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.

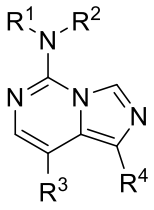
Background

[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

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



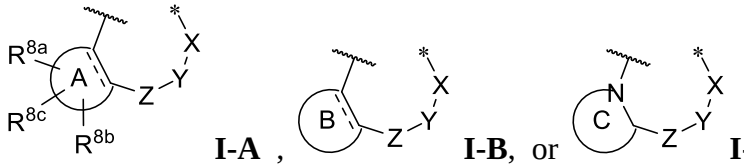
I,

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, C_3-C_8 cycloalkyl, 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, C_3-C_8 cycloalkyl, 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 a fused 3- to 8-membered cycloalkyl or fused 4- to 8-membered heterocyclo;



is a 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**;

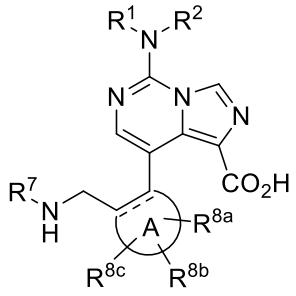
or a pharmaceutically acceptable salt or solvate thereof.

[0003b] In another 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 a proliferative disease.

[0003c] 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 a proliferative disease.

[0003d] 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.

[0003e] 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, C_3-C_8 cycloalkyl, C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

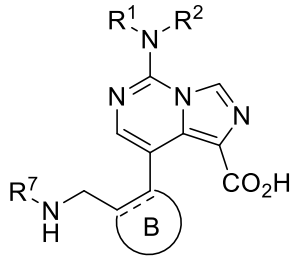
R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and alkylsulfonyl;

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.

[0003f] 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;

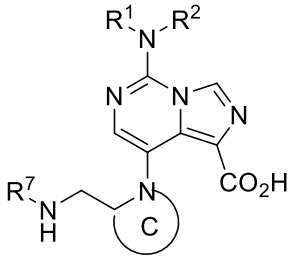
R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

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

--- is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

[0003g] 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;

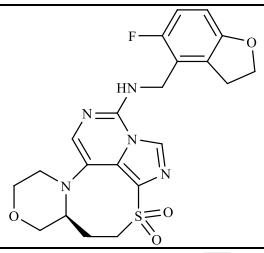
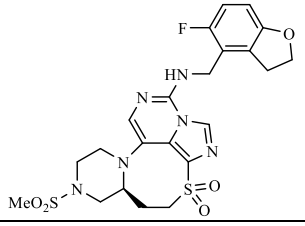
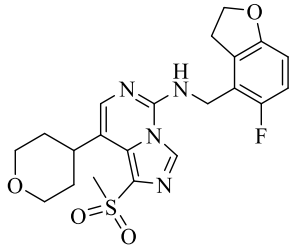
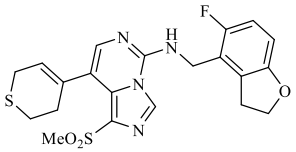
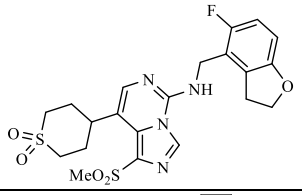
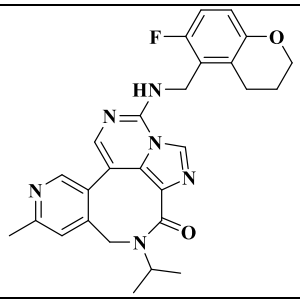
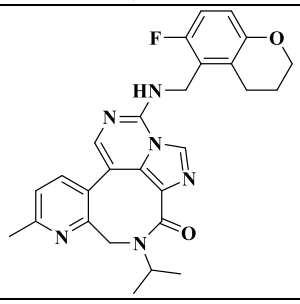
R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl; and



is 4- to 8-membered heterocyclo,

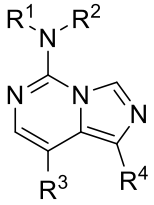
or a pharmaceutically acceptable salt or solvate thereof.

[0004] In one 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

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
159		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

What is claimed is:

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

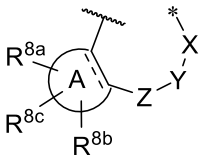
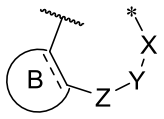
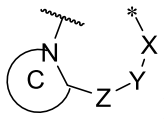
 **I**,

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, C_3-C_8 cycloalkyl, 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, C_3-C_8 cycloalkyl, 4- to 8-membered heterocyclo, (heterocyclo)C_1-C_4 alkyl, and alkylsulfonyl;

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

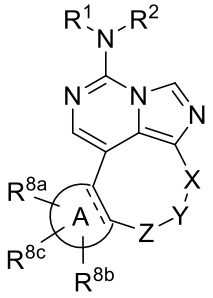
B is a fused 3- to 8-membered cycloalkyl or fused 4- to 8-membered heterocyclo;

C is a 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 a pharmaceutically acceptable salt or solvate thereof.

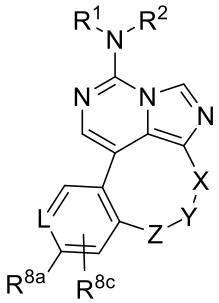
2. The compound of claim 1 of Formula **II**:



II,

or a pharmaceutically acceptable salt or solvate thereof.

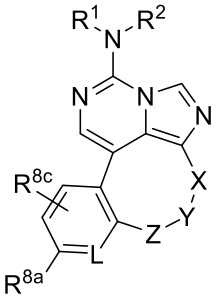
3. The compound of claim 2 of Formula **III**:



III,

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

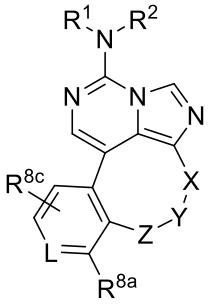
the compound of claim 2 of Formula **IV**:



IV,

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

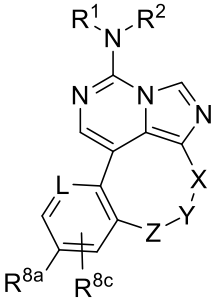
the compound of claim 2 of Formula **V**:



V,

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

the compound of claim 2 of Formula **VI**:



VI,

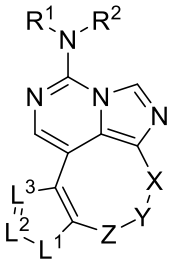
wherein L is selected from the group consisting of -C(R^{8b})= and -N=, or a pharmaceutically acceptable salt or solvate thereof.

4. The compound of claim 3, 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.

5. The compound of claim 2 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=;

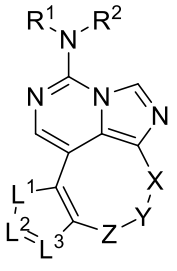
R^{8a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

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

the compound of claim 2 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=;

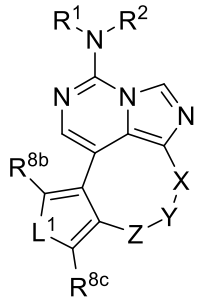
R^{8a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

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.

6. The compound of claim 2 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;

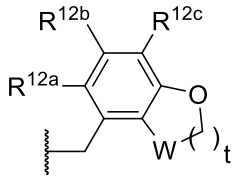
R^{8b} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; and

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.

7. The compound of any one of claims 1-6, wherein:

R^1 is R^1-1:



R^1-1;

R^{12a}, R^{12b}, and R^{12c} are each independently selected from the group consisting of hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, and C_1-C_4 alkoxy;

W is selected from the group consisting of -CH_2- and -C(=O)-; and

t is 1 or 2,

or a pharmaceutically acceptable salt or solvate thereof.

