IMIDAZOPYRIMIDINES AS EED INHIBITORS AND THE USE THEREOF

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present disclosure provides embryonic ectoderm development (EED) inhibitors, synthetic intermediates used to prepare EED inhibitors, and therapeutic methods of treating conditions and diseases, e.g., cancer, wherein the inhibition EED protein provides a benefit.

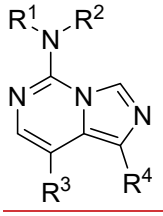
Background

[0002] Polycomb group (PcG) proteins are chromatin modifying enzymes that are dysregulated in many human cancers. The Polycomb Repressive Complex 2 (PRC2), which includes SUZ12 (suppressor of zeste 12), EED, and the catalytic subunit, EZH2 (enhancer of zeste homolog 2), represses genes by methylating the core histone H3 lysine 27 (H3K27me3) at and around the promoter regions of target genes. PRC2 is the critical component of cellular machinery involved in the epigenetic regulation of gene transcription and plays a critical function in development, tissue differentiation, and regeneration. *See, e.g.,* Moritz and Trievel, *J. Biol. Chem. 293(36)*:13805-13814 (2018); Fiskus *et al*., *Mol Cancer Ther 5(12)*:3096-3014 (2006).

[0003] PRC2 requires at least EED and SUZ12 for its methyltransferase activity. EED, SUZ12 and EZH2 are overexpressed in many cancers including, but not limited to, breast cancer, prostate cancer, and hepatocellular carcinoma. There exists for a need in the art for small molecules that inhibit the activity of EED for the treatment of cancer and other diseases.

BRIEF SUMMARY ~~OF THE INVENTION~~

[0003a] In one aspect of the present disclosure, there is provided A compound of Formula **I**:



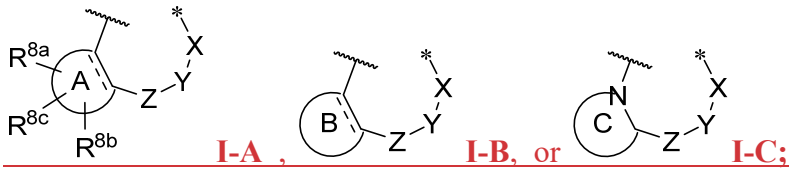
I,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^3 and R^4 taken together with the carbon atoms to which they are attached form a radical of Formula **I-A**, **I-B**, or **I-C**:



I-A, **I-B**, or **I-C**;

X is selected from the group consisting of $-C(R^{5a})(R^{5b})-$, -C(=O)-, and $-S(=O)_2-$;

R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

Y is selected from the group consisting of $-C(R^{6a})(R^{6b})-$, -S-, -O-, and $-N(R^7)-$; or

X and Y taken together form a 5-membered heteroarylenyl;

Z is $-C(R^{6c})(R^{6d})_m-$;

R^{6a} and R^{6b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

each R^{6c} and R^{6d} is independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

m is 0, 1, or 2;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, carboxamido, optionally substituted C_3-C_8 cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, (heterocyclo)C_1-C_4 alkyl, and alkylsulfonyl;


is a fused phenyl, fused 5-membered heteroaryl, or fused 6-membered heteroaryl;


is an optionally substituted fused 3- to 8-membered cycloalkyl or optionally substituted fused 4- to 8-membered heterocyclo;


is an optionally substituted fused 4- to 8-membered heterocyclo;

the bond designated with a "〰" is attached at the R^3 position of Formula **I** and the bond designated with an "*" is attached at the R^4 position of Formula **I**; or

R^3 is R^{3a};

R^4 is R^{4a};

R^{3a} is selected from group consisting of optionally substituted aryl, optionally substituted 5- to 10-membered heteroaryl, and optionally substituted 4- to 8-membered heterocyclo; and

R^{4a} is selected from the group consisting of hydrogen, halo, C_1-C_4 haloalkyl, $-S(=O)_2R^9$, $-P(=O)(R^{10a})(R^{10b})$, $-C(=O)OR^{11a}$, $-C(=O)NR^{11b}R^{11c}$ and $-S(=O)(=NR^{13a})R^{13b}$;

R^9 is selected from the group consisting of C_1-C_4 alkyl and C_3-C_6 cycloalkyl;

R^{10a} and R^{10b} are independently C_1-C_4 alkyl;

R^{11a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^{11b} and R^{11c} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl; or

R^{11b} and R^{11c} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

R^{13a} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and hydroxyalkyl;

R^{13b} is selected from the group consisting of C_1-C_6 alkyl and C_3-C_6 cycloalkyl; or

R^{13a} and R^{13b} taken together form a 5- to 7-membered heterocyclo; and

is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

[0003b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the compound disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

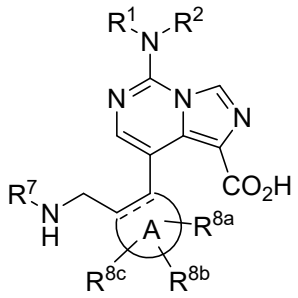
[0003c] In a further aspect of the present disclosure, there is provided a use of the compound disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating cancer in a subject in need thereof.

[0003d] In another aspect of the present disclosure, there is provided a pharmaceutical composition disclosed herein for use in treating cancer.

[0003e] In a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, for use in treating of cancer.

[0003f] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for inhibiting EED protein within a cell of a subject in need thereof.

[0003g] In a further aspect of the present disclosure, there is provided a compound of Formula **XVII**:



XVII,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and alkylsulfonyl;

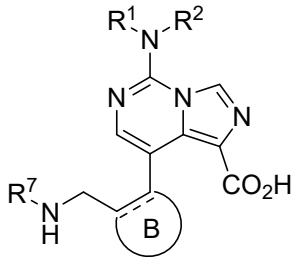


is phenyl, 5-membered heteroaryl, or 6-membered heteroaryl; and

--- is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

[0003h] In another aspect of the present disclosure, there is provided a compound of Formula **XVIII**:



XVIII,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

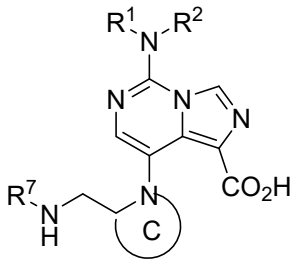
R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

B is optionally substituted 3- to 8-membered cycloalkyl or optionally substituted 4- to 8-membered heterocyclo; and

--- is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

[0003i] In a further aspect of the present disclosure, there is provided a compound of Formula **XIX**:



XIX,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl; and

 is optionally substituted 4- to 8-membered heterocyclo,

or a pharmaceutically acceptable salt or solvate thereof.

[0004] In one ~~aspect~~example, the present disclosure provides compounds represented by any one of Formulae **I-XI**, **XI-A**, **XI-B**, **XII**, **XII-A**, **XII-B**, **XIII**, **XIII-A**, **XIII-B, XIV**, **XIV-A**, **XIV-B**, **XV**, **XV-A**, **XV-B**, or **XVI**, below, and the pharmaceutically acceptable salts and solvates, e.g., hydrates, thereof, collectively referred to as "Compounds of the Disclosure." Compounds of the Disclosure are EED inhibitors and/or synthetic intermediates that can be

used to prepare EED inhibitors. Certain Compounds of the Disclosure are thus useful in treating or preventing diseases or conditions such as cancer wherein the inhibition of EED protein provides a benefit.

[0005] In another ~~aspect~~example, the present disclosure provides methods of treating or preventing a condition or disease by administering a therapeutically effective amount of a Compound of the Disclosure to a subject, e.g., a human patient, in need thereof. The disease or condition of interest that is treatable or preventable by inhibition or of EED is, for example, a cancer, a chronic autoimmune disorder, an inflammatory condition, a proliferative disorder, sepsis, or a viral infection. Also provided are methods of preventing the proliferation of unwanted proliferating cells, such as in cancer, in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure to a subject at risk of developing a condition characterized by unwanted proliferating cells. In some ~~embodiment~~examples, Compounds of the Disclosure may reduce the proliferation of unwanted cells by inducing apoptosis in those cells. In some ~~embodiment~~examples, Compounds of the Disclosure are administered in combination with an optional therapeutic agent.

[0006] In another ~~aspect~~example, the present disclosure provides a method of inhibiting EED in a subject, comprising administering to the subject a therapeutically effective amount of a Compound of the Disclosure.

[0007] In another ~~aspect~~example, the present disclosure provides a pharmaceutical composition comprising a Compound of the Disclosure and an excipient and/or pharmaceutically acceptable carrier.

[0008] In another ~~aspect~~example, the present disclosure provides a composition comprising a Compound of the Disclosure and an excipient and/or pharmaceutically acceptable carrier for use treating or preventing diseases or conditions wherein inhibition of EED provides a benefit, e.g., cancer.

[0009] In another ~~aspect~~example, the present disclosure provides a composition comprising: (a) a Compound of the Disclosure; (b) a second therapeutically active agent; and (c) optionally an excipient and/or pharmaceutically acceptable carrier.

[0010] In another ~~aspect~~example, the present disclosure provides a Compound of the Disclosure for use in the treatment or prevention of a disease or condition of interest, e.g., cancer.

[0011] In another ~~aspect~~example, the present disclosure provides a use of a Compound of the Disclosure for the manufacture of a medicament for treating a disease or condition of interest, e.g., cancer.

[0012] In another ~~aspect~~example, the present disclosure provides a kit comprising a Compound of the Disclosure, and, optionally, a packaged composition comprising an optional therapeutic agent useful in the treatment of a disease or condition of interest, and a package insert containing directions for use in the treatment of a disease or condition, e.g., cancer.

[0013] In another ~~aspect~~example, the present disclosure provides methods of preparing Compounds of the Disclosure and Intermediates of the Disclosure.

[0014] Additional embodiments and advantages of the disclosure will be set forth, in part, in the description that follows, and will flow from the description, or can be learned by practice of the disclosure. The embodiments and advantages of the disclosure will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

[0015] It is to be understood that both the foregoing summary and the following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed.

BRIEF DESCRIPTION OF DRAWINGS

[0016] Fig. 1 is a line graph showing the anti-tumor efficacy of representative Compounds of the Disclosure in the KARPAS422 tumor model in mice.

[0017] Fig. 2 is a line graph showing the body weight change of tumor-bearing mice treated with representative Compounds of the Disclosure in the KARPAS422 tumor model in mice.

DETAILED DESCRIPTION OF THE INVENTION

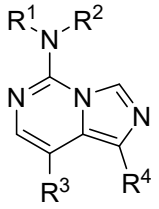
I. Compounds of the Disclosure

[0018] Compounds of the Disclosure are EED inhibitors and/or synthetic intermediates that can be used to prepare EED inhibitors.

[0019] In one embodiment, Compounds of the Disclosure are compounds of Formula **I**:

What is claimed is:

1. A compound of Formula **I**:

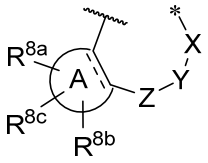
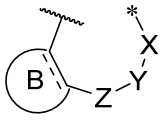
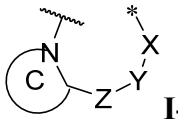
 **I**,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^3 and R^4 taken together with the carbon atoms to which they are attached form a radical of Formula **I-A**, **I-B**, or **I-C**:

 **I-A** ,  **I-B**, or  **I-C;**

X is selected from the group consisting of -C(R^{5a})(R^{5b})-, -C(=O)-, and -S(=O)$_2$-;

R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

Y is selected from the group consisting of -C(R^{6a})(R^{6b})-, -S-, -O-, and -N(R^7)-; or

X and Y taken together form a 5-membered heteroarylenyl;

Z is -C(R^{6c})(R^{6d})$_m$-;

R^{6a} and R^{6b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

each R^{6c} and R^{6d} is independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

m is 0, 1, or 2;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, carboxamido, optionally substituted C_3-C_8

cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, (heterocyclo)C_1-C_4 alkyl, and alkylsulfonyl;



is a fused phenyl, fused 5-membered heteroaryl, or fused 6-membered heteroaryl;



is an optionally substituted fused 3- to 8-membered cycloalkyl or optionally substituted fused 4- to 8-membered heterocyclo;



is an optionally substituted fused 4- to 8-membered heterocyclo;

the bond designated with a "〰" is attached at the R^3 position of Formula **I** and the bond designated with an "*" is attached at the R^4 position of Formula **I**; or

R^3 is R^{3a};

R^4 is R^{4a};

R^{3a} is selected from group consisting of optionally substituted aryl, optionally substituted 5- to 10-membered heteroaryl, and optionally substituted 4- to 8-membered heterocyclo; and

R^{4a} is selected from the group consisting of hydrogen, halo, C_1-C_4 haloalkyl, $-S(=O)_2R^9$, $-P(=O)(R^{10a})(R^{10b})$, $-C(=O)OR^{11a}$, $-C(=O)NR^{11b}R^{11c}$ and $-S(=O)(=NR^{13a})R^{13b}$;

R^9 is selected from the group consisting of C_1-C_4 alkyl and C_3-C_6 cycloalkyl;

R^{10a} and R^{10b} are independently C_1-C_4 alkyl;

R^{11a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^{11b} and R^{11c} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl; or

R^{11b} and R^{11c} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

R^{13a} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and hydroxyalkyl;

R^{13b} is selected from the group consisting of C_1-C_6 alkyl and C_3-C_6 cycloalkyl; or

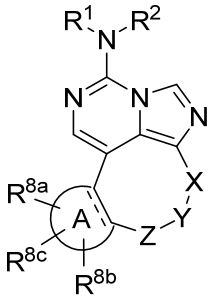
R^{13a} and R^{13b} taken together form a 5- to 7-membered heterocyclo; and

=== is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

~~2. The compound of claim 1, wherein R^3 and R^4 taken together with the carbon atoms to which they are attached form a radical of Formula **I-A**, **I-B**, or **I-C**, or a pharmaceutically acceptable salt or solvate thereof.~~

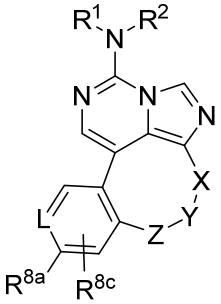
~~3~~2. The compound of claim ~~2~~1 of Formula **II**:



II,

or a pharmaceutically acceptable salt or solvate thereof.

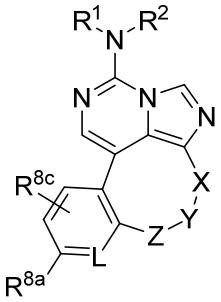
~~4~~3. The compound of claim 2~~3~~ of Formula **III**:



III,

wherein L is selected from the group consisting of -C(R^{8b})= and -N=, or a pharmaceutically acceptable salt or solvate thereof~~.~~; or

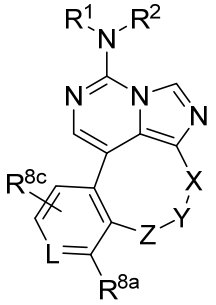
~~5. The compound of claim 3 of~~ Formula **IV**:



IV,

wherein L is selected from the group consisting of -C(R^{8b})= and -N=, or a pharmaceutically acceptable salt or solvate thereof~~.~~; or

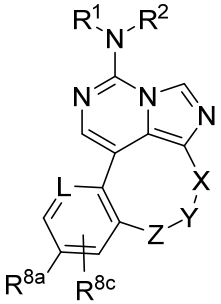
~~6. The compound of claim 3 of~~ Formula **V**:



V,

wherein L is selected from the group consisting of -C(R^{8b})= and -N=, or a pharmaceutically acceptable salt or solvate thereof~~.~~; or

~~7. The compound of claim 3 of~~ Formula **VI**:



VI,

wherein L is selected from the group consisting of -C(R^{8b})= and -N=, or a pharmaceutically acceptable salt or solvate thereof.

