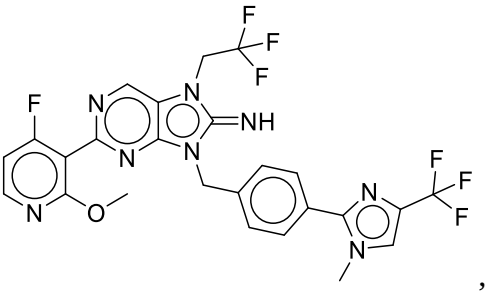
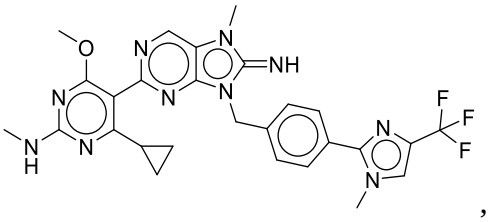
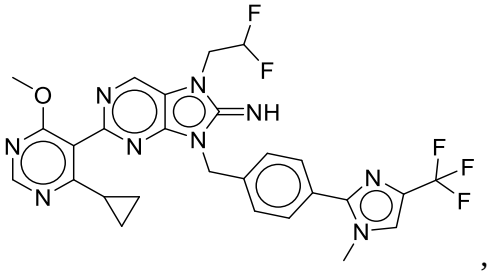
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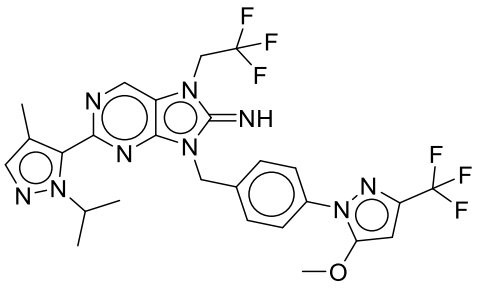
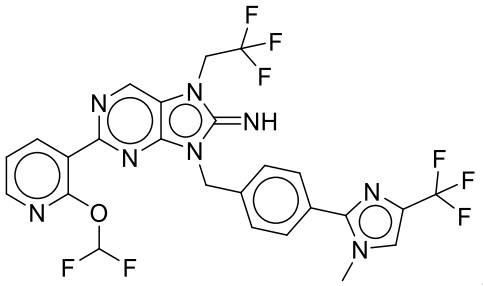
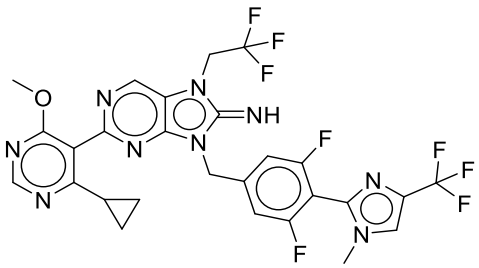
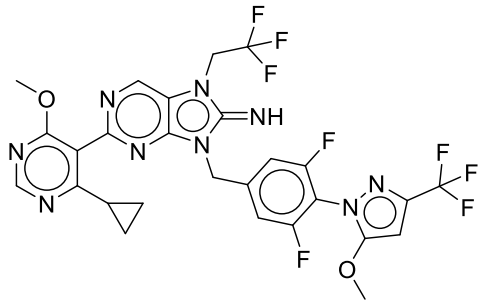
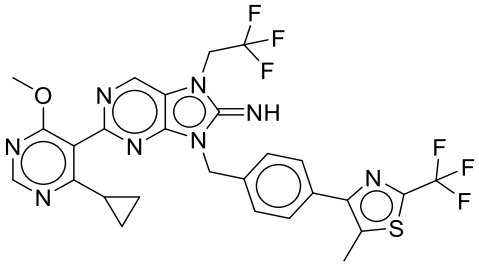
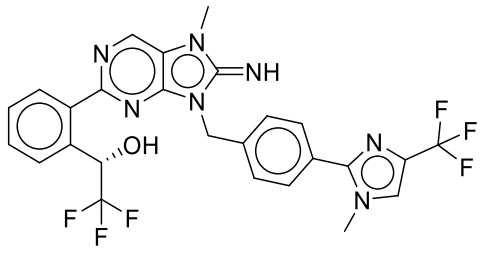
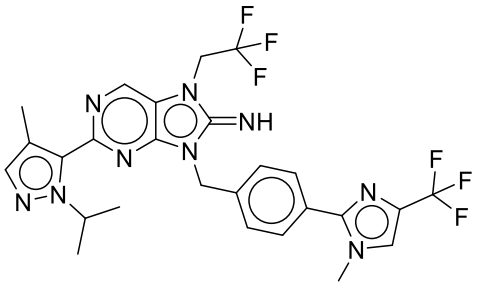
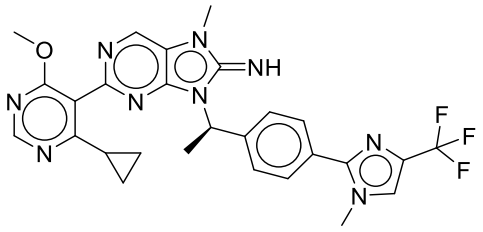
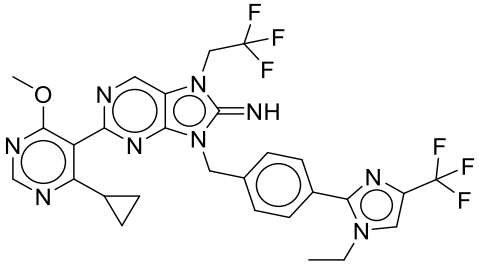
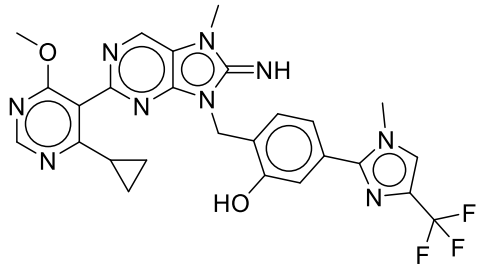