8. The compound of claim 7, wherein W is -C(=O)- and t is 1, or a pharmaceutically acceptable salt or solvate thereof.

9. The compound of any one of claims 7-8, wherein:

R^{12a} is fluoro; and

R^{12b} and R^{12c} are independently selected from the group consisting of hydrogen and fluoro,

or a pharmaceutically acceptable salt or solvate thereof.

10. The compound of claim 9, wherein:

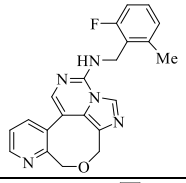
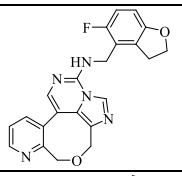
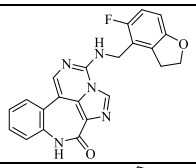
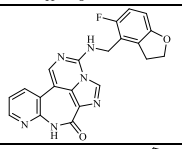
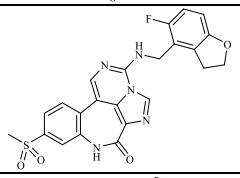
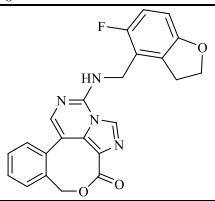
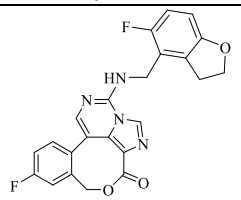
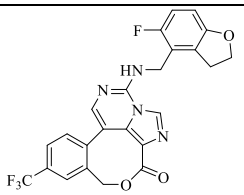
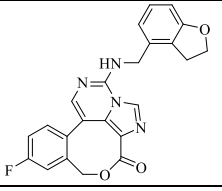
R^{12a} is fluoro; and

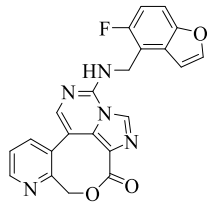
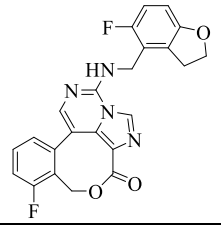
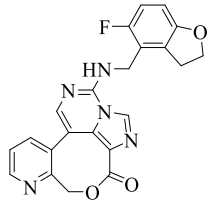
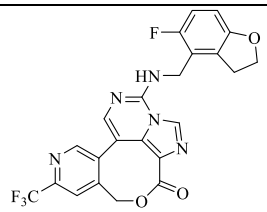
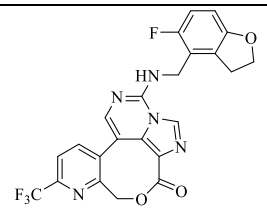
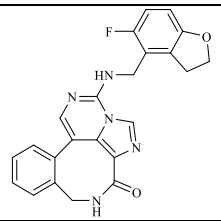
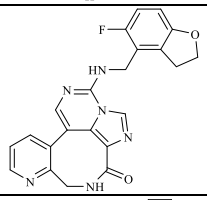
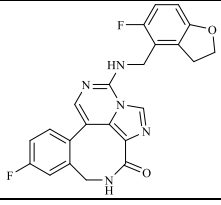
R^{12b} and R^{12c} are hydrogen,

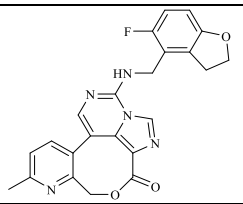
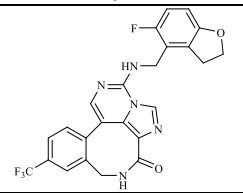
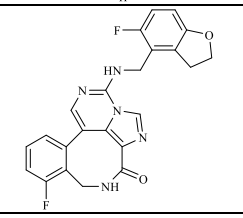
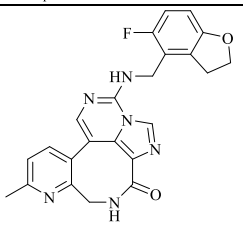
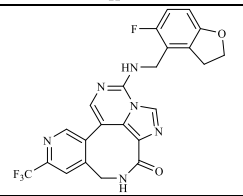
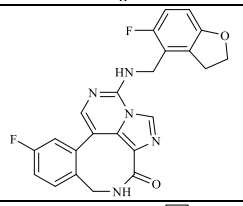
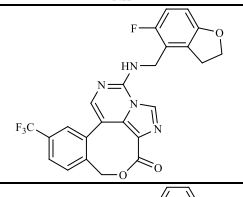
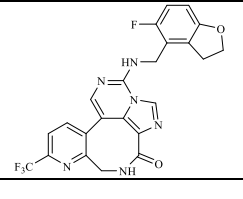
or a pharmaceutically acceptable salt or solvate thereof.

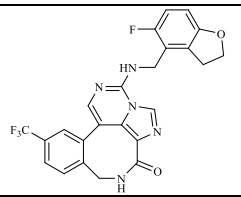
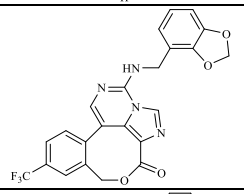
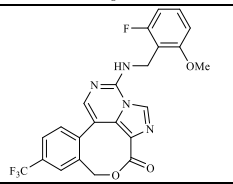
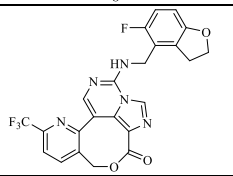
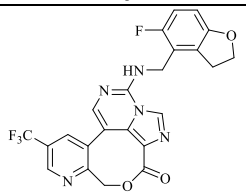
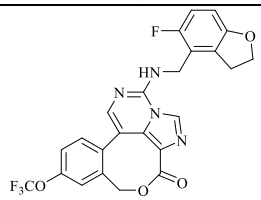
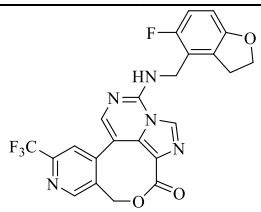
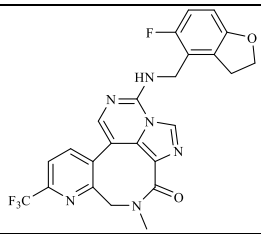
11. The compound of claim 1 selected from any one or more of the following compounds, or a pharmaceutically acceptable salt or solvate thereof:

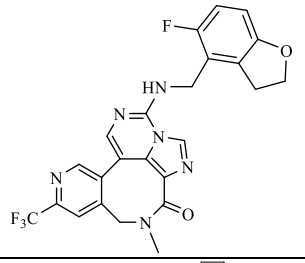
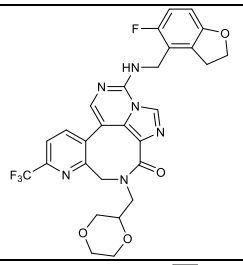
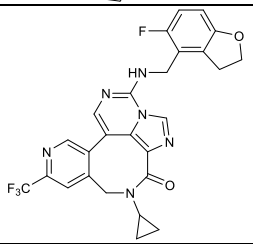
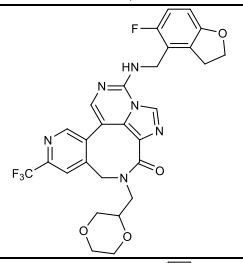
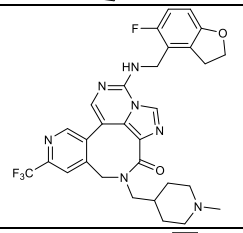
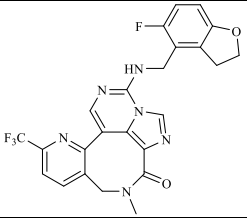
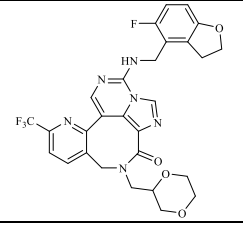
Cpd. No.	**Structure**	**Name**