~~8. The compound of claim 4, wherein L is -C(R^{8b})=, or a pharmaceutically acceptable salt or solvate thereof.~~

~~9. The compound of any one of claims 3-7, wherein L is -N=, or a pharmaceutically acceptable salt or solvate thereof.~~

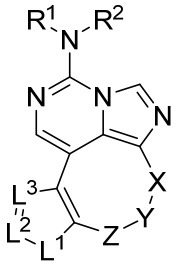
~~10. The compound of any one of claims 1-9, wherein R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 cycloalky, optionally substituted 4- to 8-membered heterocyclo, and (heterocyclo)C_1-C_4 alkyl,, or a pharmaceutically acceptable salt or solvate thereof.~~

~~4~~11. The compound of any one of claims 1-3~~claim 10~~, wherein:

R^{8a} is selected from the group consisting of -CF_3, -CH_3, -CHF_2, -CD_3, and cyclopropyl; and

R^{8b} and R^{8c} are hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

~~12~~5. The compound of claim ~~2~~3 of Formula **VII**:



VII,

wherein:

L^1 is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

L^2 is selected from the group consisting of -C(R^{8b})= and -N=;

L^3 is selected from the group consisting of -C(R^{8c})= and -N=;

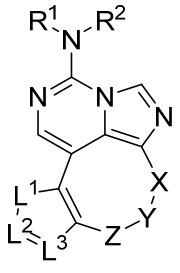
R^{8a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^{8b} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl,

or a pharmaceutically acceptable salt or solvate thereof~~.~~; or

~~13. The compound of claim 3 of~~ Formula **VIII**:



VIII,

wherein:

L^1 is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

L^2 is selected from the group consisting of -C(R^{8b})= and -N=;

L^3 is selected from the group consisting of -C(R^{8c})= and -N=;

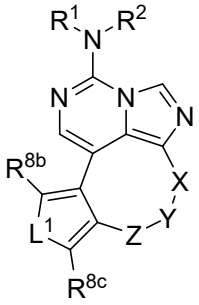
R^{8a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^{8b} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl,

or a pharmaceutically acceptable salt or solvate thereof.

~~146~~. The compound of claim ~~32~~ of Formula **IX**:



IX,

wherein:

L^1 is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

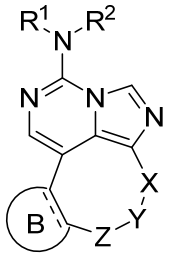
R^{8a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^{8b} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl,

or a pharmaceutically acceptable salt or solvate thereof.

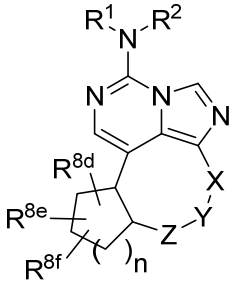
~~15~~7. The compound of claim 1~~2~~ of Formula **X**:



X,

or a pharmaceutically acceptable salt or solvate thereof.

~~16~~8. The compound of claim ~~15~~7 of Formula **XI**:



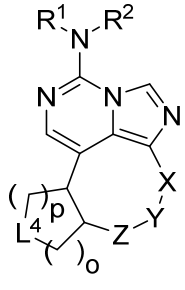
XI,

wherein:

R^{8d}, R^{8e}, and R^{8f} are independently selected from the group consisting of hydrogen, halo, and C_1-C_4 alkyl; and

n is 1, 2, or 3, or a pharmaceutically acceptable salt or solvate thereof.

~~17~~9. The compound of claim ~~15~~7 of Formula **XII**:



XII,

wherein:

L^4 is selected from the group consisting of -S-, -O-, and -N(R^{8g})-;

R^{8g} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, optionally substituted C_3-C_6 cycloalkyl, and optionally substituted 4- to 8-membered heterocyclo;

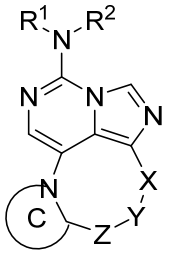
o is 0, 1, 2, or 3; and

p is 0, 1, 2, or 3;

wherein the sum of o and p is 1, 2, 3, 4, or 5,

or a pharmaceutically acceptable salt or solvate thereof.

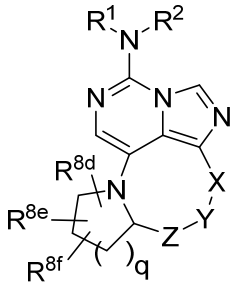
~~18~~10. The compound of claim 1~~2~~ of Formula **XIII**:



XIII,

or a pharmaceutically acceptable salt or solvate thereof.

~~19~~11. The compound of claim 10~~18~~ of Formula **XIV**:



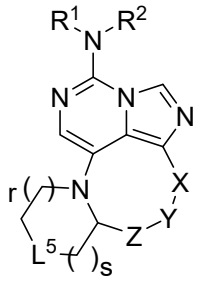
XIV,

wherein:

R^{8d}, R^{8e}, and R^{8f} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl; and

q is 1, 2, or 3, or a pharmaceutically acceptable salt or solvate thereof.

~~20~~12. The compound of claim 10~~18~~ of Formula **XV**:



XV,

wherein:

L^5 is selected from the group consisting of -S-, -O-, and -N(R^{8h})-;

R^{8h} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, optionally substituted C_3-C_6 cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, -C(=O)R^{14a}, and -S(=O)$_2R^{14b}$;

R^{14a} and R^{14b} are independently selected from the group consisting of C_1-C_6 alkyl and optionally substituted C_3-C_8 cycloalkyl;

r is 1, 2, or 3; and

s is 1, 2, or 3,

or a pharmaceutically acceptable salt or solvate thereof.

~~21. The compound of any one of claims 1-20, wherein Z is -CH_2-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~22. The compound of any one of claims 1-21, wherein:~~

~~X is selected from the group consisting of -C(R^{5a})(R^{5b})-, -C(=O)-, and -S(=O)$_2$-; and~~

~~Y is selected from the group consisting of -C(R^{6a})(R^{6b})-, -S-, -O-, and -N(R^7)-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~23. The compound of any one of claims 1-22, wherein X is -CH_2-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~24. The compound of any one of claims 1-22, wherein X is -C(=O)-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~25. The compound of any one of claims 1-22, wherein X is -S(=O)$_2$-, or a pharmaceutically acceptable salt or solvate thereof.~~

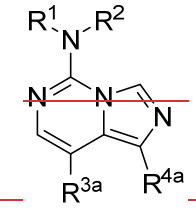
~~26. The compound of any one of claims 1-25, wherein Y is -O-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~27. The compound of any one of claims 1-25, wherein Y is -N(R^7)-, or a pharmaceutically acceptable salt or solvate thereof.~~

~~28. The compound of claim 27, wherein R^7 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, and optionally substituted C_3-C_8 cycloalkyl, or a pharmaceutically acceptable salt or solvate thereof.~~

~~29. The compound of any one of claims 1-21, wherein X and Y taken together form a 5-membered heteroarylenyl, or a pharmaceutically acceptable salt or solvate thereof.~~

~~30. The compound of claim 1 of Formula **XVI**:~~



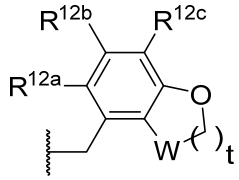
~~**XVI**,~~

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

~~31. The compound of any one of claims 1-30, wherein R^2 is hydrogen, or a pharmaceutically acceptable salt or solvate thereof.~~

~~32~~13. The compound of any one of claims 1-~~31~~12, wherein:

R^1 is R^1-1:



R1-1;

R12a, R12b, and R12c are each independently selected from the group consisting of hydrogen, halo, C1-C4 alkyl, C1-C4 haloalkyl, and C1-C4 alkoxy;

W is selected from the group consisting of -CH2- and -C(=O)-; and

t is 1 or 2,

or a pharmaceutically acceptable salt or solvate thereof.

~~33~~14. The compound of claim ~~32~~13, wherein W is -C(=O)- and t is 1, or a pharmaceutically acceptable salt or solvate thereof.

~~34. The compound of claim 32, wherein W is -CH2- and t is 2, or a pharmaceutically acceptable salt or solvate thereof.~~

~~35. The compound of claim 32, wherein W is -CH2- and t is 1, or a pharmaceutically acceptable salt or solvate thereof.~~

~~36~~15. The compound of claim 13 or 14~~any one of claims 32-35~~, wherein:

R12a is fluoro; and

R12b and R12c are independently selected from the group consisting of hydrogen and fluoro,

or a pharmaceutically acceptable salt or solvate thereof.

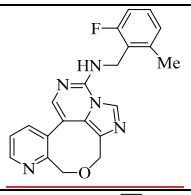
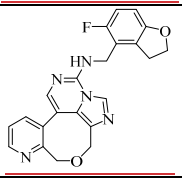
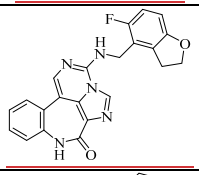
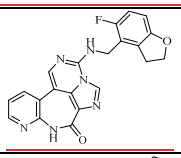
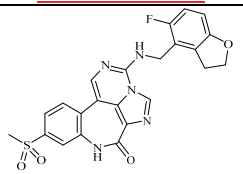
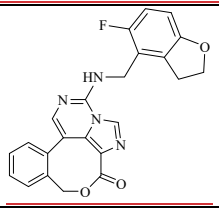
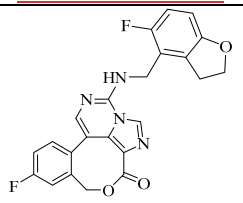
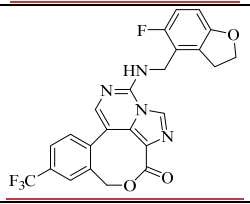
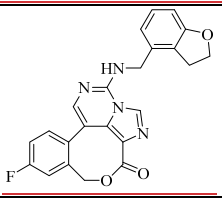
~~37~~16. The compound of claim ~~36~~15, wherein:

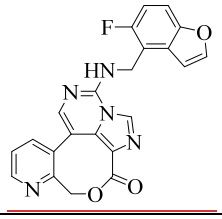
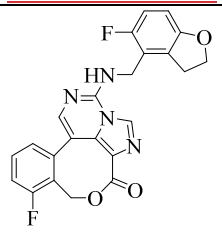
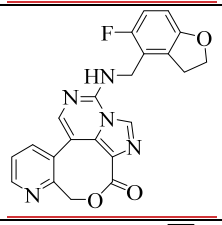
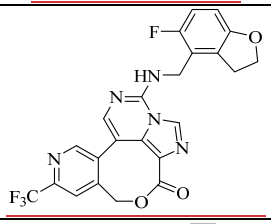
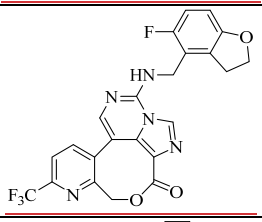
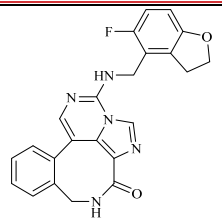
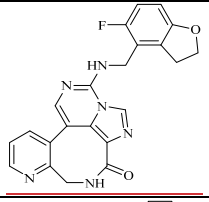
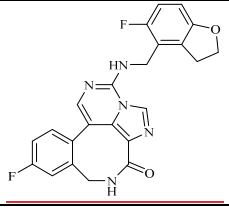
R12a is fluoro; and

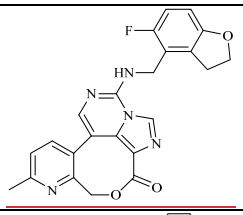
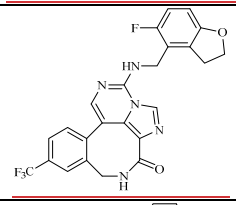
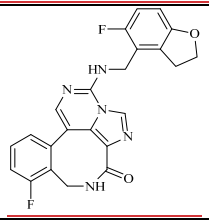
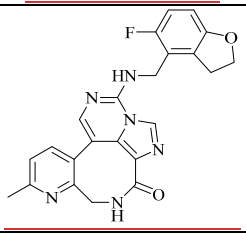
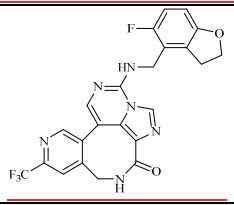
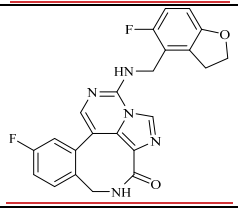
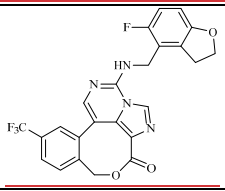
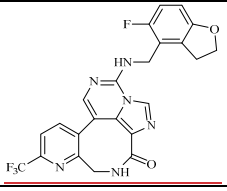
R12b and R12c are hydrogen,

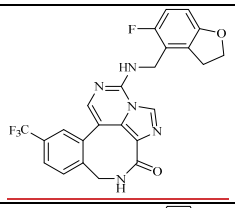
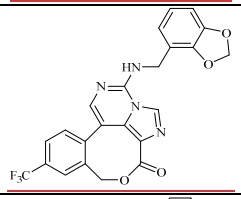
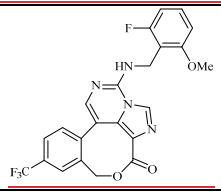
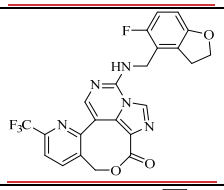
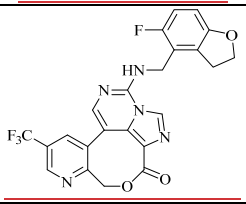
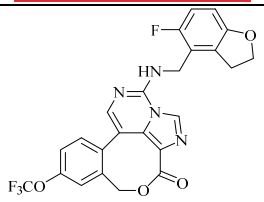
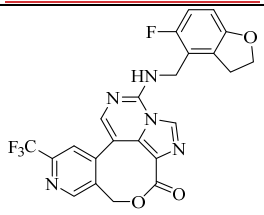
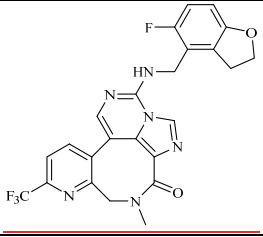
or a pharmaceutically acceptable salt or solvate thereof.

