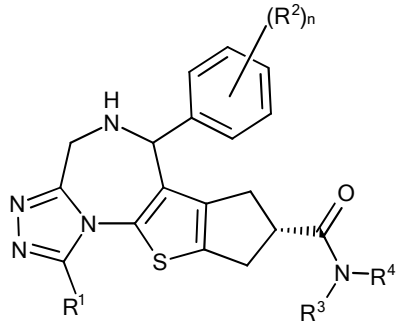
Claims

1. A compound of formula (I.0)



(I.0)

,

wherein

R^1 is selected from the group consisting of C_{1-4}-alkyl optionally substituted with 1 to 3 F and of C_{3-4}-cycloalkyl;

R^2 is selected from the group consisting of F, Cl, Br, I, C_{1-4}-alkyl optionally substituted with 1 to 3 F or optionally substituted with 1 -CN, with 1 OH, or with 1 -O-C_{1-4}-alkyl, further consisting of C_{3-4}-cycloalkyl, -CN, -$CONH_2$, -CONH(C_{1-4}-alkyl), -CON(C_{1-4}-alkyl)$_2$, -COOH, -COO-C_{1-4}-alkyl, OH, -O-C_{1-4}-alkyl optionally substituted with 1 to 3 F, and consisting of -$S(O)_r$-C_{1-4}-alkyl with r = 0, 1, or 2;

n is selected from the group consisting of 0, 1, 2, and 3;

R^3 is selected from the group consisting of H and C_{1-4}-alkyl optionally substituted with 1 to 5 F; and

R^4 is selected from the group consisting of C_{1-6}-alkyl

optionally substituted with 1 to 3 F and

optionally substituted with 1 to 2 substituents independently selected from -CN, -$CONH_2$, -CONH(C_{1-4}-alkyl), -CON(C_{1-4}-alkyl)$_2$, -COOH, -COO-C_{1-4}-alkyl, C_{1-3}-alkyl-CO-NH-, C_{1-3}-alkyl-$S(=O)_2$-NH-, OH, and -O-C_{1-3}-alkyl optionally substituted with 1 to 3 F;

or

R^4 is selected from the group consisting of -C_{0-3}-alkylene-C_{3-10}-cycloalkyl and -C_{0-3}-alkylene-C_{3-10}-heterocyclyl,

wherein said alkylene is optionally substituted with 1 to 2 substituents selected from F and CH_3,

wherein the 2 H atoms of 1 >CH_2 group of said alkylene are optionally replaced by an ethylene (-CH_2-CH_2-) bridge to form a cyclopropylene moiety >C(-CH_2-CH_2-),

wherein said cycloalkyl and heterocyclyl are saturated mono- or bicyclic ring systems,

wherein said heterocyclyl contains 1 to 2 ring members independently selected from N, NH, >N(C_{1-4}-alkyl), >NCO(C_{1-4}-alkyl), >$NS(=O)_2$(C_{1-4}-alkyl), and O, and optionally 1 ring member selected from >C=O and >$S(=O)_r$, with r = 0, 1, or 2,

provided that said heterocyclyl does not contain any heteroatom-heteroatom bonds other than N-N, N-O, and N-$S(=O)_{r=1,2}$ between ring members, and

wherein said cycloalkyl and heterocyclyl are optionally substituted with 1 to 2 F and optionally substituted with 1 to 2 substituents independently selected from Cl, -CN, -$CONH_2$, -$CONH(C_{1-4}$-alkyl), -$CON(C_{1-4}$-$alkyl)_2$, -COOH, -COO-C_{1-4}-alkyl, OH, -O-C_{1-3}-alkyl optionally substituted with 1 to 3 F, and from C_{1-4}-alkyl optionally substituted with 1 to 3 F or with 1 substituent selected from -CN, OH, -O-C_{1-4}-alkyl;

or

R^4 is selected from the group consisting of -C_{0-3}-alkylene-phenyl and -C_{0-3}-alkylene-heteroaryl,

wherein said alkylene is optionally substituted with 1 to 2 substituents selected from F and CH_3,

wherein the 2 H atoms of 1 >CH_2 group of said alkylene are optionally replaced by an ethylene (-CH_2-CH_2-) bridge to form a cyclopropylene moiety >C(-CH_2-CH_2-),

wherein said heteroaryl is a 5-membered monocycle containing 1 ring member selected from N, NH, O, and S and optionally further containing 1 to 2 ring members N, or a 6-membered monocycle containing 1 to 2 ring members N, and