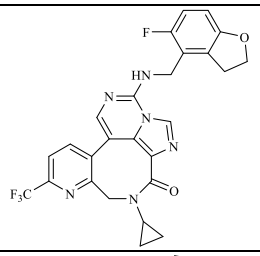
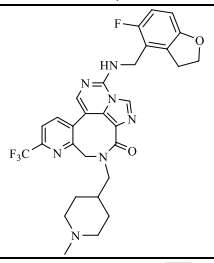
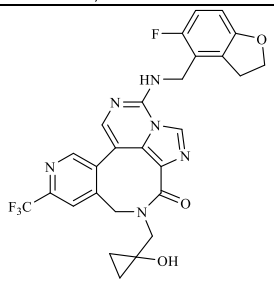
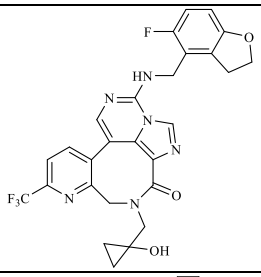
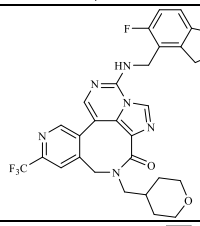
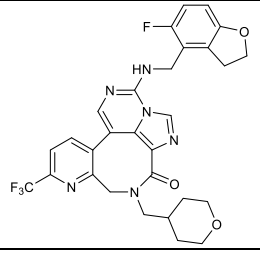
1		N-(2-fluoro-6-methylbenzyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-12-amine
2		N-((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-12-amine
3		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-2,4,10,11a-tetraazadibenzo[cd,f]azulen-3(4H)-one
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

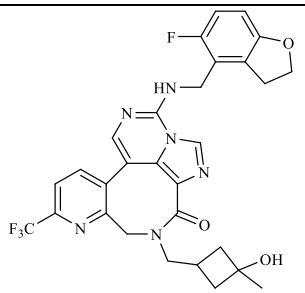
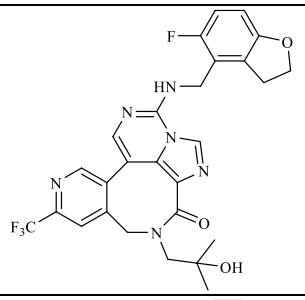
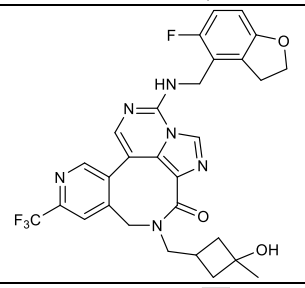
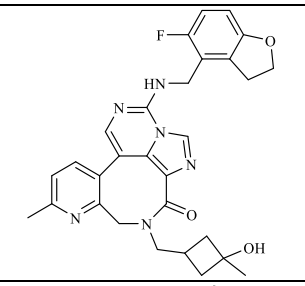
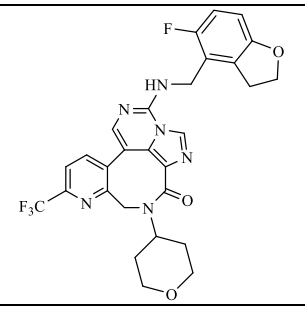
10		12-(((5-fluorobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
11		6-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
12		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[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

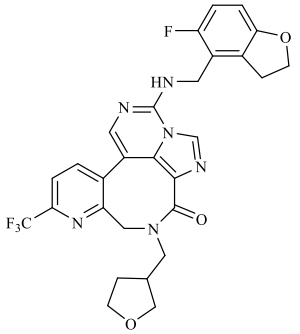
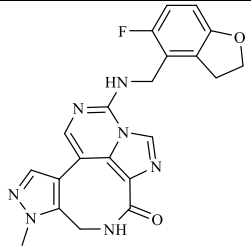
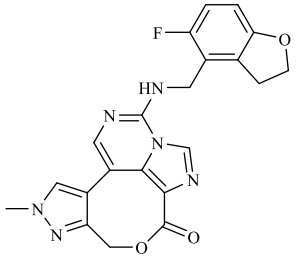
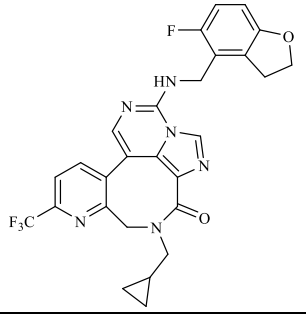
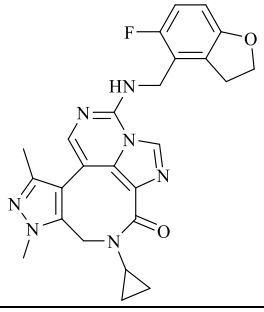
18		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-3H,5H-4-oxa-2,6,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
19		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
20		6-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)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

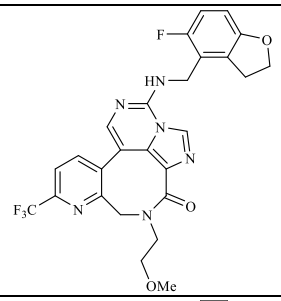
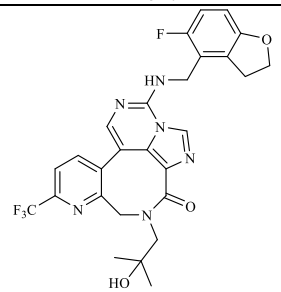
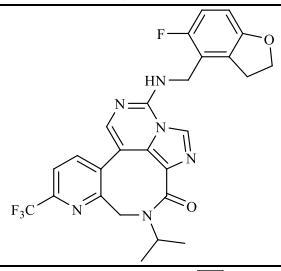
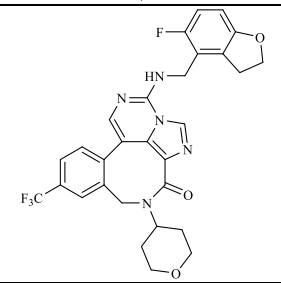
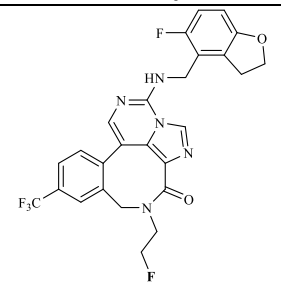
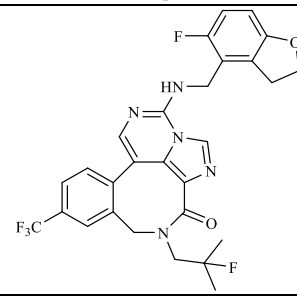
26		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-8-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
27		12-((benzo[d][1,3]dioxol-4-ylmethyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2,11,12a-triazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
28		12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-3H,5H-4-oxa-2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

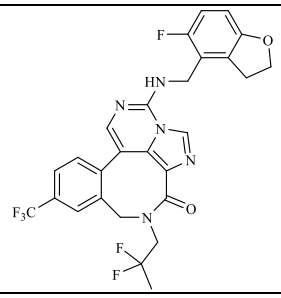
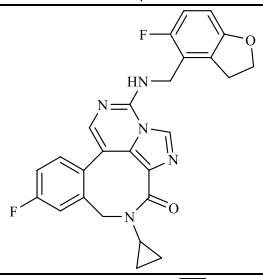
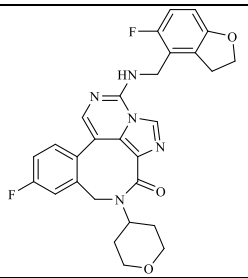
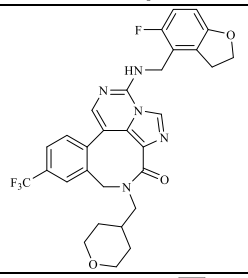
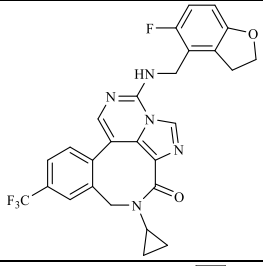
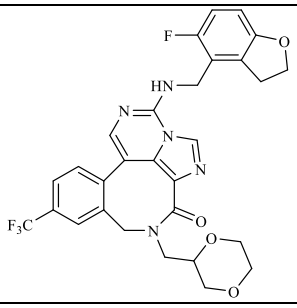
34		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
35		4-((1,4-dioxan-2-yl)methyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