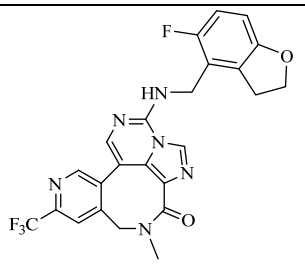
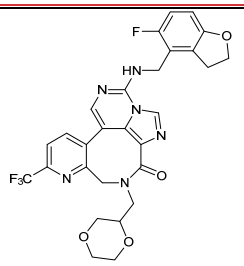
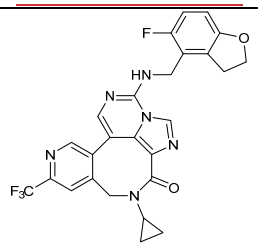
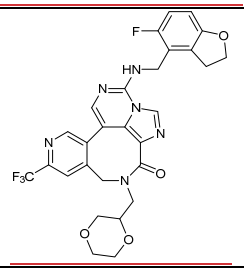
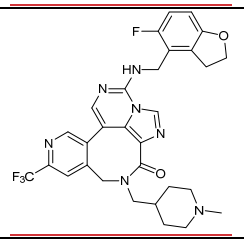
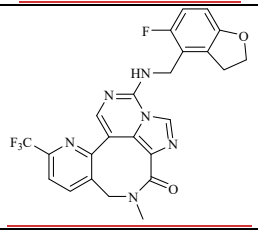
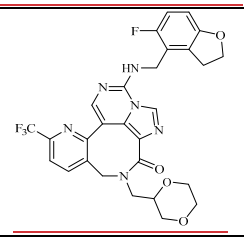
~~38~~17. The compound of claim 1 selected from any one or more of the following compounds~~ of Table 1~~, or a pharmaceutically acceptable salt or solvate thereof~~.~~:

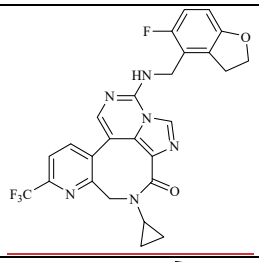
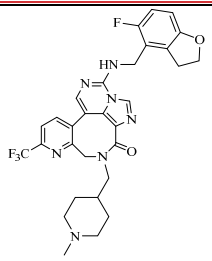
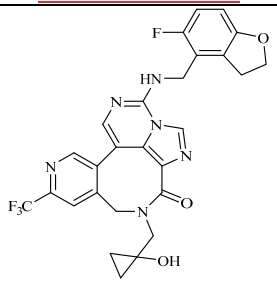
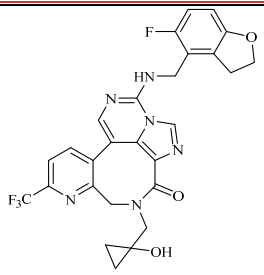
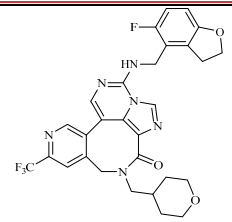
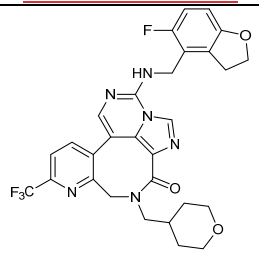
Cpd. No.	Structure	Name
1		N-(2-fluoro-6-methylbenzyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-12-amine
2		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-12-amine
3		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-2,4,10,11a-tetraazadibenzo[cd,f]azulen-3(4H)-one
4		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-2,4,5,10,11a-pentaazadibenzo[cd,f]azulen-3(4H)-one
5		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-(methylsulfonyl)-2,4,10,11a-tetraazadibenzo[cd,f]azulen-3(4H)-one
6		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
7		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
8		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
9		12-(((2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-fluoro-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

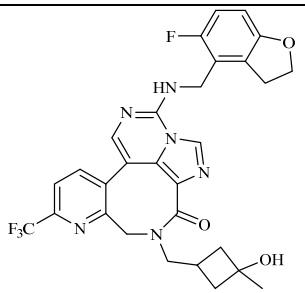
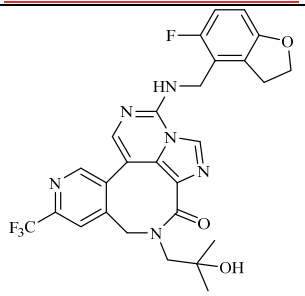
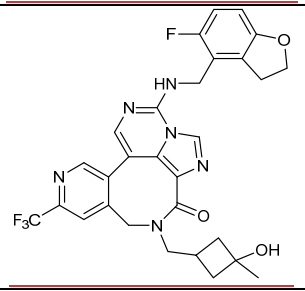
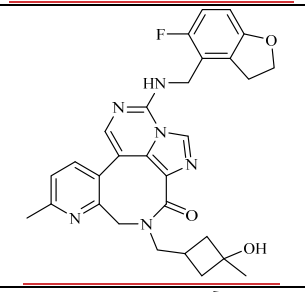
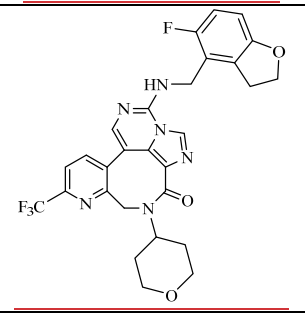
10		12-(((5-fluorobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
11		6-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
12		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
13		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,8,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
14		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
15		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
16		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
17		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

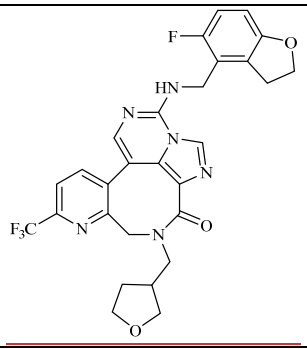
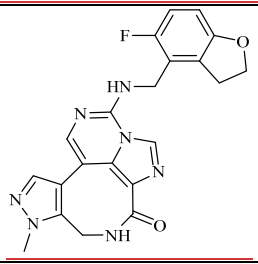
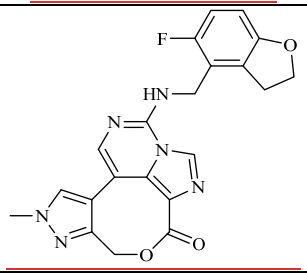
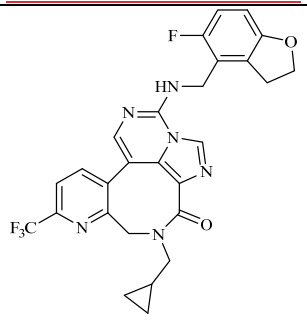
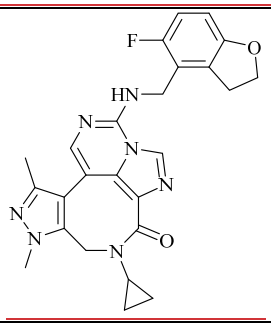
18		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
19		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
20		6-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
21		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
22		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
23		8-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
24		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
25		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

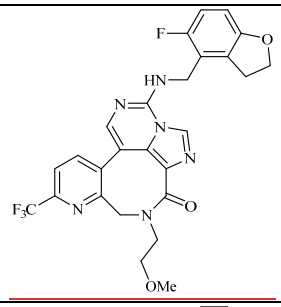
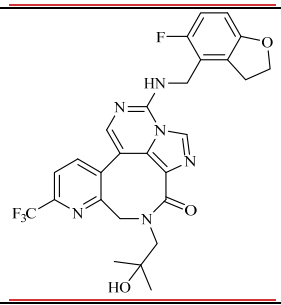
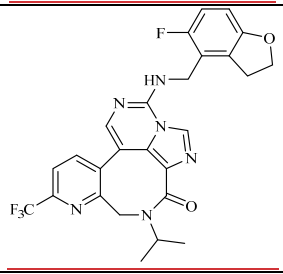
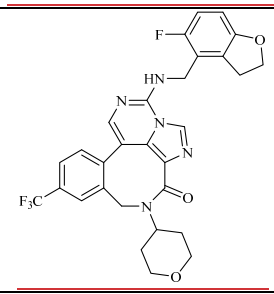
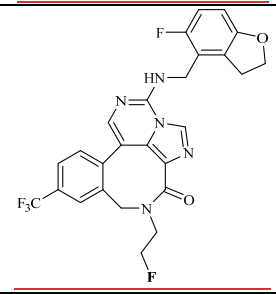
26		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
27		12-((benzo[d][1,3]dioxol-4-ylmethyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
28		12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
29		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-3H,5H-4-oxa-2,9,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
30		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
31		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethoxy)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
32		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-3H,5H-4-oxa-2,7,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
33		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

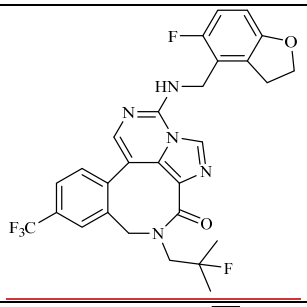
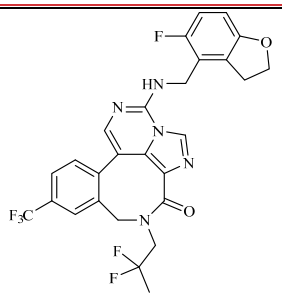
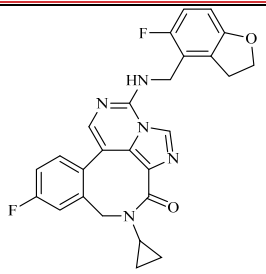
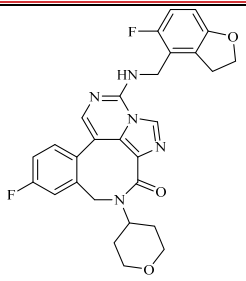
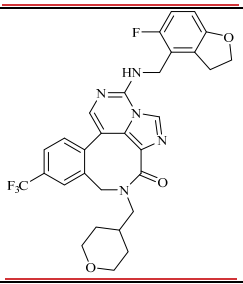
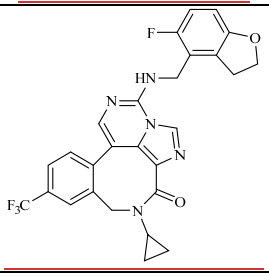
34		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
35		4-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
36		4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
37		4-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
38		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((1-methylpiperidin-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
39		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-8-(trifluoromethyl)-4,5-dihydro-3H-2,4,9,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
40		4-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-4,5-dihydro-3H-2,4,9,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

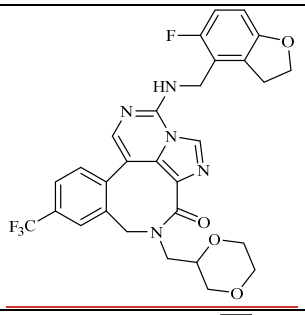
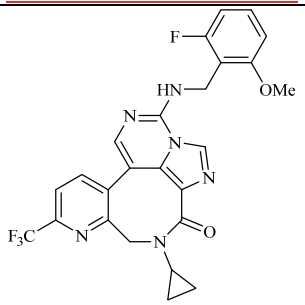
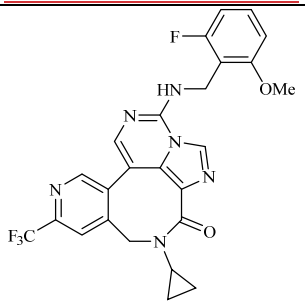
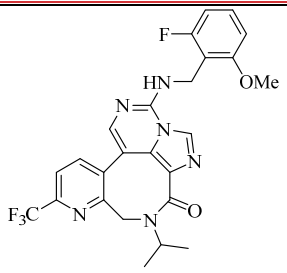
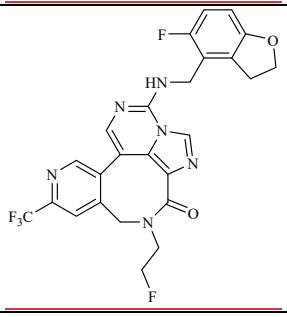
41		4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
42		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((1-methylpiperidin-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
43		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((1-hydroxycyclopropyl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
44		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((1-hydroxycyclopropyl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
45		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((tetrahydro-2H-pyran-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
46		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((tetrahydro-2H-pyran-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

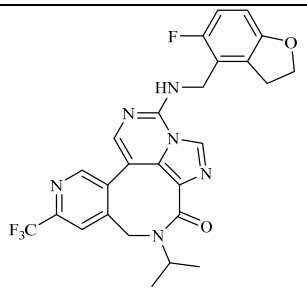
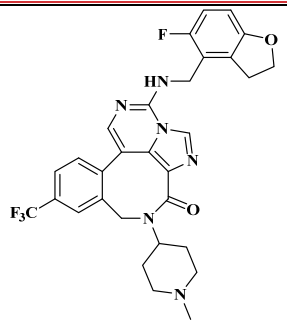
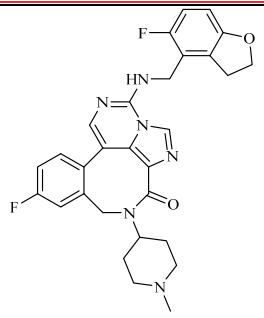
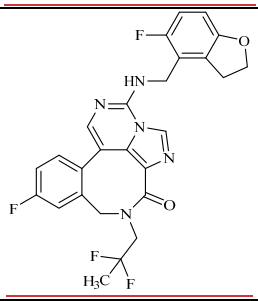
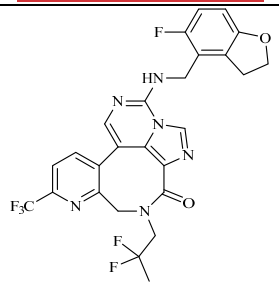
47		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((3-hydroxy-3-methylcyclobutyl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
48		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-hydroxy-2-methylpropyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
49		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((3-hydroxy-3-methylcyclobutyl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
50		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((3-hydroxy-3-methylcyclobutyl)methyl)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
51		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(tetrahydro-2H-pyran-4-yl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

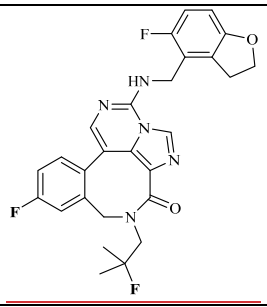
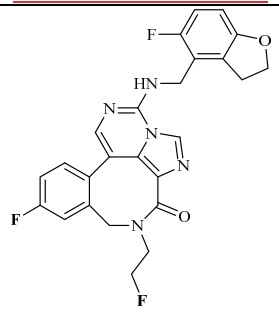
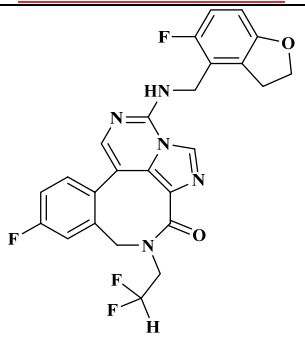
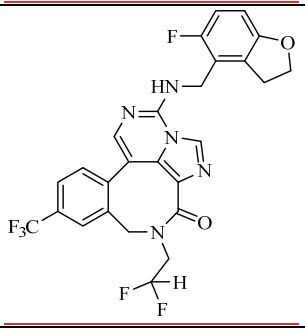
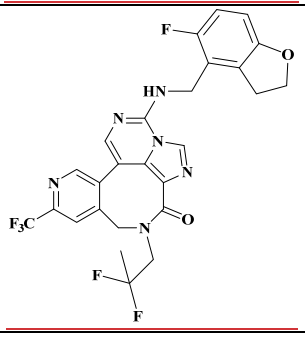
52		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((tetrahydrofuran-3-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
53		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-5,6-dihydro-2,4,6,7,10,11a-hexaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
54		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-5,7-dihydro-3H-4-oxa-2,6,7,10,11a-pentaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3-one
55		4-(cyclopropylmethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
56		4-cyclopropyl-11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6,8-dimethyl-5,6-dihydro-2,4,6,7,10,11a-hexaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one