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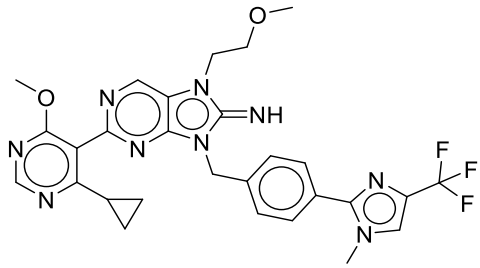
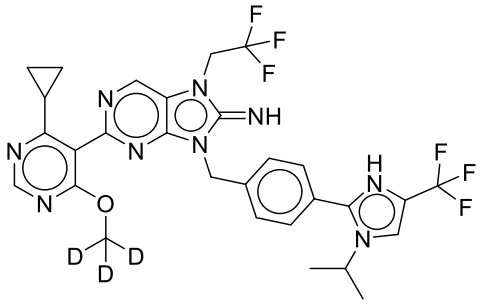
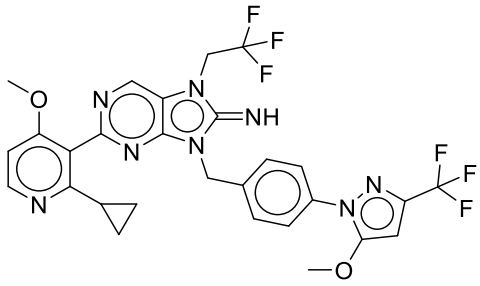
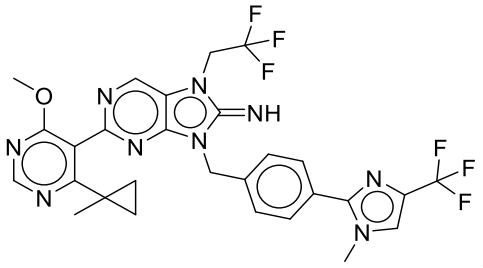
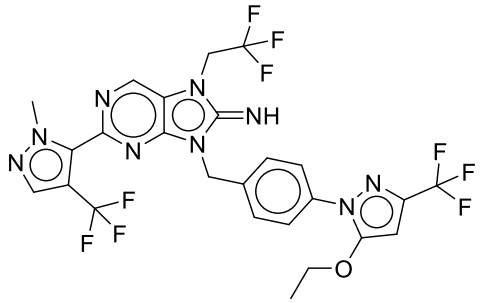
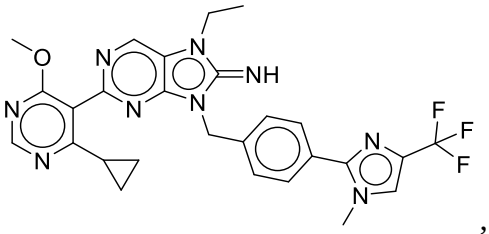
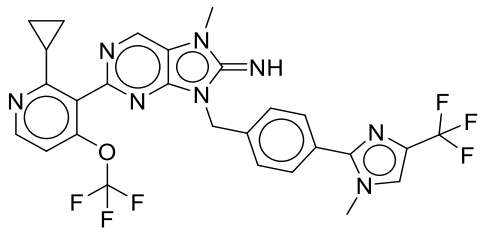
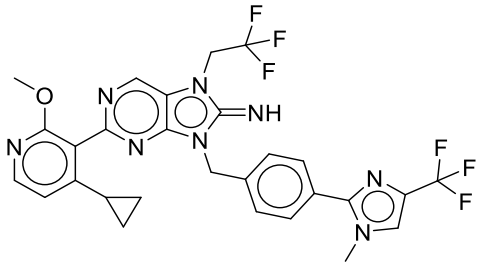
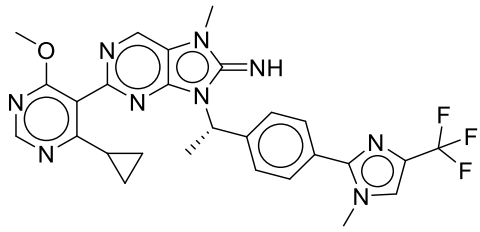
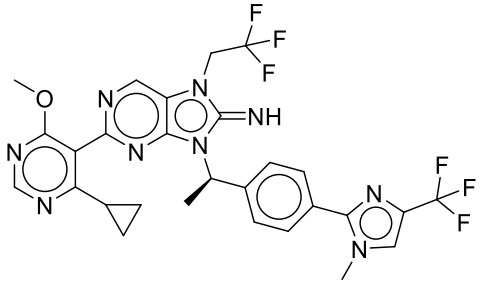