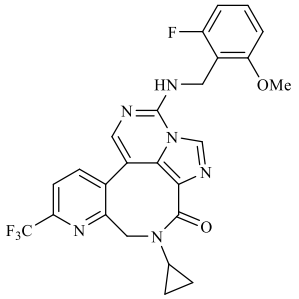
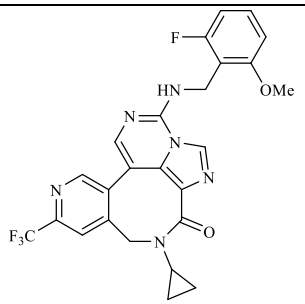
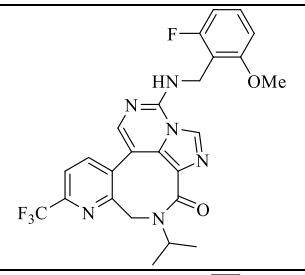
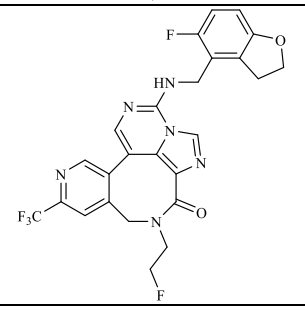
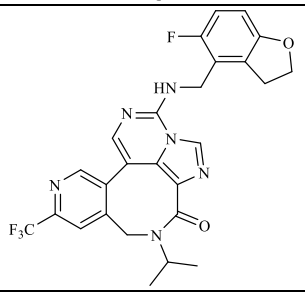
41		4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
42		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((1-methylpiperidin-4-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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

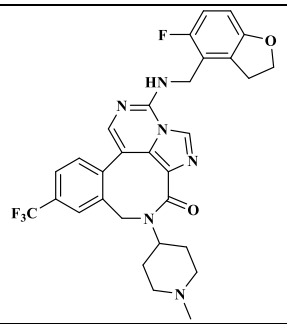
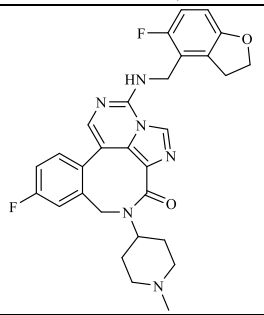
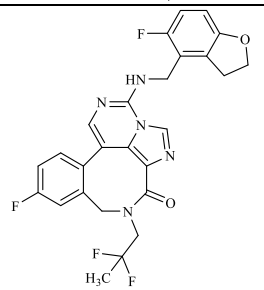
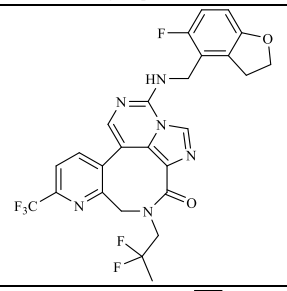
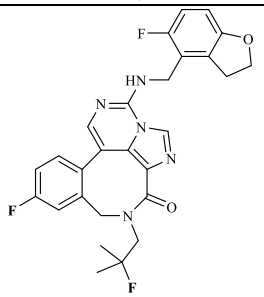
47		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((3-hydroxy-3-methylcyclobutyl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
48		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-hydroxy-2-methylpropyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1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

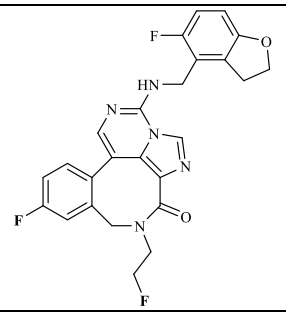
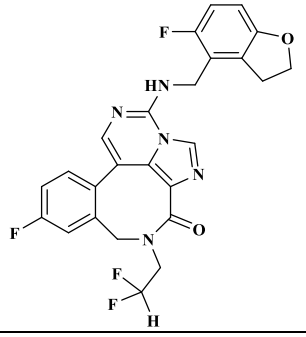
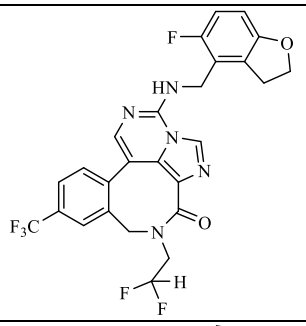
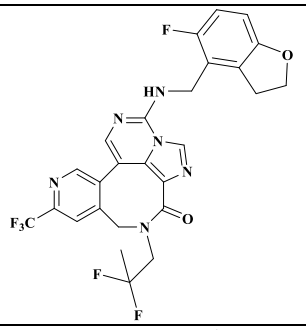
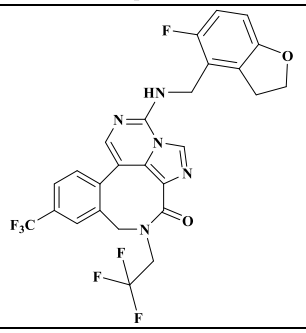
52		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-((tetrahydrofuran-3-yl)methyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
53		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-5,6-dihydro-2,4,6,7,10,11a-hexaazacyclopenta[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
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

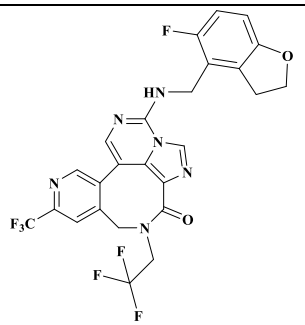
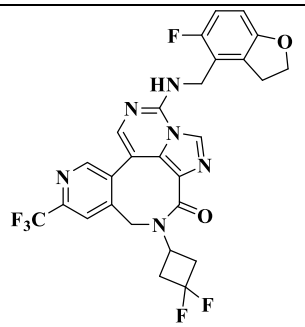
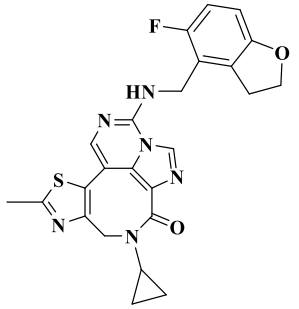
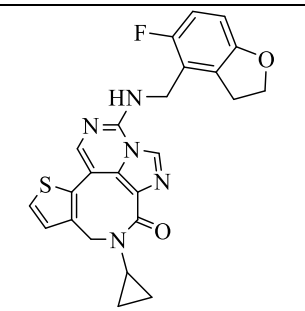
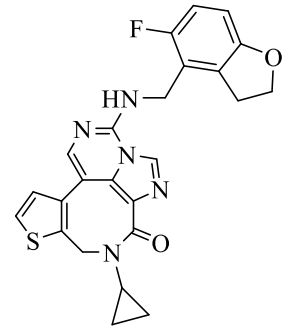
57		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-methoxyethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
58		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-hydroxy-2-methylpropyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