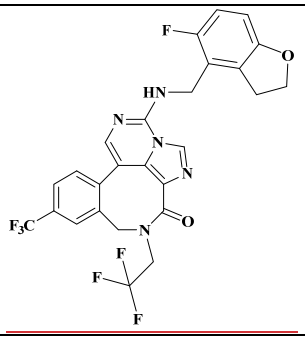
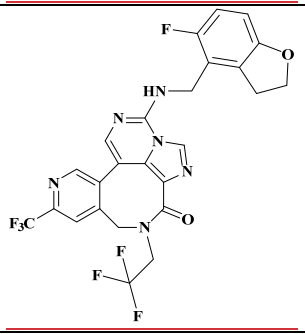
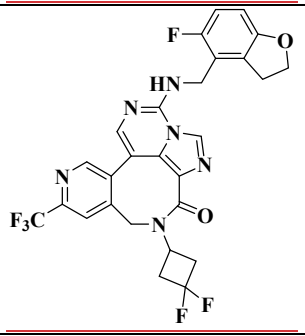
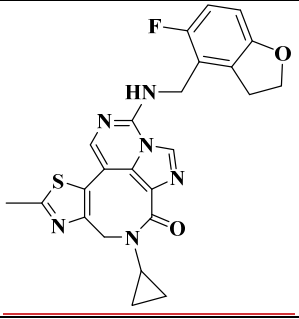
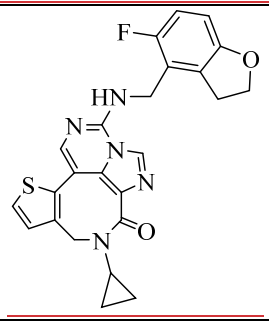
57		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-methoxyethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
58		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-hydroxy-2-methylpropyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
59		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
60		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(tetrahydro-2H-pyran-4-yl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
61		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

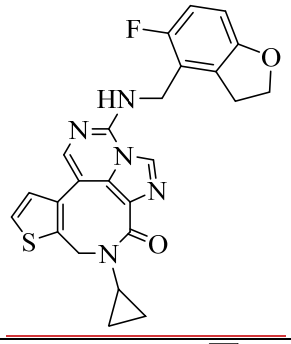
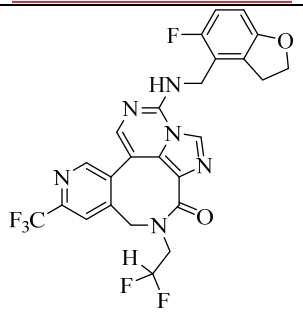
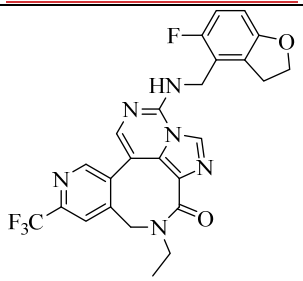
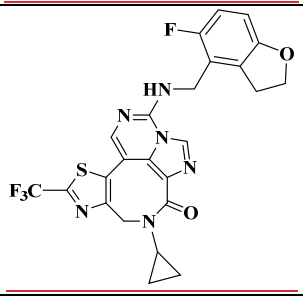
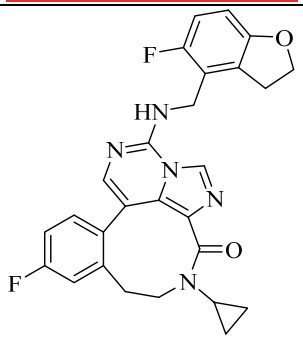
62		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoro-2-methylpropyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
63		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
64		4-cyclopropyl-7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
65		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
66		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((tetrahydro-2H-pyran-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
67		4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

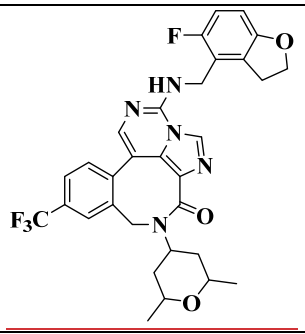
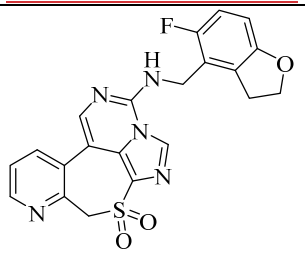
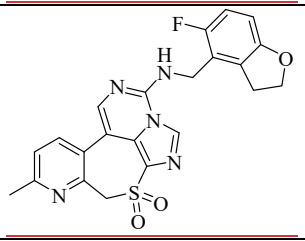
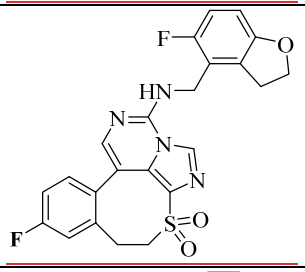
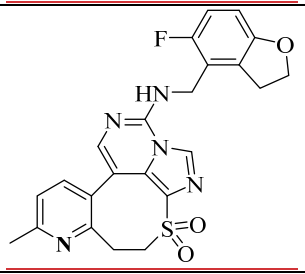
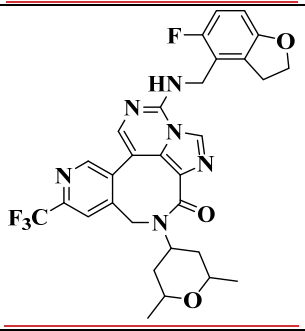
68		4-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
69		4-cyclopropyl-12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
70		4-cyclopropyl-12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
71		12-((2-fluoro-6-methoxybenzyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
72		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

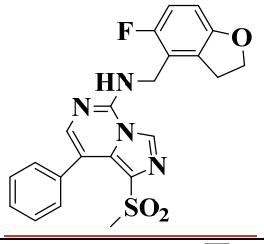
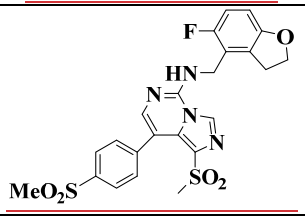
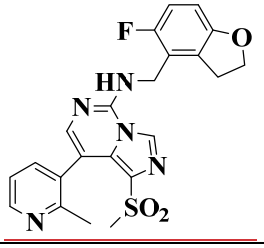
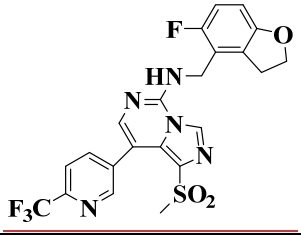
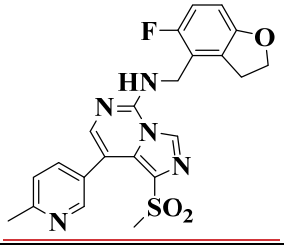
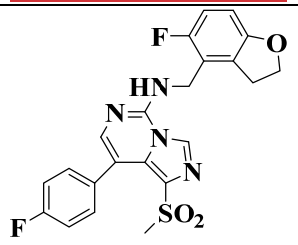
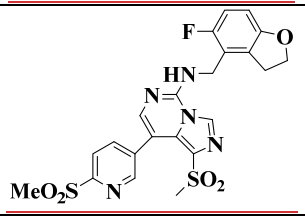
73		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
74		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(1-methylpiperidin-4-yl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
75		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(1-methylpiperidin-4-yl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
76		4-(2,2-difluoropropyl)-7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
77		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

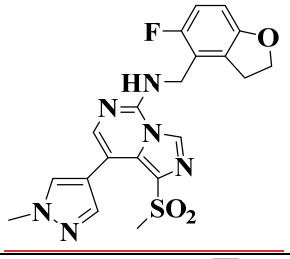
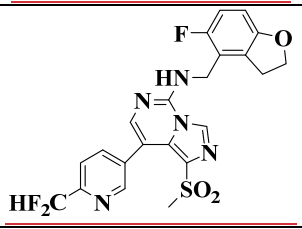
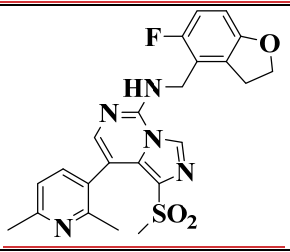
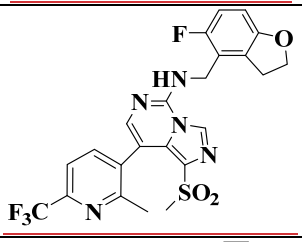
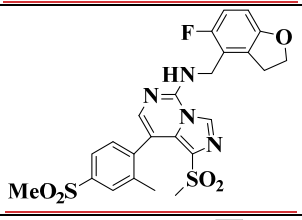
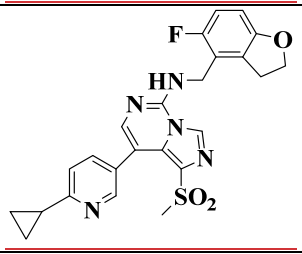
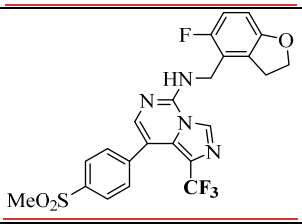
78		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoro-2-methylpropyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
79		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoroethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
80		4-(2,2-difluoroethyl)-7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
81		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
82		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

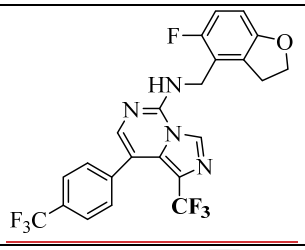
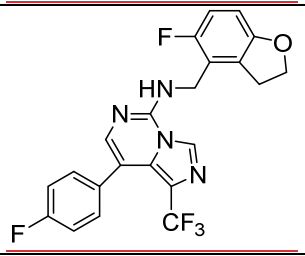
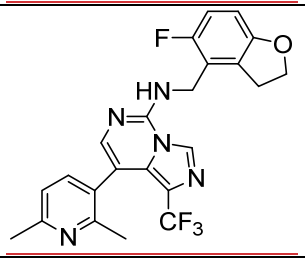
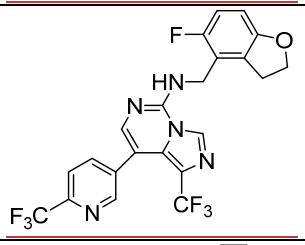
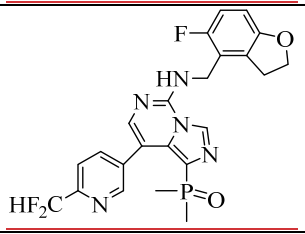
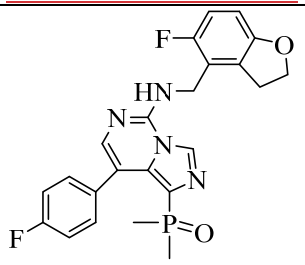
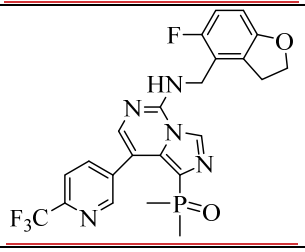
83		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
84		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
85		4-(3,3-difluorocyclobutyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
86		4-cyclopropyl-11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-8-thia-2,4,6,10,11a-pentaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3-one
87		4-cyclopropyl-11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-8-thia-2,4,10,11a-tetraazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3-one

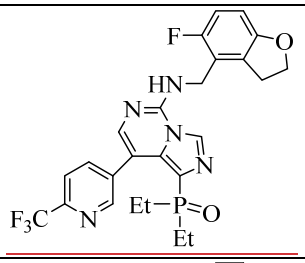
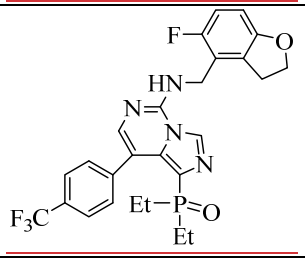
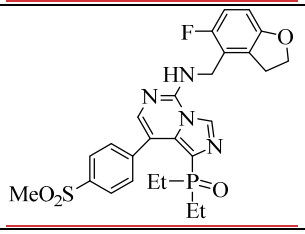
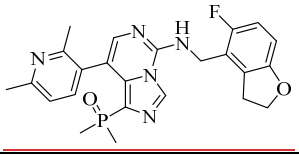
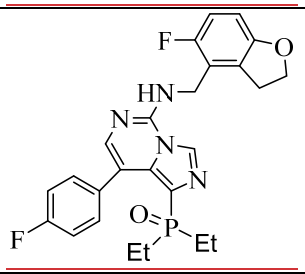
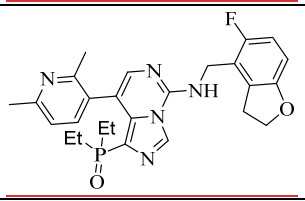
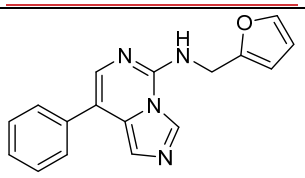
88		4-cyclopropyl-11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-6-thia-2,4,10,11a-tetraazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3-one
89		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
90		4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
91		4-cyclopropyl-11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-8-thia-2,4,6,10,11a-pentaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3-one
92		4-cyclopropyl-8-fluoro-13-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-5,6-dihydro-2,4,12,13a-tetraazabenzo[4,5]cyclonona[1,2,3-cd]inden-3(4H)-one

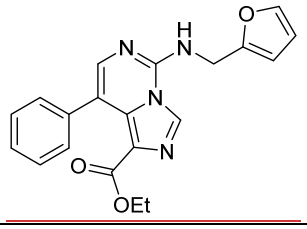
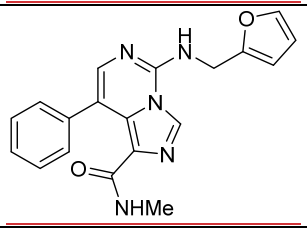
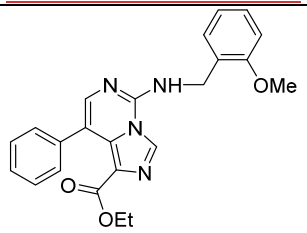
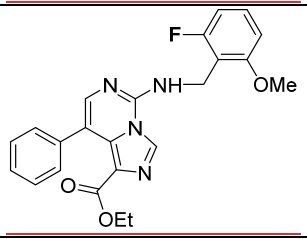
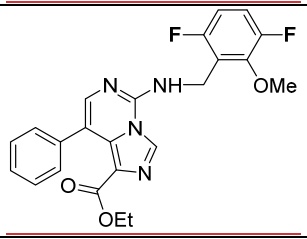
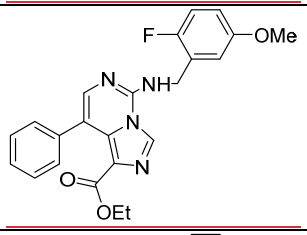
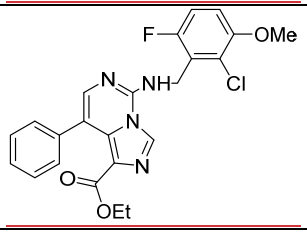
93		4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
94		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide
95		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide
96		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3-thia-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
97		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3-thia-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
98		4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