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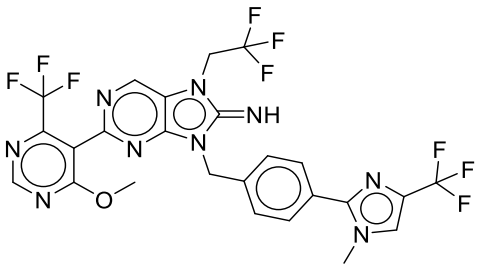
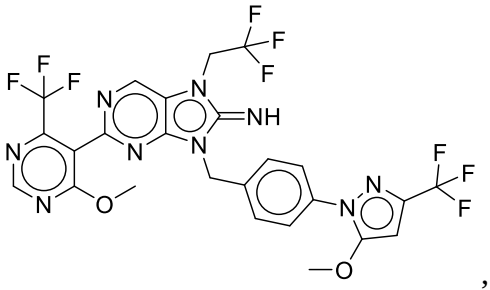
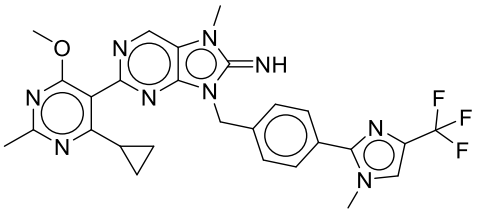
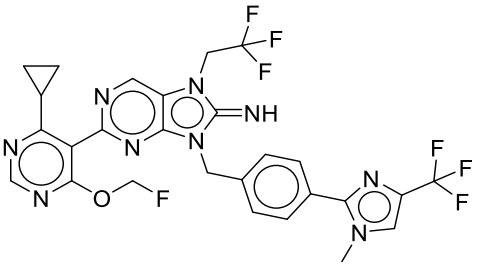
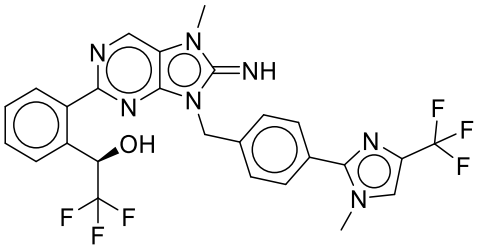

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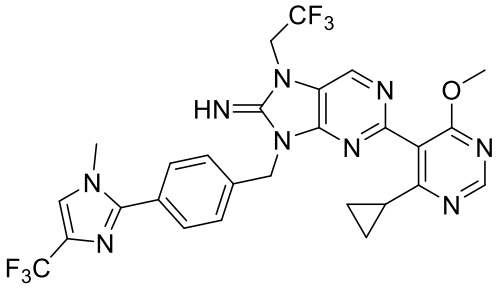

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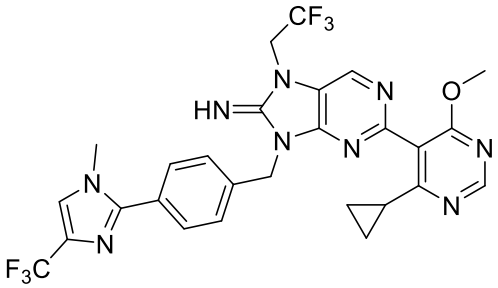

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and

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31. The compound of claim 1, wherein the compound is


or a pharmaceutically acceptable salt thereof.