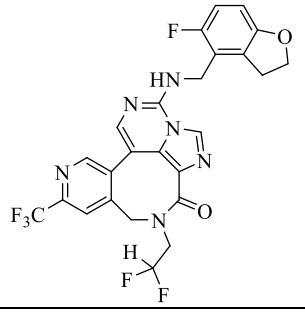
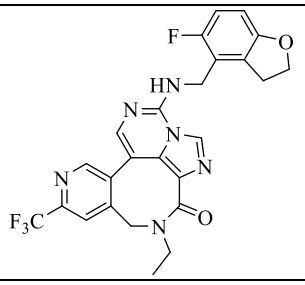
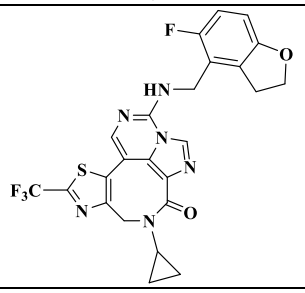
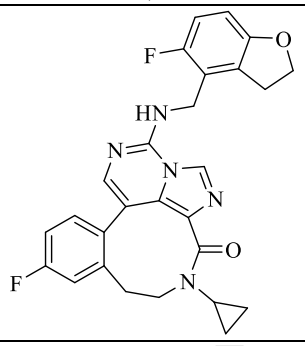
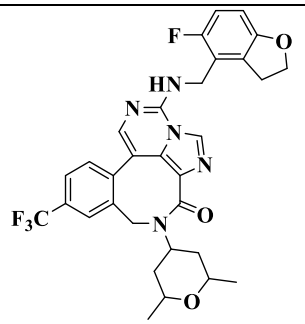
63		4-(2,2-difluoropropyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
64		4-cyclopropyl-7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

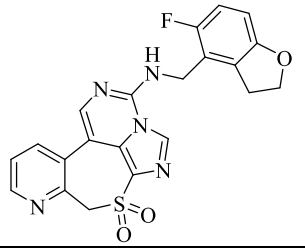
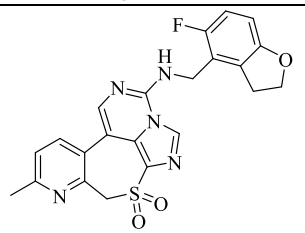
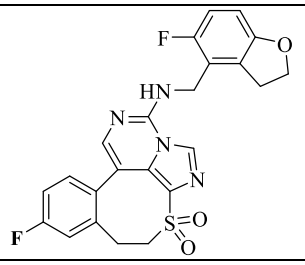
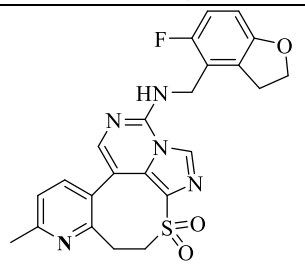
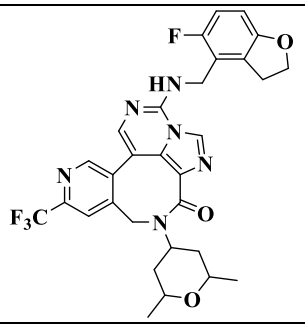
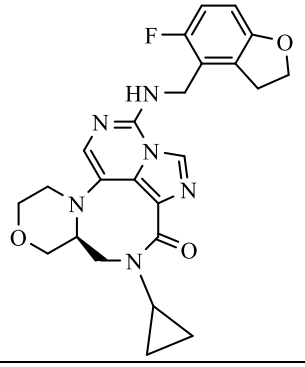
69		4-cyclopropyl-12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
70		4-cyclopropyl-12-((2-fluoro-6-methoxybenzyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

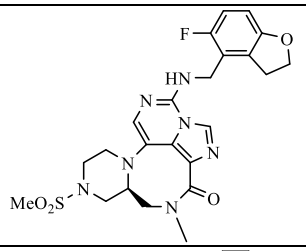
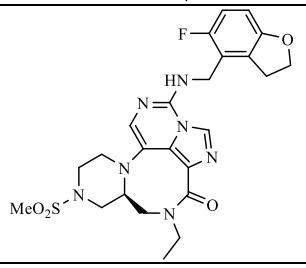
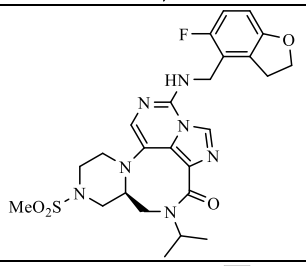
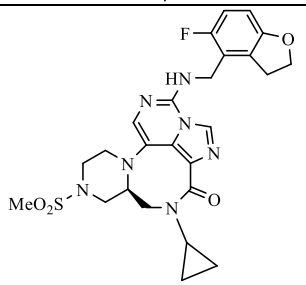
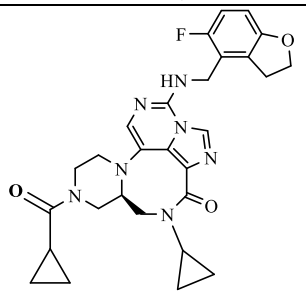
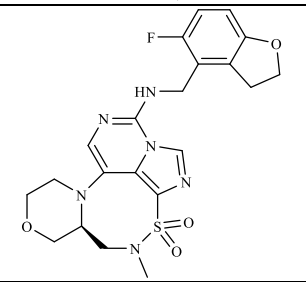
74		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(1-methylpiperidin-4-yl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
75		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(1-methylpiperidin-4-yl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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

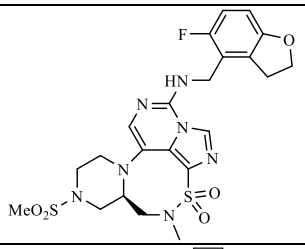
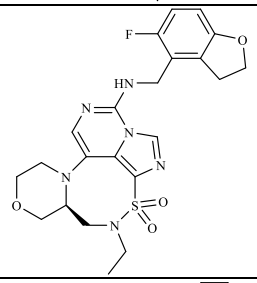
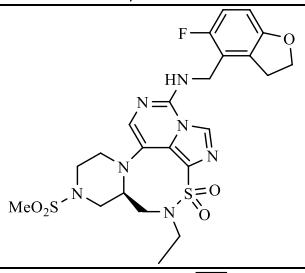
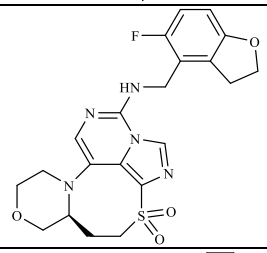
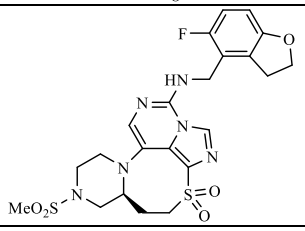
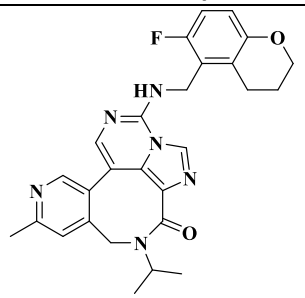
79		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2-fluoroethyl)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
80		4-(2,2-difluoroethyl)-7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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