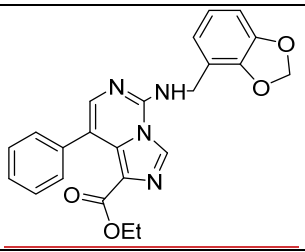
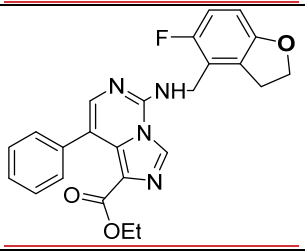
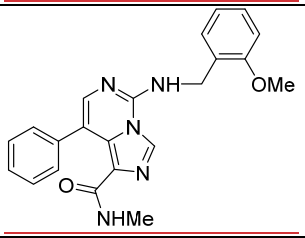
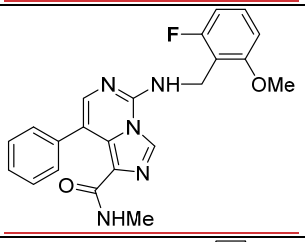
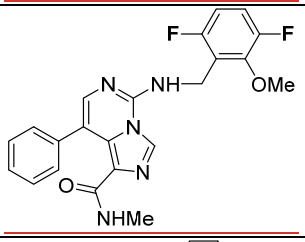
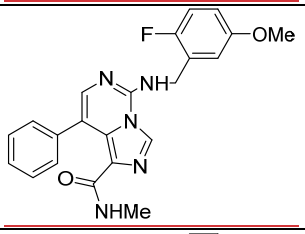
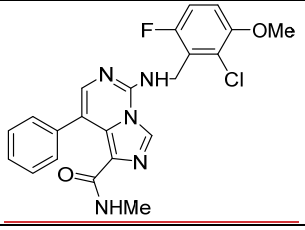
99		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)-8-phenylimidazo[1,5-c]pyrimidin-5-amine
100		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)-8-(4 (methylsulfonyl)phenyl)imidazo[1,5-c]pyrimidin-5-amine
101		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(2-methylpyridin-3-yl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
102		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)-8-(6-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-5-amine
103		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(6-methylpyridin-3-yl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
104		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(4-fluorophenyl)-1 (methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
105		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)-8-(6-(methylsulfonyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-5-amine

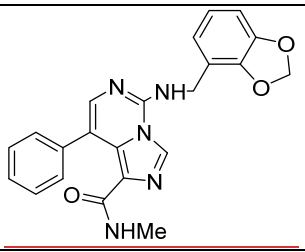
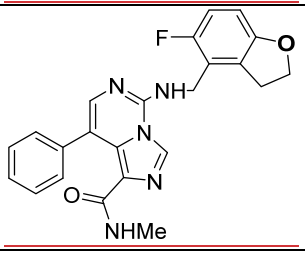
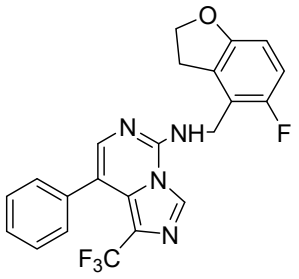
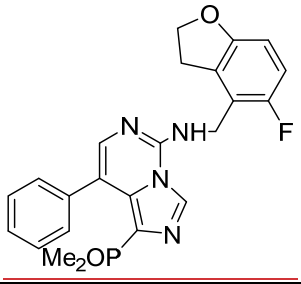
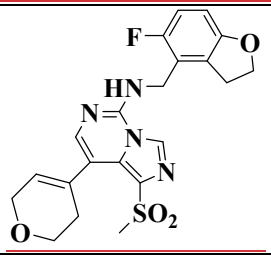
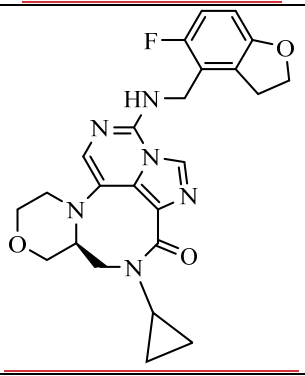
106		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(1-methyl-1H-pyrazol-4-yl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
107		8-(6-(difluoromethyl)pyridin-3-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
108		8-(2,6-dimethylpyridin-3-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
109		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(2-methyl-6-(trifluoromethyl)pyridin-3-yl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
110		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(2-methyl-4-(methylsulfonyl)phenyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
111		8-(6-cyclopropylpyridin-3-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
112		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(4-(methylsulfonyl)phenyl)-1-(trifluoromethyl)imidazo[1,5-c]pyrimidin-5-amine

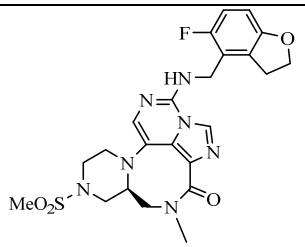
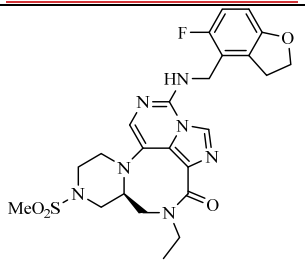
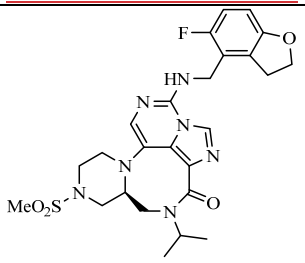
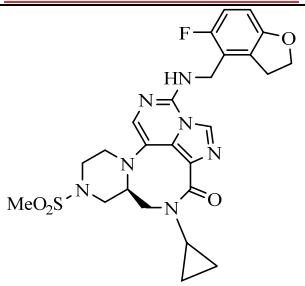
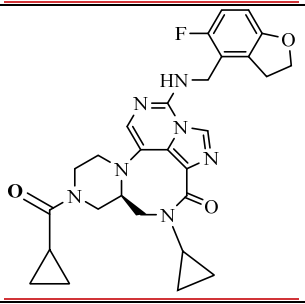
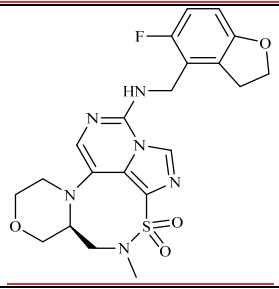
113		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(trifluoromethyl)-8-(4-(trifluoromethyl)phenyl)imidazo[1,5-c]pyrimidin-5-amine
114		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(4-fluorophenyl)-1-(trifluoromethyl)imidazo[1,5-c]pyrimidin-5-amine
115		8-(2,6-dimethylpyridin-3-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(trifluoromethyl)imidazo[1,5-c]pyrimidin-5-amine
116		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(trifluoromethyl)-8-(6-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-5-amine
117		(8-(6-(difluoromethyl)pyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)dimethylphosphine oxide
118		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(4-fluorophenyl)imidazo[1,5-c]pyrimidin-1-yl)dimethylphosphine oxide
119		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(6-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)dimethylphosphine oxide

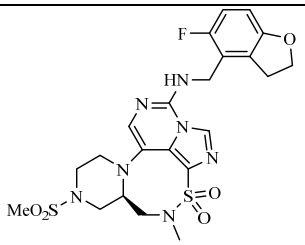
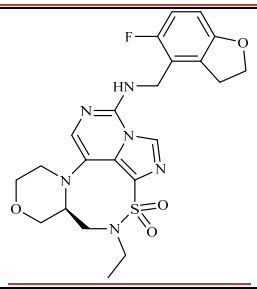
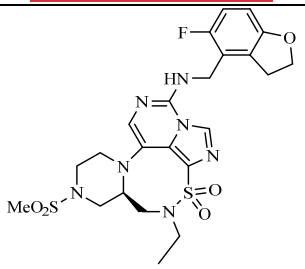
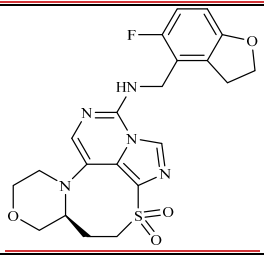
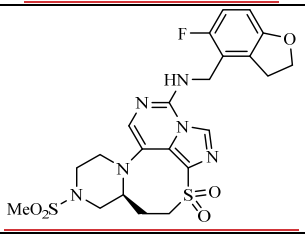
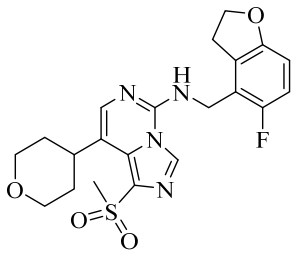
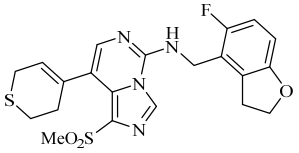
120		diethyl(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(6-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)phosphine oxide
121		diethyl(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(4-(trifluoromethyl)phenyl)imidazo[1,5-c]pyrimidin-1-yl)phosphine oxide
122		diethyl(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(4-(methylsulfonyl)phenyl)imidazo[1,5-c]pyrimidin-1-yl)phosphine oxide
123		(8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)dimethylphosphine oxide
124		diethyl(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(4-fluorophenyl)imidazo[1,5-c]pyrimidin-1-yl)phosphine oxide
125		(8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)diethylphosphine oxide
126		N-(furan-2-ylmethyl)-8-phenylimidazo[1,5-c]pyrimidin-5-amine

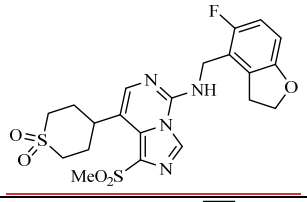
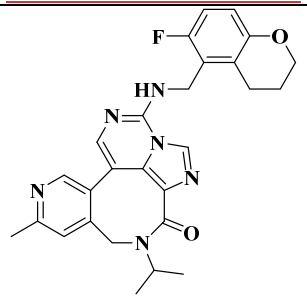
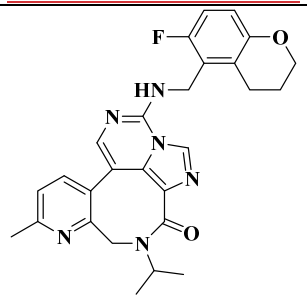
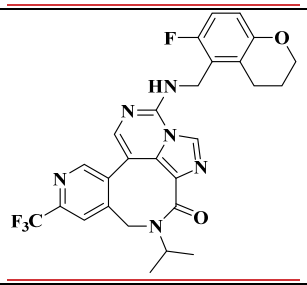
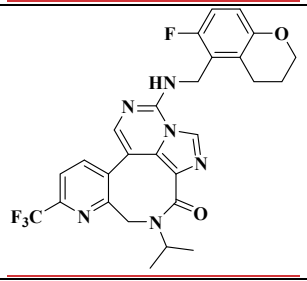
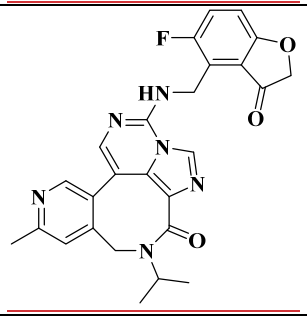
127		ethyl 5-((furan-2-ylmethyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
128		5-((furan-2-ylmethyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
129		ethyl 5-((2-methoxybenzyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
130		ethyl 5-((2-fluoro-6-methoxybenzyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
131		ethyl 5-((2,6-difluoro-3-methoxybenzyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
132		ethyl 5-((2-fluoro-5-methoxybenzyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
133		ethyl 5-((2-chloro-6-fluoro-3-methoxybenzyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate

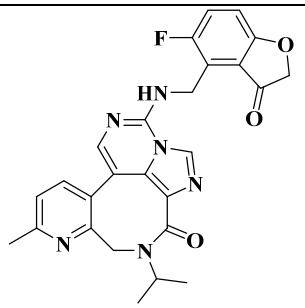
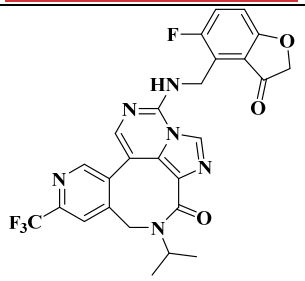
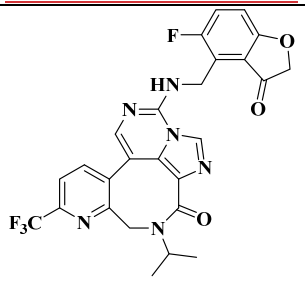
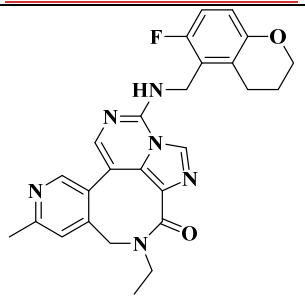
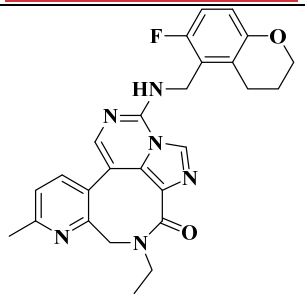
134		ethyl 5-((benzo[d][1,3]dioxol-4-ylmethyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
135		ethyl 5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-phenylimidazo[1,5-c]pyrimidine-1-carboxylate
136		5-((2-methoxybenzyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
137		5-((2-fluoro-6-methoxybenzyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
138		5-((3,6-difluoro-2-methoxybenzyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
139		5-((2-fluoro-5-methoxybenzyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
140		5-((2-chloro-6-fluoro-3-methoxybenzyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide

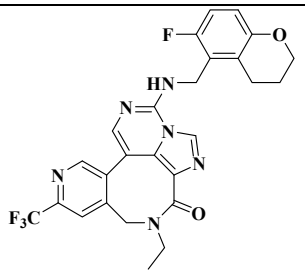
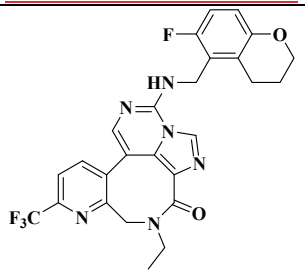
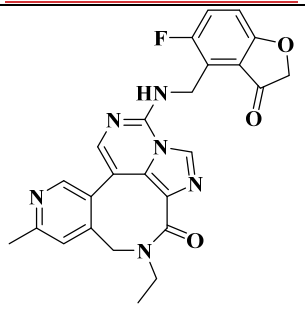
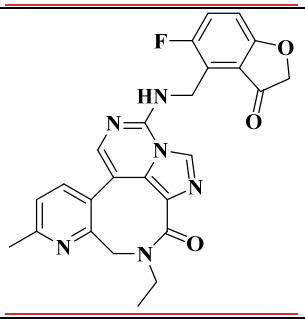
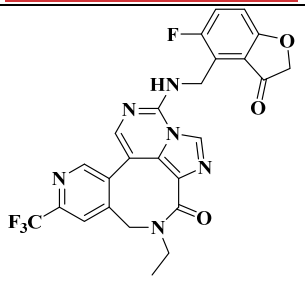
141		5-((benzo[d][1,3]dioxol-4-ylmethyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
142		5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-N-methyl-8-phenylimidazo[1,5-c]pyrimidine-1-carboxamide
143		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-phenyl-1-(trifluoromethyl)imidazo[1,5-c]pyrimidin-5-amine
144		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-phenylimidazo[1,5-c]pyrimidin-1-yl)dimethylphosphine oxide
146		8-(3,6-dihydro-2H-pyran-4-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine
147		(*S*)-4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5,5a,6,8,9-hexahydro-3H-7-oxa-2,4,9a,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