32. The compound of claim 1, wherein the compound is


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33. A pharmaceutical composition comprising a compound of any one of claims 1 to 32 or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof and a pharmaceutically acceptable carrier.

34. Use of a compound of any one of claims 1-32 in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the compound or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof is to be administered to the patient.

35. Use of a composition of claim 33 in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the composition is to be administered to the patient.

36. The use of claim 34 or 35, wherein the cancer is a cancer that is sensitive to USP1 inhibition.

37. The use of claim 34 or 35, wherein the cancer is a BRCA1 and/or a BRCA2 mutant cancer.

38. The use of claim 34 or 35, wherein the cancer is a BRCA1 and/or a BRCA2 deficient cancer.

39. The use of claim 34 or 35, wherein the cancer is an ATM mutant cancer.

40. The use of claim 34 or 35, wherein the cancer is a PARP inhibitor resistant or refractory cancer.

41. The use of claim 34 or 35, wherein the cancer is a an HRD+ cancer.

42. The use of any one of claims 34 to 41, wherein an additional therapeutic agent is to be administered to the patient.

43. The use of claim 42, wherein the additional therapeutic agent is a PARP inhibitor.

44. The use of any one of claims 34 to 43, wherein the cancer is selected from adrenocortical carcinoma, AIDS-related lymphoma, AIDS-related malignancies, anal cancer, cerebellar astrocytoma, extrahepatic bile duct cancer, bladder cancer osteosarcoma/malignant fibrous histiocytoma, brain stem glioma, ependymoma, visual pathway and hypothalamic gliomas, breast cancer, bronchial adenomas/carcinoids, carcinoid tumors, gastrointestinal carcinoid tumors, carcinoma, adrenocortical, islet cell carcinoma, primary central nervous system lymphoma, cerebellar astrocytoma, cervical cancer, chronic lymphocytic leukemia, chronic myelogenous leukemia, clear cell sarcoma of tendon sheaths, colon cancer, colorectal cancer, cutaneous t-cell lymphoma, endometrial cancer, ependymoma, esophageal cancer, Ewing's sarcoma/family of tumors, extracranial germ cell tumors, extragonadal germ cell tumors, extrahepatic bile duct cancer, eye cancers, including intraocular melanoma, and retinoblastoma, gallbladder cancer, gastrointestinal carcinoid tumor, ovarian germ cell tumor, gestational trophoblastic tumor, hairy cell leukemia, head and neck cancer, Hodgkin's disease, hypopharyngeal cancer, hypothalamic and visual pathway glioma, intraocular

melanoma, Kaposi's sarcoma, laryngeal cancer, acute lymphoblastic leukemia, acute myeloid leukemia, liver cancer, non-small cell lung cancer, small cell lung cancer, non-Hodgkin's lymphoma, Waldenstrom's macroglobulinemia, malignant mesothelioma, malignant thymoma, medulloblastoma, melanoma, intraocular melanoma, merkel cell carcinoma, metastatic squamous neck cancer with occult primary, multiple endocrine neoplasia syndrome, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndrome, chronic myelogenous leukemia, myeloid leukemia, multiple myeloma, myeloproliferative disorders, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cancer, oral cavity and lip cancer, oropharyngeal cancer, osteosarcoma/malignant fibrous histiocytoma of bone, ovarian cancer, ovarian low malignant potential tumor, pancreatic cancer, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, prostate cancer, rectal cancer, renal cell (kidney) cancer, transitional cell cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, malignant fibrous histiocytoma of bone, soft tissue sarcoma, Sezary syndrome, skin cancer, small intestine cancer, stomach (gastric) cancer, supratentorial primitive neuroectodennal and pineal tumors, cutaneous t-cell lymphoma, testicular cancer, malignant thymoma, thyroid cancer, gestational trophoblastic tumor, urethral cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Wilms' tumor.

45. The use of any one of claims 34 to 43, wherein the cancer is breast cancer.

46. The use of any one of claims 34 to 43, wherein the cancer is ovarian cancer.

47. The use of any one of claims 34 to 43, wherein the cancer is pancreatic cancer.

48. The use of any one of claims 34 to 43, wherein the cancer is prostate cancer.

49. A compound of any one of claims 1-32, or a pharmaceutical composition of claim 33, for use in therapy.