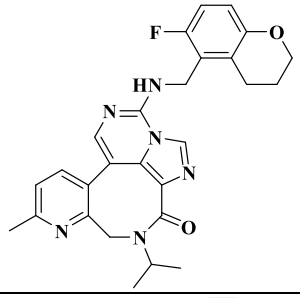
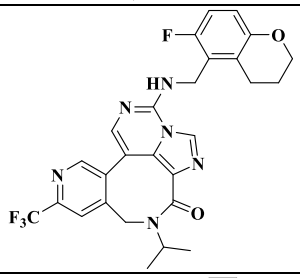
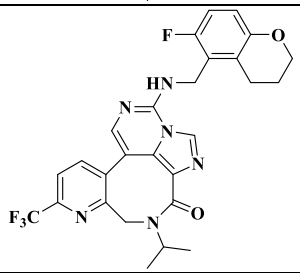
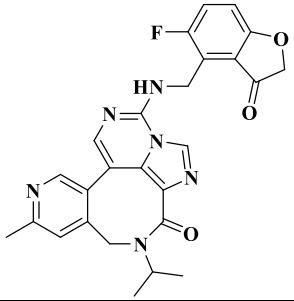
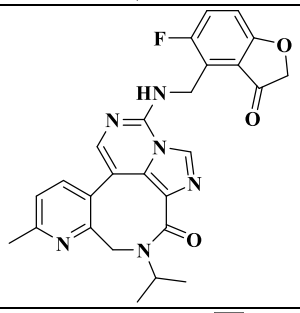
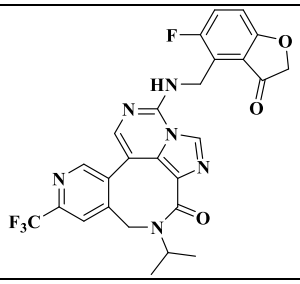
84		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
85		4-(3,3-difluorocyclobutyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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

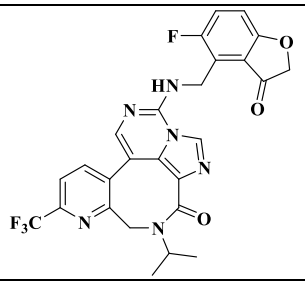
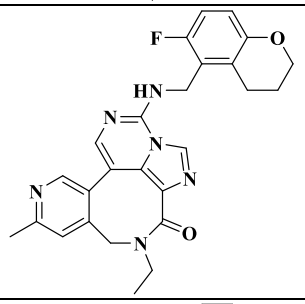
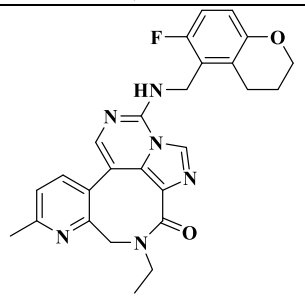
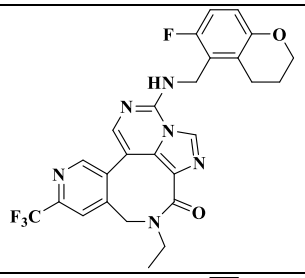
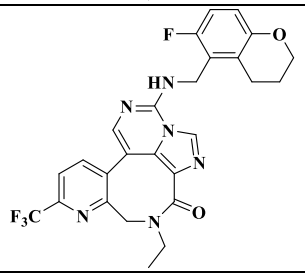
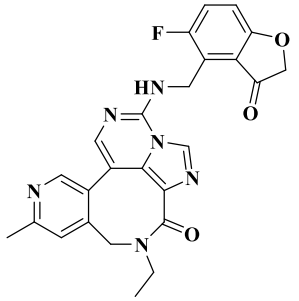
89		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
90		4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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

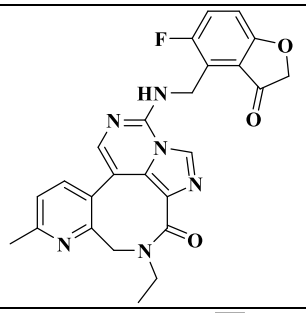
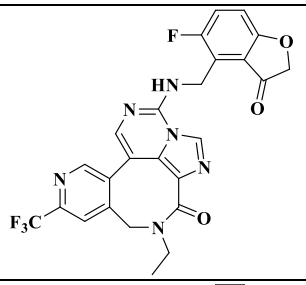
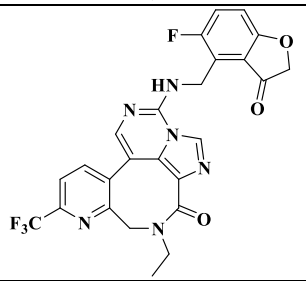
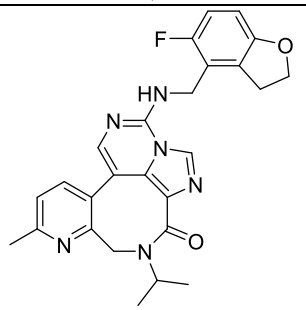
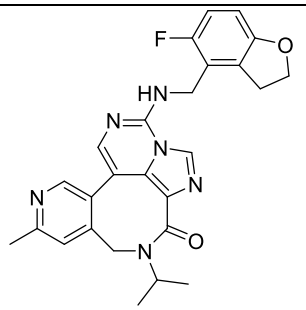
94		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide
95		11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide
96		7-fluoro-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5-dihydro-3-thia-2,11,12a-triazabenzo[4,5]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
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

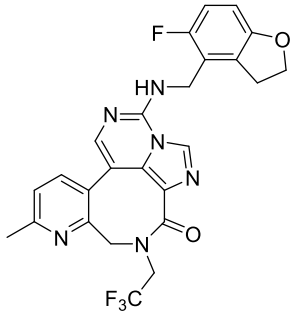
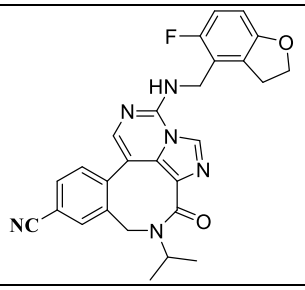
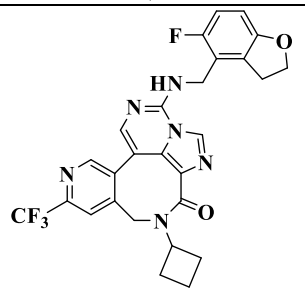
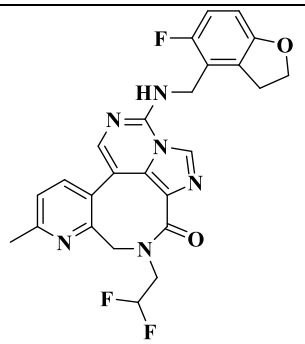
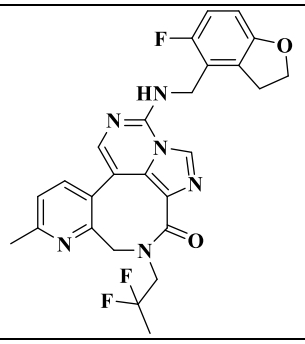
148		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
149		(S)-4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3(4H)-one
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

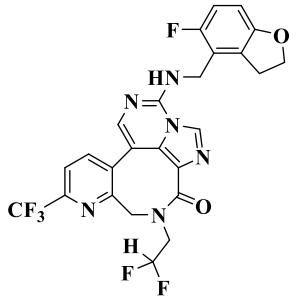
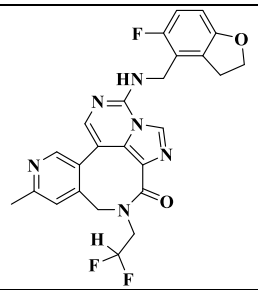
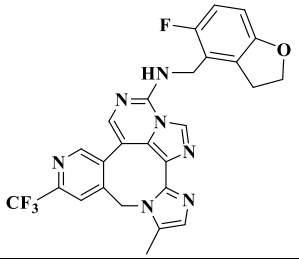
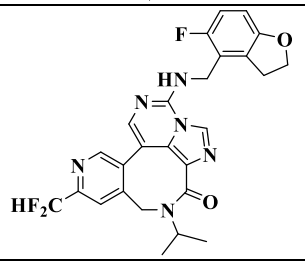
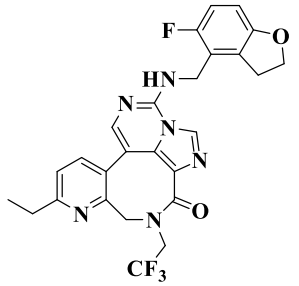
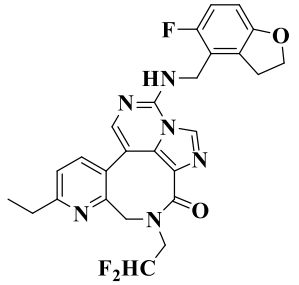
154		(S)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-methyl-7-(methylsulfonyl)-5,5a,6,7,8,9-hexahydro-4H-3-thia-2,4,7,9a,11,12a-hexaazabenzo[4,5]cycloocta[1,2,3-cd]indene 3,3-dioxide
155		(S)-4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4,5,5a,6,8,9-hexahydro-7-oxa-3-thia-2,4,9a,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]indene 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
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