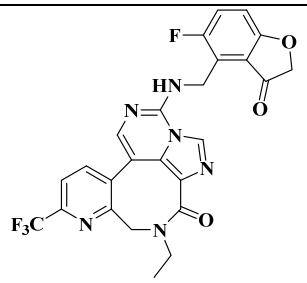
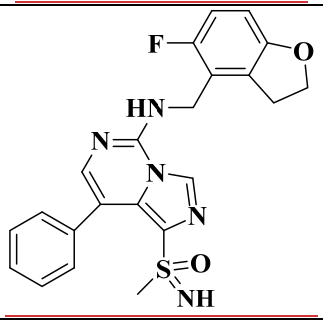
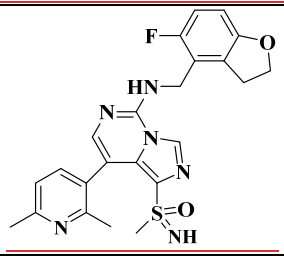
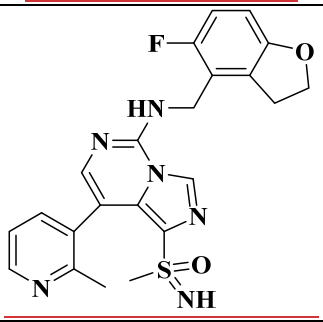
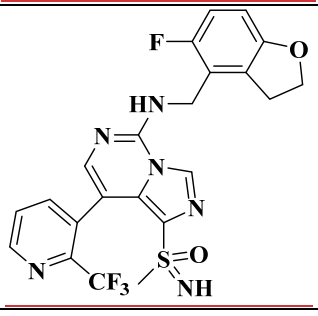
148		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
149		(S)-4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
150		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
151		(S)-4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
152		(R)-7-(cyclopropanecarbonyl)-4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
153		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-4,5,5a,6,8,9-hexahydro-7-oxa-3-thia-2,4,9a,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide

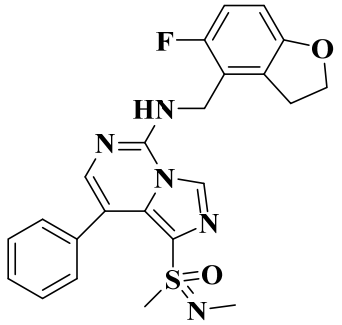
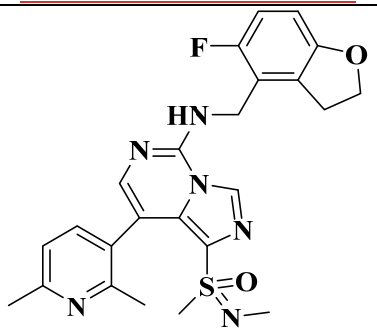
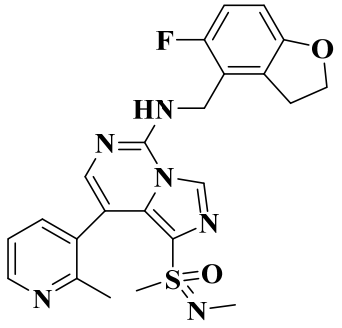
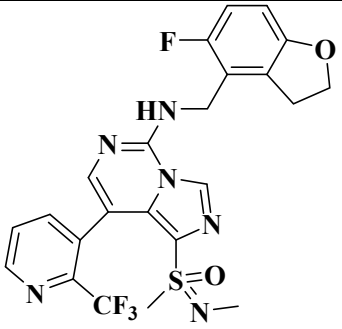
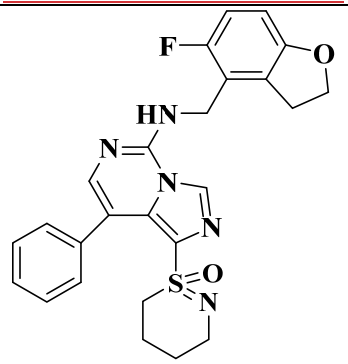
154		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-4H-3-thia-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
155		(S)-4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5,5a,6,8,9-hexahydro-7-oxa-3-thia-2,4,9a,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
156		(R)-4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-4H-3-thia-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
157		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5,5a,6,8,9-hexahydro-7-oxa-3-thia-2,9a,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
158		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-4H-3-thia-2,7,9a,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
169		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)-8-(tetrahydro-2H-pyran-4-yl)imidazo[1,5-c]pyrimidin-5-amine
160		8-(3,6-dihydro-2H-thiopyran-4-yl)-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-5-amine

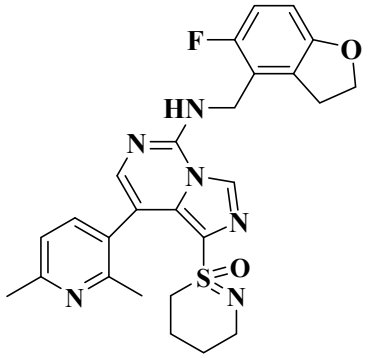
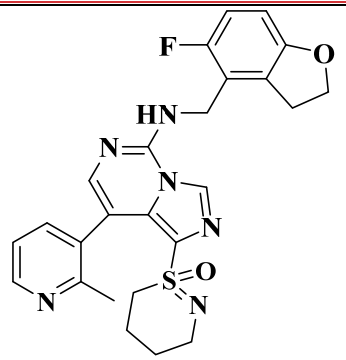
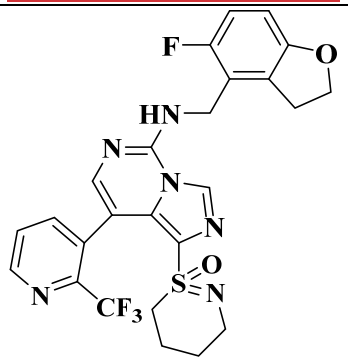
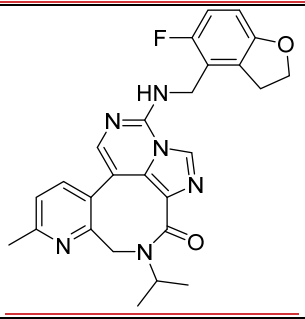
161		4-(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-1-(methylsulfonyl)imidazo[1,5-c]pyrimidin-8-yl)tetrahydro-2H-thiopyran 1,1-dioxide
162		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
163		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
164		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
165		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
166		12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

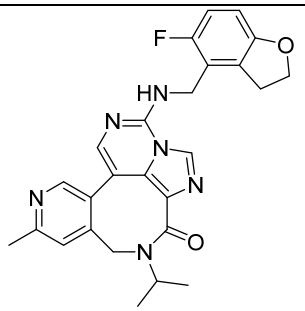
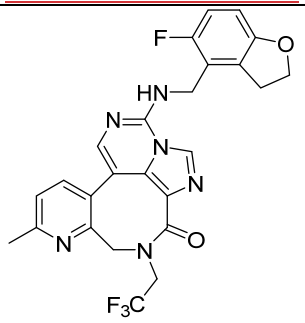
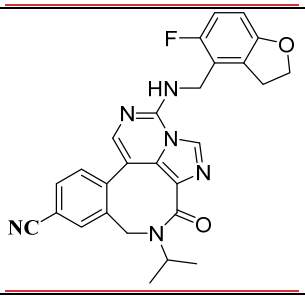
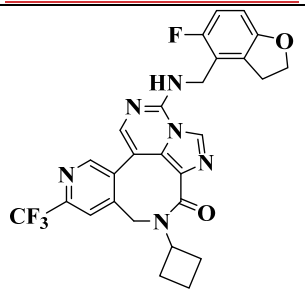
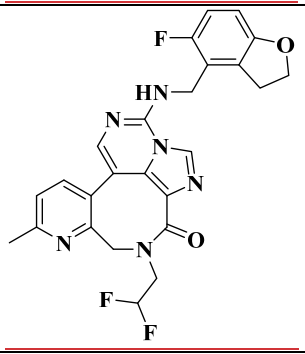
167		12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
168		12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
169		12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
170		4-ethyl-12-(((6-fluorochroman-5-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
171		4-ethyl-12-(((6-fluorochroman-5-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

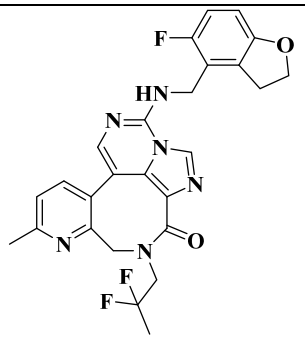
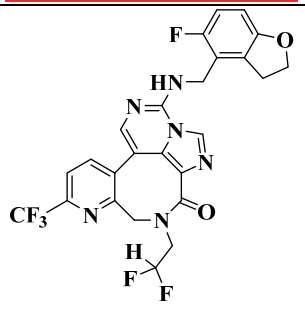
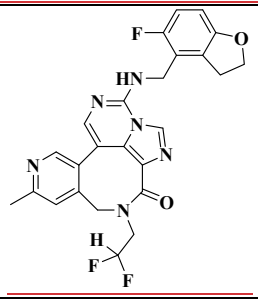
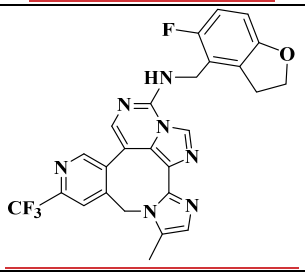
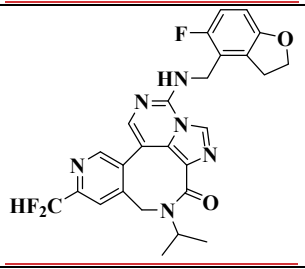
172		4-ethyl-12-(((6-fluorochroman-5-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
173		4-ethyl-12-(((6-fluorochroman-5-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
174		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
175		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
176		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

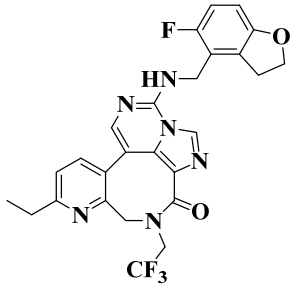
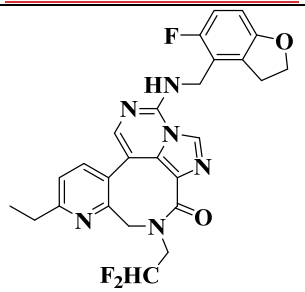
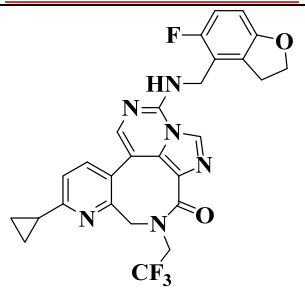
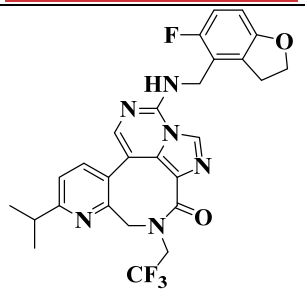
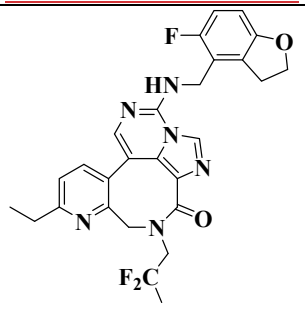
177		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
178		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-phenylimidazo[1,5-c]pyrimidin-1-yl)(imino)(methyl)-l6-sulfanone
179		(8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)(imino)(methyl)- sulfanone
180		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-methylpyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)(imino)(methyl)-sulfanone
181		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)(imino)(methyl)-l6-sulfanone

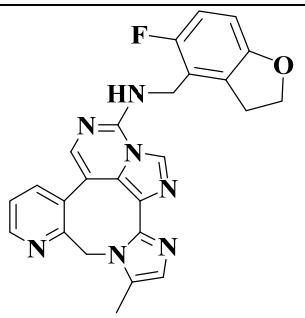
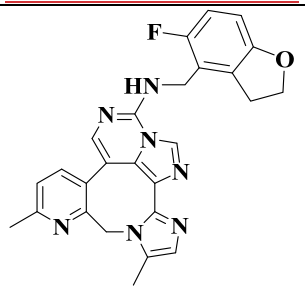
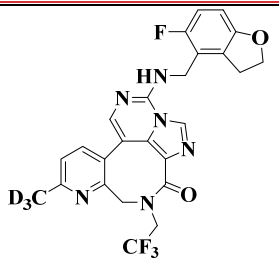
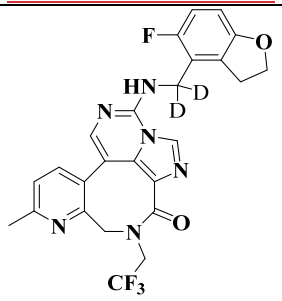
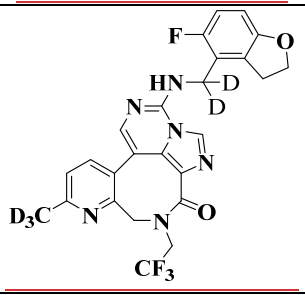
182		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-phenylimidazo[1,5-c]pyrimidin-1-yl)(methyl)(methylimino)-l6-sulfanone
183		(8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)(methyl)(methylimino)-l6-sulfanone
184		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-methylpyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)(methyl)(methylimino)-l6-sulfanone
185		(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)(methyl)(methylimino)-l6-sulfanone
186		1-(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-phenylimidazo[1,5-c]pyrimidin-1-yl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide

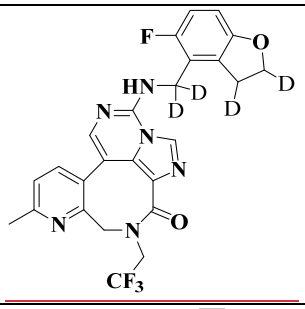
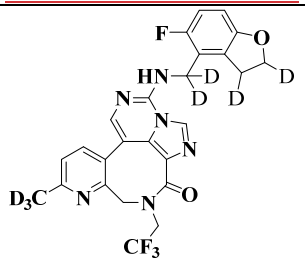
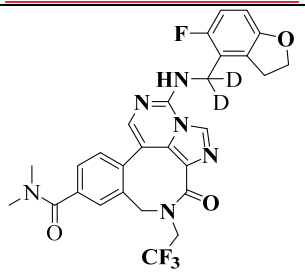
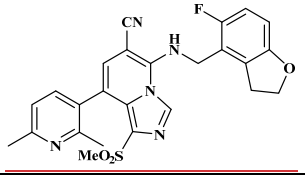
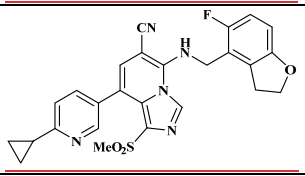
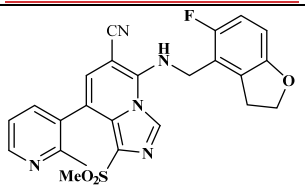
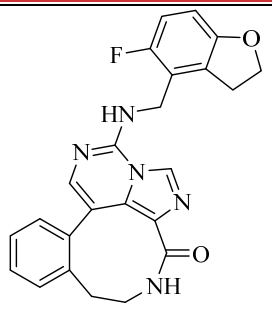
187		1-(8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)imidazo[1,5-c]pyrimidin-1-yl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide
188		1-(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-methylpyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide
189		1-(5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-(trifluoromethyl)pyridin-3-yl)imidazo[1,5-c]pyrimidin-1-yl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide
E 1		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