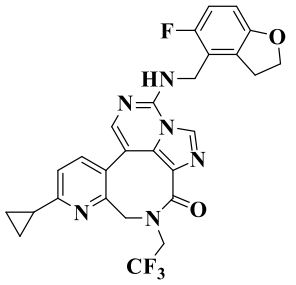
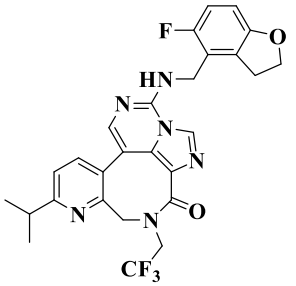
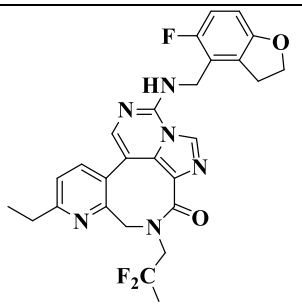
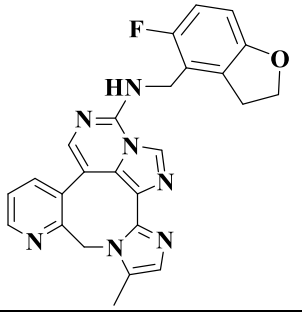
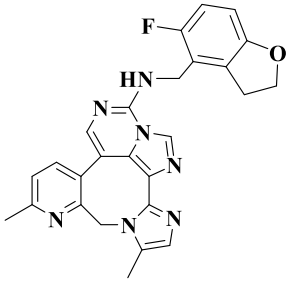
163		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
164		12-(((6-fluorochroman-5-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
165		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-pentaazabenzo[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-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one

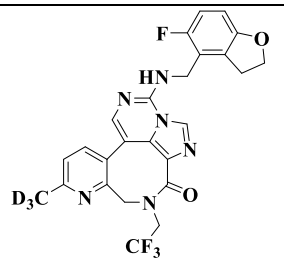
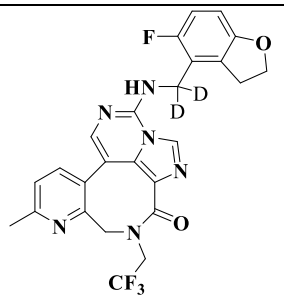
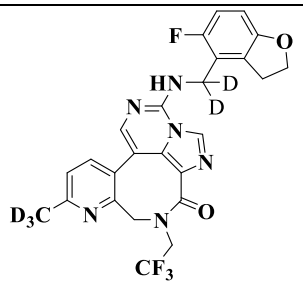
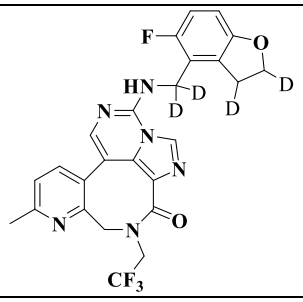
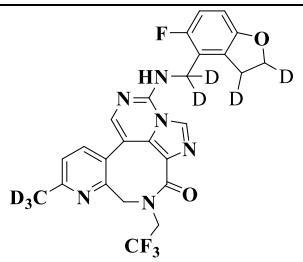
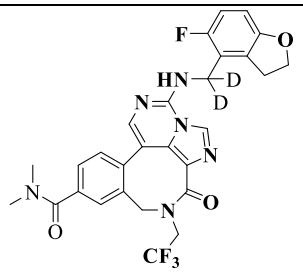
169		12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
170		4-ethyl-12-(((6-fluorochroman-5-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

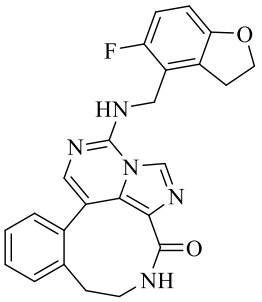
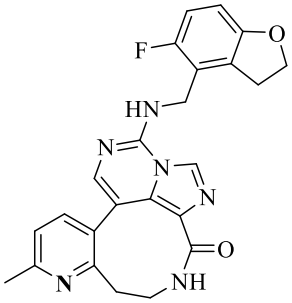
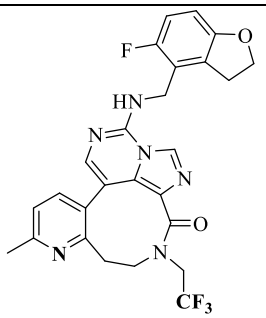
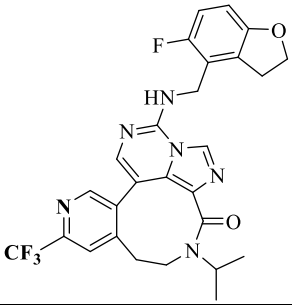
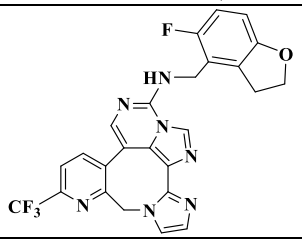
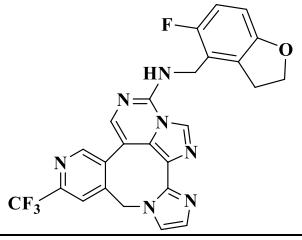
175		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,6,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
176		4-ethyl-12-(((5-fluoro-3-oxo-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

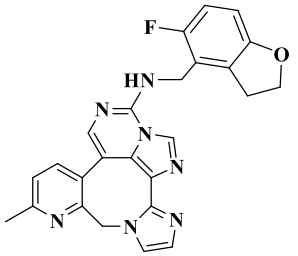
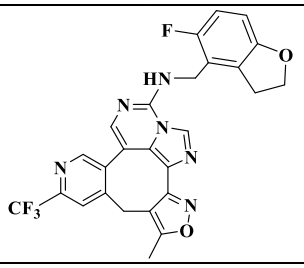
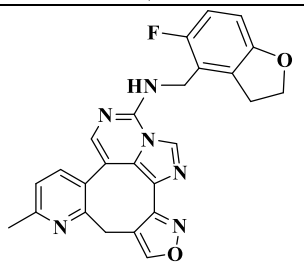
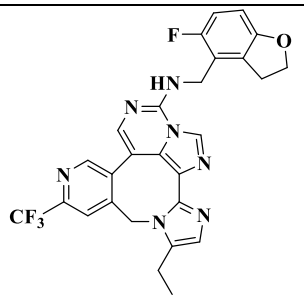
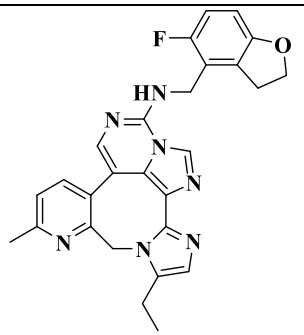
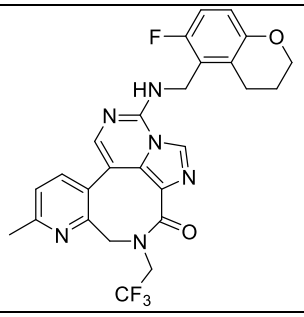
E 3		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 4		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-3-oxo-4,5-dihydro-3H-2,4,11,12a-tetraazabenzo[4,5]cycloocta[1,2,3-cd]indene-7-carbonitrile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

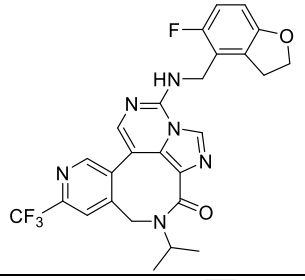
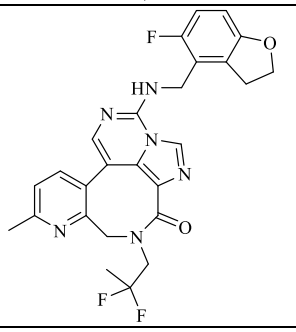
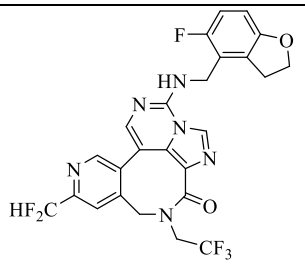
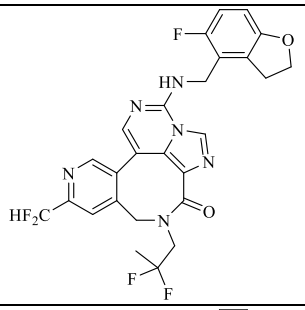
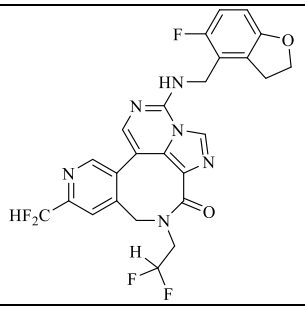
E 8		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 9		4-(2,2-difluoroethyl)-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-methyl-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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-pentaazabenzo[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

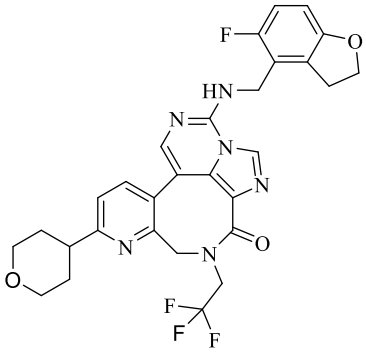
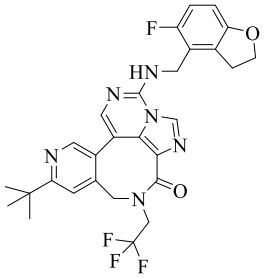
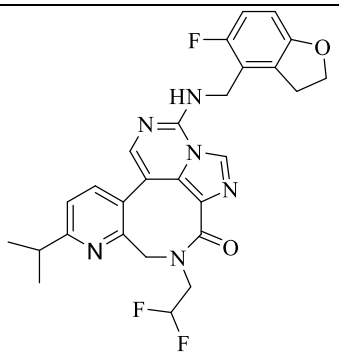
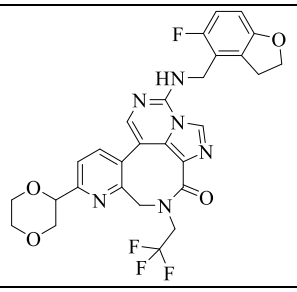
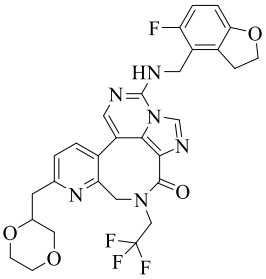
E 14		7-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 15		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-isopropyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one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

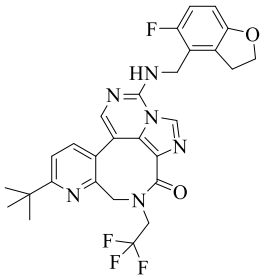
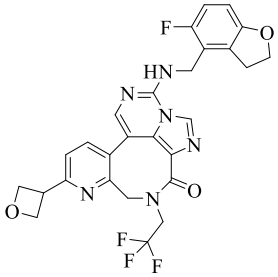
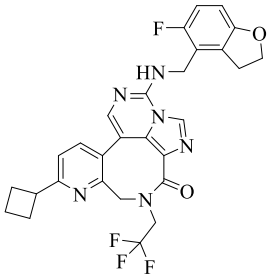
E 19		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(methyl-d3)-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
E 20		12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl-d2)amino)-7-methyl-4-(2,2,2-trifluoroethyl)-4,5-dihydro-3H-2,4,6,11,12a-pentaazabenzo[4,5]cycloocta[1,2,3-cd]inden-3-one
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 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

12. The compound of claim 11 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.

13. Use of the compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating a proliferative disease.

14. The use of claim 13, wherein the proliferative disease is any one or more of the following:

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			

15. A compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, for use in treating a proliferative disease.

16. The compound for use of claim 25, wherein the proliferative disease is any one or more of the following:

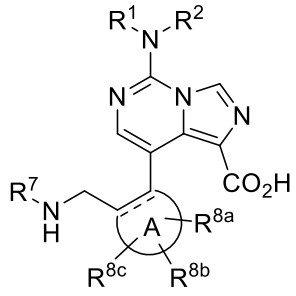
adrenal cancer	acinic cell carcinoma	acoustic neuroma	acral lentigious melanoma
acrospiroma	acute eosinophilic leukemia	acute erythroid leukemia	acute lymphoblastic leukemia
acute megakaryoblastic leukemia	acute monocytic leukemia	acute promyelocytic leukemia	adenocarcinoma
adenoid cystic carcinoma	adenoma	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	anaplastic thyroid	angioimmunoblastic	angiomyolipoma

lymphoma	cancer	T-cell lymphoma	
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	medulloblastoma	melanoma	meningioma

cancer			
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			

17. Use of a compound of any one of claims 1-12, 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.

18. 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, C_3-C_8 cycloalkyl, 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;

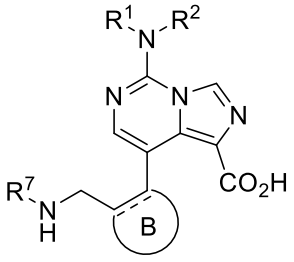


is phenyl, 5-membered heteroaryl, or 6-membered heteroaryl; and

is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

19. 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, C_3-C_8 cycloalkyl, C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

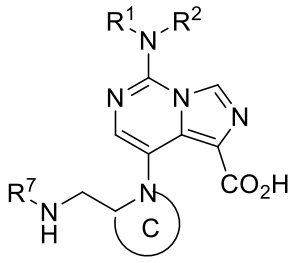


is 3- to 8-membered cycloalkyl or 4- to 8-membered heterocyclo; and

is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

20. 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;

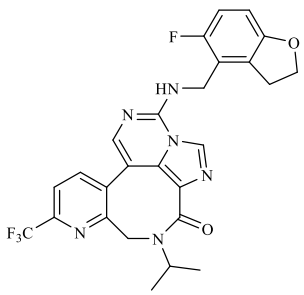
R^7 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl; and



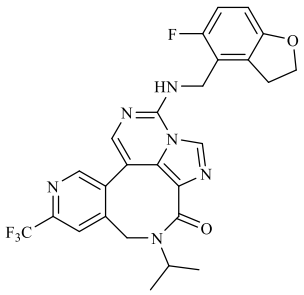
is 4- to 8-membered heterocyclo,

or a pharmaceutically acceptable salt or solvate thereof.

21. The compound of claim 1 having a structure



or



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