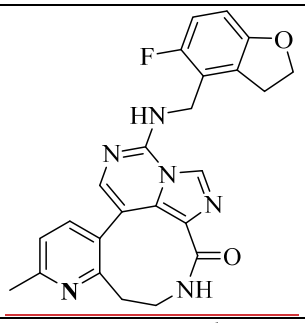
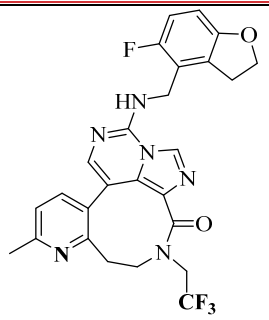
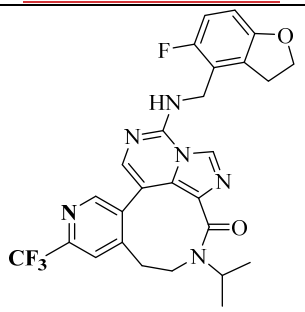
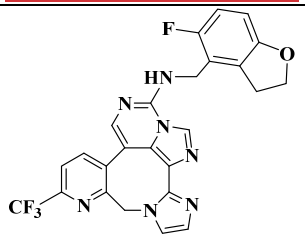
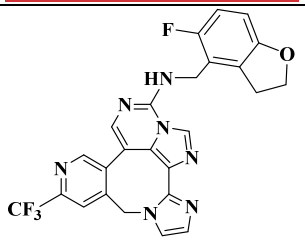
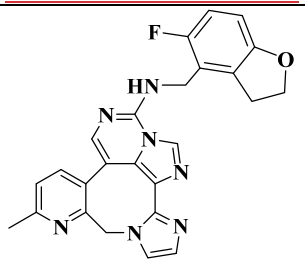
E 2		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 3		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 4		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-3-oxo-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]indene-7-carbonitrile
E 5		4-cyclobutyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 6		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

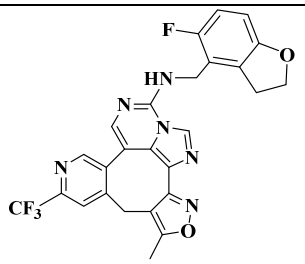
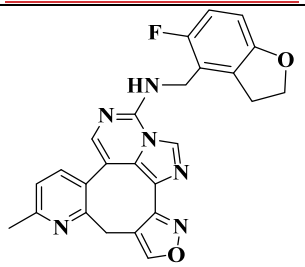
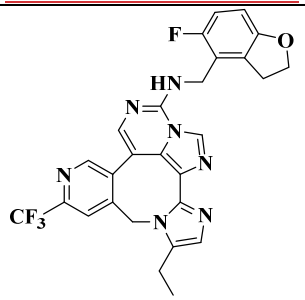
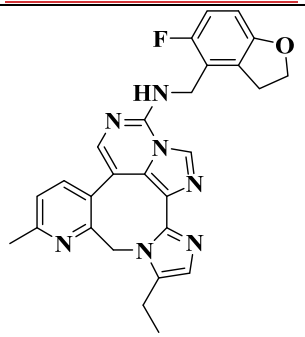
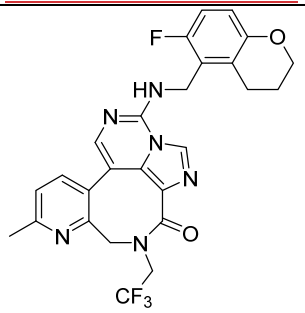
E 7		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 8		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 9		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 10		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-5-methyl-8-(trifluoromethyl)-6H-2,3,5a,9,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 11		7-(difluoromethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-4,5-dihydro-3H-2,4,8,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

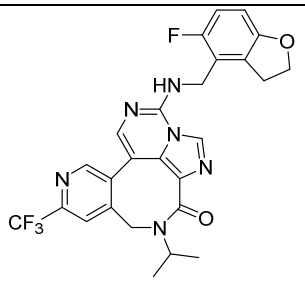
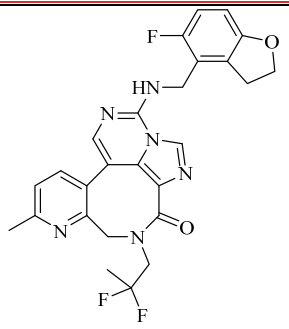
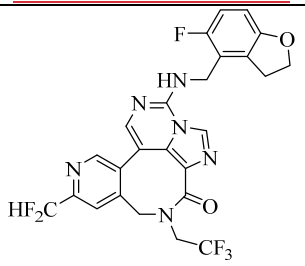
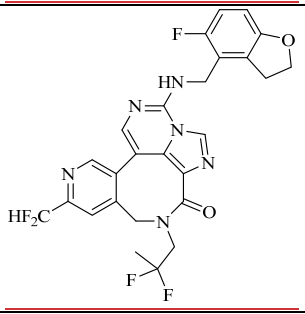
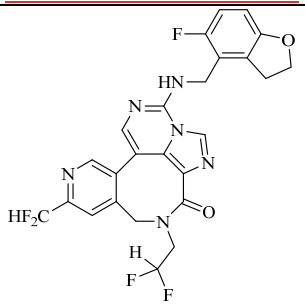
E 12		7-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 13		4-(2,2-difluoroethyl)-7-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 14		7-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 15		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-isopropyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 16		4-(2,2-difluoropropyl)-7-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

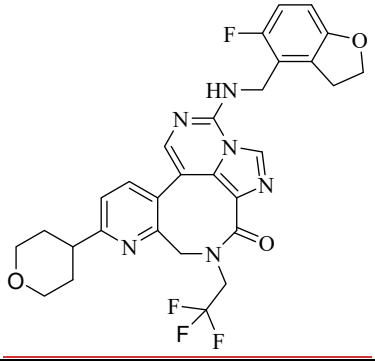
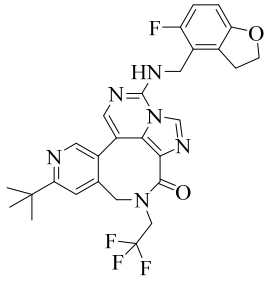
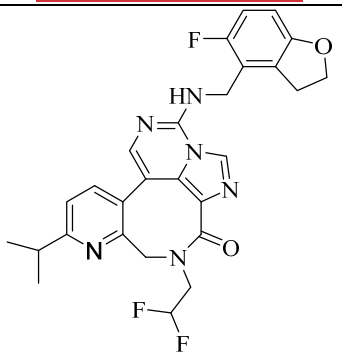
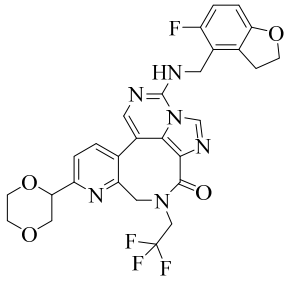
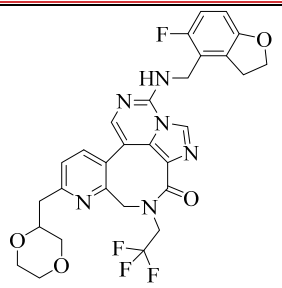
E 17		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-5-methyl-6H-2,3,5a,7,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 18		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-5,8-dimethyl-6H-2,3,5a,7,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 19		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methyl-d3)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 20		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl-d2)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 21		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl-d2)amino)-7-(methyl-d3)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

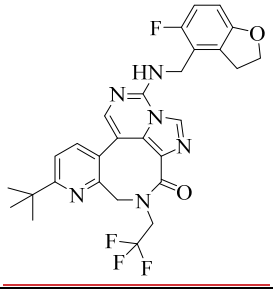
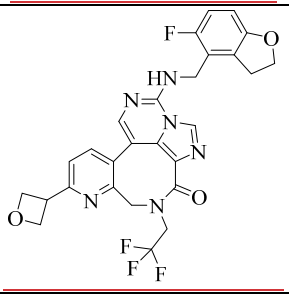
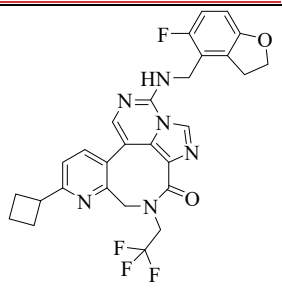
E 22		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl-2,3-d2)methyl-d2)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 23		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl-2,3-d2)methyl-d2)amino)-7-(methyl-d3)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 24		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl-d2)amino)-N,N-dimethyl-3-oxo-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]indene-7-carboxamide
E 25		8-(2,6-dimethylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-1-(methylsulfonyl)imidazo[1,5-a]pyridine-6-carbonitrile
E 26		8-(6-cyclopropylpyridin-3-yl)-5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-1-(methylsulfonyl)imidazo[1,5-a]pyridine-6-carbonitrile
E 27		5-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(2-methylpyridin-3-yl)-1-(methylsulfonyl)imidazo[1,5-a]pyridine-6-carbonitrile
E 28		13-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-5,6-dihydro-2,4,12,13a-tetraazabenzo[4,5]cyclonona[1,2,3-cd]inden-3(4H)-one

E 29		13-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-methyl-5,6-dihydro-2,4,7,12,13a-pentaazabenzo[4,5]cyclonona[1,2,3-cd]inden-3(4H)-one
E 30		13-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-methyl-4-(2,2,2-trifluoroethyl)-5,6-dihydro-2,4,7,12,13a-pentaazabenzo[4,5]cyclonona[1,2,3-cd]inden-3(4H)-one
E 31		13-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-8-(trifluoromethyl)-5,6-dihydro-2,4,9,12,13a-pentaazabenzo[4,5]cyclonona[1,2,3-cd]inden-3(4H)-one
E 32		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(trifluoromethyl)-6H-2,3,5a,7,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 33		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(trifluoromethyl)-6H-2,3,5a,9,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 34		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-methyl-6H-2,3,5a,7,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine

E 35		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-5-methyl-8-(trifluoromethyl)-6H-4-oxa-2,3,9,12,13a-pentaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 36		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-methyl-6H-4-oxa-2,3,7,12,13a-pentaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 37		5-ethyl-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-(trifluoromethyl)-6H-2,3,5a,9,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 38		5-ethyl-N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-8-methyl-6H-2,3,5a,7,12,13a-hexaazabenzo[4,5]cyclopenta[7,8]cycloocta[1,2,3-cd]inden-13-amine
E 39		12-(((6-fluorochroman-5-yl)methyl)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

E 40		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 41		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 42		7-(difluoromethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 43		7-(difluoromethyl)-4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 44		4-(2,2-difluoroethyl)-7-(difluoromethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

E 45		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(tetrahydro-2H-pyran-4-yl)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 46		7-(tert-butyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 47		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-isopropyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 48		7-(1,4-dioxan-2-yl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 49		7-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

E 50		7-(tert-butyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 51		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(oxetan-3-yl)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 52		7-cyclobutyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

~~39~~18. The compound of claim ~~38~~ 17 selected from group consisting of:

4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one;

12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one;

4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one;

12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one; and

11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide,

or a pharmaceutically acceptable salt or solvate thereof.

~~40~~19. A pharmaceutical composition comprising the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

~~41~~20. Use of the compound of any one of claims 1-18, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for ~~A method of~~ treating cancer in a subject in need thereof~~, the method comprising administering to the subject a therapeutically effective amount of the compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof~~.

~~42~~21. The ~~method~~ use of claim ~~41~~20, wherein the cancer is any one or more of the following cancers~~ of Table 3.~~:

adrenal cancer	acinic cell carcinoma	acoustic neuroma	acral lentigious melanoma
acrospiroma	acute eosinophilic leukemia	acute erythroid leukemia	acute lymphoblastic leukemia
acute megakaryoblastic leukemia	acute monocytic leukemia	acute promyelocytic leukemia	adenocarcinoma
adenoid cystic carcinoma	adenoma	adenomatoid odontogenic tumor	adenosquamous carcinoma
adipose tissue neoplasm	adrenocortical carcinoma	adult T-cell leukemia/lymphoma	aggressive NK-cell leukemia
AIDS-related lymphoma	alveolar rhabdomyosarcoma	alveolar soft part sarcoma	ameloblastic fibroma
anaplastic large cell lymphoma	anaplastic thyroid cancer	angioimmunoblastic T-cell lymphoma	angiomyolipoma
angiosarcoma	astrocytoma	atypical teratoid rhabdoid tumor	B-cell chronic lymphocytic

			leukemia
B-cell prolymphocytic leukemia	B-cell lymphoma	basal cell carcinoma	biliary tract cancer
bladder cancer	blastoma	bone cancer	Brenner tumor
Brown tumor	Burkitt's lymphoma	breast cancer	brain cancer
carcinoma	carcinoma in situ	carcinosarcoma	cartilage tumor
cementoma	myeloid sarcoma	chondroma	chordoma
choriocarcinoma	choroid plexus papilloma	clear-cell sarcoma of the kidney	craniopharyngioma
cutaneous T-cell lymphoma	cervical cancer	colorectal cancer	Degos disease
desmoplastic small round cell tumor	diffuse large B-cell lymphoma	dysembryoplastic neuroepithelial tumor	dysgerminoma
embryonal carcinoma	endocrine gland neoplasm	endodermal sinus tumor	enteropathy-associated T-cell lymphoma
esophageal cancer	fetus in fetu	fibroma	fibrosarcoma
follicular lymphoma	follicular thyroid cancer	ganglioneuroma	gastrointestinal cancer
germ cell tumor	gestational choriocarcinoma	giant cell fibroblastoma	giant cell tumor of the bone
glial tumor	glioblastoma multiforme	glioma	gliomatosis cerebri
glucagonoma	gonadoblastoma	granulosa cell tumor	gynandroblastoma
gallbladder cancer	gastric cancer	hairy cell leukemia	hemangioblastoma
head and neck cancer	hemangiopericytoma	hematological cancer	hepatoblastoma
hepatosplenic T-cell lymphoma	Hodgkin's lymphoma	non-Hodgkin's lymphoma	invasive lobular carcinoma
intestinal cancer	kidney cancer	laryngeal cancer	lentigo maligna
lethal midline carcinoma	leukemia	leydig cell tumor	liposarcoma
lung cancer	lymphangioma	lymphangiosarcoma	lymphoepithelioma
lymphoma	acute lymphocytic leukemia	acute myelogeous leukemia	chronic lymphocytic leukemia
liver cancer	small cell lung cancer	non-small cell lung cancer	MALT lymphoma
malignant fibrous histiocytoma	malignant peripheral nerve sheath tumor	malignant triton tumor	mantle cell lymphoma
marginal zone B-cell lymphoma	mast cell leukemia	mediastinal germ cell tumor	medullary carcinoma of the breast
medullary thyroid cancer	medulloblastoma	melanoma	meningioma
merkel cell cancer	mesothelioma	metastatic urothelial carcinoma	mixed Mullerian tumor

mucinous tumor	multiple myeloma	muscle tissue neoplasm	mycosis fungoides
myxoid liposarcoma	myxoma	myxosarcoma	nasopharyngeal carcinoma
neurinoma	neuroblastoma	neurofibroma	neuroma
nodular melanoma	ocular cancer	oligoastrocytoma	oligodendroglioma
oncocytoma	optic nerve sheath meningioma	optic nerve tumor	oral cancer
osteosarcoma	ovarian cancer	Pancoast tumor	papillary thyroid cancer
paraganglioma	pinealoblastoma	pineocytoma	pituicytoma
pituitary adenoma	pituitary tumor	plasmacytoma	polyembryoma
precursor T-lymphoblastic lymphoma	primary central nervous system lymphoma	primary effusion lymphoma	preimary peritoneal cancer
prostate cancer	pancreatic cancer	pharyngeal cancer	pseudomyxoma periotonei
renal cell carcinoma	renal medullary carcinoma	retinoblastoma	rhabdomyoma
rhabdomyosarcoma	Richter's transformation	rectal cancer	sarcoma
Schwannomatosis	seminoma	Sertoli cell tumor	sex cord-gonadal stromal tumor
signet ring cell carcinoma	skin cancer	small blue round cell tumors	small cell carcinoma
soft tissue sarcoma	somatostatinoma	soot wart	spinal tumor
splenic marginal zone lymphoma	squamous cell carcinoma	synovial sarcoma	Sezary's disease
small intestine cancer	squamous carcinoma	stomach cancer	T-cell lymphoma
testicular cancer	thecoma	thyroid cancer	transitional cell carcinoma
throat cancer	urachal cancer	urogenital cancer	urothelial carcinoma
uveal melanoma	uterine cancer	verrucous carcinoma	visual pathway glioma
vulvar cancer	vaginal cancer	Waldenstrom's macroglobulinemia	Warthin's tumor
Wilms' tumor			

~~43~~22. The ~~method~~ use of claims 20 or 21~~41 or 42~~, wherein ~~further comprising administering~~ a therapeutically effective amount of an optional therapeutic agent useful in the treatment of cancer is to be administered to the subject.

~~44~~23. The pharmaceutical composition of claim ~~40~~ 19 for use in treating cancer.

~~45~~24. The pharmaceutical composition for use of claim 23~~44~~, wherein the cancer is any one or more of the following cancers ~~of Table 3.~~:

adrenal cancer	acinic cell carcinoma	acoustic neuroma	acral lentigious melanoma
acrospiroma	acute eosinophilic leukemia	acute erythroid leukemia	acute lymphoblastic leukemia
acute megakaryoblastic leukemia	acute monocytic leukemia	acute promyelocytic leukemia	adenocarcinoma
adenoid cystic carcinoma	adenoma	adenomatoid odontogenic tumor	adenosquamous carcinoma
adipose tissue neoplasm	adrenocortical carcinoma	adult T-cell leukemia/lymphoma	aggressive NK-cell leukemia
AIDS-related lymphoma	alveolar rhabdomyosarcoma	alveolar soft part sarcoma	ameloblastic fibroma
anaplastic large cell lymphoma	anaplastic thyroid cancer	angioimmunoblastic T-cell lymphoma	angiomyolipoma
angiosarcoma	astrocytoma	atypical teratoid rhabdoid tumor	B-cell chronic lymphocytic leukemia
B-cell prolymphocytic leukemia	B-cell lymphoma	basal cell carcinoma	biliary tract cancer
bladder cancer	blastoma	bone cancer	Brenner tumor
Brown tumor	Burkitt's lymphoma	breast cancer	brain cancer
carcinoma	carcinoma in situ	carcinosarcoma	cartilage tumor
cementoma	myeloid sarcoma	chondroma	chordoma
choriocarcinoma	choroid plexus papilloma	clear-cell sarcoma of the kidney	craniopharyngioma
cutaneous T-cell lymphoma	cervical cancer	colorectal cancer	Degos disease
desmoplastic small round cell tumor	diffuse large B-cell lymphoma	dysembryoplastic neuroepithelial tumor	dysgerminoma
embryonal carcinoma	endocrine gland neoplasm	endodermal sinus tumor	enteropathy-associated T-cell lymphoma
esophageal cancer	fetus in fetu	fibroma	fibrosarcoma
follicular lymphoma	follicular thyroid cancer	ganglioneuroma	gastrointestinal cancer
germ cell tumor	gestational	giant cell	giant cell tumor of

	choriocarcinoma	fibroblastoma	the bone
glial tumor	glioblastoma multiforme	glioma	gliomatosis cerebri
glucagonoma	gonadoblastoma	granulosa cell tumor	gynandroblastoma
gallbladder cancer	gastric cancer	hairy cell leukemia	hemangioblastoma
head and neck cancer	hemangiopericytoma	hematological cancer	hepatoblastoma
hepatosplenic T-cell lymphoma	Hodgkin's lymphoma	non-Hodgkin's lymphoma	invasive lobular carcinoma
intestinal cancer	kidney cancer	laryngeal cancer	lentigo maligna
lethal midline carcinoma	leukemia	leydig cell tumor	liposarcoma
lung cancer	lymphangioma	lymphangiosarcoma	lymphoepithelioma
lymphoma	acute lymphocytic leukemia	acute myelogeous leukemia	chronic lymphocytic leukemia
liver cancer	small cell lung cancer	non-small cell lung cancer	MALT lymphoma
malignant fibrous histiocytoma	malignant peripheral nerve sheath tumor	malignant triton tumor	mantle cell lymphoma
marginal zone B-cell lymphoma	mast cell leukemia	mediastinal germ cell tumor	medullary carcinoma of the breast
medullary thyroid cancer	medulloblastoma	melanoma	meningioma
merkel cell cancer	mesothelioma	metastatic urothelial carcinoma	mixed Mullerian tumor
mucinous tumor	multiple myeloma	muscle tissue neoplasm	mycosis fungoides
myxoid liposarcoma	myxoma	myxosarcoma	nasopharyngeal carcinoma
neurinoma	neuroblastoma	neurofibroma	neuroma
nodular melanoma	ocular cancer	oligoastrocytoma	oligodendroglioma
oncocytoma	optic nerve sheath meningioma	optic nerve tumor	oral cancer
osteosarcoma	ovarian cancer	Pancoast tumor	papillary thyroid cancer
paraganglioma	pinealoblastoma	pineocytoma	pituicytoma
pituitary adenoma	pituitary tumor	plasmacytoma	polyembryoma
precursor T-lymphoblastic lymphoma	primary central nervous system lymphoma	primary effusion lymphoma	preimary peritoneal cancer
prostate cancer	pancreatic cancer	pharyngeal cancer	pseudomyxoma periotonei
renal cell carcinoma	renal medullary carcinoma	retinoblastoma	rhabdomyoma
rhabdomyosarcoma	Richter's transformation	rectal cancer	sarcoma

Schwannomatosis	seminoma	Sertoli cell tumor	sex cord-gonadal stromal tumor
signet ring cell carcinoma	skin cancer	small blue round cell tumors	small cell carcinoma
soft tissue sarcoma	somatostatinoma	soot wart	spinal tumor
splenic marginal zone lymphoma	squamous cell carcinoma	synovial sarcoma	Sezary's disease
small intestine cancer	squamous carcinoma	stomach cancer	T-cell lymphoma
testicular cancer	thecoma	thyroid cancer	transitional cell carcinoma
throat cancer	urachal cancer	urogenital cancer	urothelial carcinoma
uveal melanoma	uterine cancer	verrucous carcinoma	visual pathway glioma
vulvar cancer	vaginal cancer	Waldenstrom's macroglobulinemia	Warthin's tumor
Wilms' tumor			

~~46~~25. A compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt or solvate thereof, for use in treating of cancer.

~~47~~26. The compound for use of claim ~~46~~25, wherein the cancer is any one or more of the following gcancers ~~of Table 3.~~:

adrenal cancer	acinic cell carcinoma	acoustic neuroma	acral lentigious melanoma
acrospiroma	acute eosinophilic leukemia	acute erythroid leukemia	acute lymphoblastic leukemia
acute megakaryoblastic leukemia	acute monocytic leukemia	acute promyelocytic leukemia	adenocarcinoma
adenoid cystic carcinoma	adenoma	adenomatoid odontogenic tumor	adenosquamous carcinoma
adipose tissue neoplasm	adrenocortical carcinoma	adult T-cell leukemia/lymphoma	aggressive NK-cell leukemia
AIDS-related lymphoma	alveolar rhabdomyosarcoma	alveolar soft part sarcoma	ameloblastic fibroma
anaplastic large cell lymphoma	anaplastic thyroid cancer	angioimmunoblastic T-cell lymphoma	angiomyolipoma
angiosarcoma	astrocytoma	atypical teratoid rhabdoid tumor	B-cell chronic lymphocytic leukemia

B-cell prolymphocytic leukemia	B-cell lymphoma	basal cell carcinoma	biliary tract cancer
bladder cancer	blastoma	bone cancer	Brenner tumor
Brown tumor	Burkitt's lymphoma	breast cancer	brain cancer
carcinoma	carcinoma in situ	carcinosarcoma	cartilage tumor
cementoma	myeloid sarcoma	chondroma	chordoma
choriocarcinoma	choroid plexus papilloma	clear-cell sarcoma of the kidney	craniopharyngioma
cutaneous T-cell lymphoma	cervical cancer	colorectal cancer	Degos disease
desmoplastic small round cell tumor	diffuse large B-cell lymphoma	dysembryoplastic neuroepithelial tumor	dysgerminoma
embryonal carcinoma	endocrine gland neoplasm	endodermal sinus tumor	enteropathy-associated T-cell lymphoma
esophageal cancer	fetus in fetu	fibroma	fibrosarcoma
follicular lymphoma	follicular thyroid cancer	ganglioneuroma	gastrointestinal cancer
germ cell tumor	gestational choriocarcinoma	giant cell fibroblastoma	giant cell tumor of the bone
glial tumor	glioblastoma multiforme	glioma	gliomatosis cerebri
glucagonoma	gonadoblastoma	granulosa cell tumor	gynandroblastoma
gallbladder cancer	gastric cancer	hairy cell leukemia	hemangioblastoma
head and neck cancer	hemangiopericytoma	hematological cancer	hepatoblastoma
hepatosplenic T-cell lymphoma	Hodgkin's lymphoma	non-Hodgkin's lymphoma	invasive lobular carcinoma
intestinal cancer	kidney cancer	laryngeal cancer	lentigo maligna
lethal midline carcinoma	leukemia	leydig cell tumor	liposarcoma
lung cancer	lymphangioma	lymphangiosarcoma	lymphoepithelioma
lymphoma	acute lymphocytic leukemia	acute myelogeous leukemia	chronic lymphocytic leukemia
liver cancer	small cell lung cancer	non-small cell lung cancer	MALT lymphoma
malignant fibrous histiocytoma	malignant peripheral nerve sheath tumor	malignant triton tumor	mantle cell lymphoma
marginal zone B-cell lymphoma	mast cell leukemia	mediastinal germ cell tumor	medullary carcinoma of the breast
medullary thyroid cancer	medulloblastoma	melanoma	meningioma
merkel cell cancer	mesothelioma	metastatic urothelial carcinoma	mixed Mullerian tumor
mucinous tumor	multiple myeloma	muscle tissue	mycosis fungoides

		neoplasm	
myxoid liposarcoma	myxoma	myxosarcoma	nasopharyngeal carcinoma
neurinoma	neuroblastoma	neurofibroma	neuroma
nodular melanoma	ocular cancer	oligoastrocytoma	oligodendroglioma
oncocytoma	optic nerve sheath meningioma	optic nerve tumor	oral cancer
osteosarcoma	ovarian cancer	Pancoast tumor	papillary thyroid cancer
paraganglioma	pinealoblastoma	pineocytoma	pituicytoma
pituitary adenoma	pituitary tumor	plasmacytoma	polyembryoma
precursor T-lymphoblastic lymphoma	primary central nervous system lymphoma	primary effusion lymphoma	preimary peritoneal cancer
prostate cancer	pancreatic cancer	pharyngeal cancer	pseudomyxoma periotonei
renal cell carcinoma	renal medullary carcinoma	retinoblastoma	rhabdomyoma
rhabdomyosarcoma	Richter's transformation	rectal cancer	sarcoma
Schwannomatosis	seminoma	Sertoli cell tumor	sex cord-gonadal stromal tumor
signet ring cell carcinoma	skin cancer	small blue round cell tumors	small cell carcinoma
soft tissue sarcoma	somatostatinoma	soot wart	spinal tumor
splenic marginal zone lymphoma	squamous cell carcinoma	synovial sarcoma	Sezary's disease
small intestine cancer	squamous carcinoma	stomach cancer	T-cell lymphoma
testicular cancer	thecoma	thyroid cancer	transitional cell carcinoma
throat cancer	urachal cancer	urogenital cancer	urothelial carcinoma
uveal melanoma	uterine cancer	verrucous carcinoma	visual pathway glioma
vulvar cancer	vaginal cancer	Waldenstrom's macroglobulinemia	Warthin's tumor
Wilms' tumor			

~~48. Use of a compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for treatment of cancer.~~

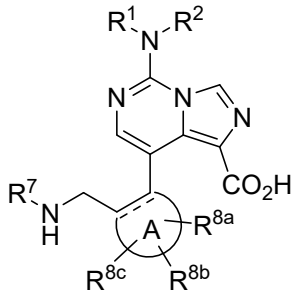
~~49. The use of claim 48, wherein the cancer is any one or more of the cancers of Table 3.~~

~~50~~27. Use of a compound of any one of claims 1-18, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for ~~A method of~~ inhibiting EED protein within a cell of a subject in need thereof~~, the method comprising administering to the subject a compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof~~.

~~51. A kit comprising the compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, and instructions for administering the compound, or a pharmaceutically acceptable salt or solvate thereof, to a subject having cancer.~~

~~52. The kit of claim 51 wherein the cancer is any one or more of the cancers of Table 3.~~

~~53~~28. A compound of Formula **XVII**:



XVII,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

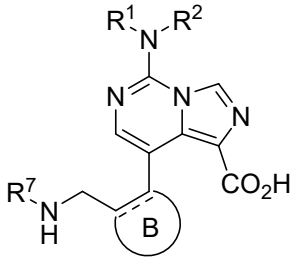
R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and alkylsulfonyl;

A is phenyl, 5-membered heteroaryl, or 6-membered heteroaryl; and

=== is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

~~54~~29. A compound of Formula **XVIII**:



XVIII,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

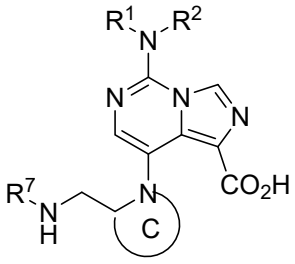
R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

B is optionally substituted 3- to 8-membered cycloalkyl or optionally substituted 4- to 8-membered heterocyclo; and

=== is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

~~55~~30. A compound of Formula **XIX**:



XIX,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, optionally substituted C_3-C_8 cycloalkyl, optionally substituted C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl; and


is optionally substituted 4- to 8-membered heterocyclo,

or a pharmaceutically acceptable salt or solvate thereof.