wherein said phenyl and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from F, Cl, Br, C_{3-4}-cycloalkyl, -CN, -$CONH_2$, -$CONH(C_{1-4}$-alkyl), -$CON(C_{1-4}$-$alkyl)_2$, -COOH, -COO-C_{1-4}-alkyl, -NHCO-C_{1-4}-alkyl, -$NHS(=O)_2$-C_{1-4}-alkyl, -$S(=O)_r$-C_{1-4}-alkyl with r = 0, 1, or 2, from -O-C_{1-4}-alkyl optionally substituted with 1 to 3 F, and from C_{1-4}-alkyl optionally substituted with 1 to 3 F or with 1 substituent selected from -CN, OH, and -O-C_{1-4}-alkyl;

or

R^3 and R^4 are selected from the group in which R^3 and R^4, together with the amide N atom they are attached to, form a saturated 3- to 8-membered monocyclic heterocyclyl

optionally further containing 1 to 2 ring members independently selected from >NH, >N(C_{1-4}-alkyl), >N(CO-C_{1-3}-alkyl), >N($S(=O)_2$-C_{1-3}-alkyl), and O, and

optionally containing 1 ring member selected from >C=O and >$S(=O)_r$, with r = 0, 1, or 2,

provided that said heterocyclyl does not contain any heteroatom-heteroatom bonds other than N-N, N-O, and N-$S(=O)_{r=1,2}$ between ring members,

wherein said heterocyclyl is optionally substituted with 1 to 4 F,

is optionally substituted with 1 to 4 C_{1-3}-alkyl optionally substituted with 1 to 3 F, and

is optionally substituted with 1 to 2 substituents selected from Cl, -CN, -$CONH_2$, -$CONH(C_{1-4}$-alkyl), -$CON(C_{1-4}$-$alkyl)_2$, -COOH, -COO-C_{1-4}-alkyl, HO-C_{1-3}-alkylene-, C_{1-3}-alkyl-O-C_{1-3}-alkylene-, C_{1-3}-alkyl-CO-NH-, C_{1-3}-alkyl-$S(=O)_2$-NH-, OH, and C_{1-3}-alkyl-O- optionally substituted with 1 to 3 F;

or

R^3 and R^4 are selected from the group in which R^3 and R^4, together with the amide N atom they are attached to, form a saturated 5- to 12-membered bicyclic heterocyclyl

optionally further containing 1 to 3 ring members independently selected from >N-, >NH, >N(C_{1-4}-alkyl), >N(CO-C_{1-3}-alkyl), >N($S(=O)_2$-C_{1-3}-alkyl), and O, and

optionally containing 1 ring member selected from >C=O and >$S(=O)_r$, with r = 0, 1, or 2,

provided that said heterocyclyl does not contain any heteroatom-heteroatom bonds other than N-N, N-O, and N-$S(=O)_{r=1,2}$ between ring members,

wherein said heterocyclyl is optionally substituted with 1 to 6 F,

is optionally substituted with 1 to 4 C_{1-3}-alkyl optionally substituted with 1 to 3 F, and

is optionally substituted with 1 to 2 substituents selected from Cl, -CN, -$CONH_2$, -CONH(C_{1-4}-alkyl), -CON(C_{1-4}-alkyl)$_2$, -COOH, -COO-C_{1-4}-alkyl, HO-C_{1-3}-alkylene-, C_{1-3}-alkyl-O-C_{1-3}-alkylene-, C_{1-3}-alkyl-CO-NH-, C_{1-3}-alkyl-S(=O)$_2$-NH-, OH, and C_{1-3}-alkyl-O-;

or

R^3 and R^4 are selected from the group in which R^3 and R^4, together with the amide N atom they are attached to, form a 7- to 12-membered fused bicyclic ring system,

wherein said bicyclic ring system is a heterocyclyl or heteroaryl consisting of

one non-aromatic ring containing said amide N atom and optionally further containing 1 to 2 ring members independently selected from =N-, >N-, >NH, >N(C_{1-4}-alkyl), >N(CO-C_{1-3}-alkyl), >N(S(=O)$_2$-C_{1-3}-alkyl), and O, and optionally containing 1 ring member selected from >C=O and >S(=O)$_r$, with r = 0, 1, or 2, provided that there are no heteroatom-heteroatom bonds other than N-N, N-O, and N-S(=O)$_{r=1,2}$ between members of said non-aromatic ring,

and of

one aromatic ring selected from 5-membered monocycles containing 1 ring member selected from NH, N, O, and S and optionally further containing 1 to 2 ring members N, and of 6-membered monocycles containing 0, 1, or 2 ring members N,

wherein said bicyclic ring system is optionally substituted with 1 to 4 F,

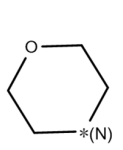
is optionally substituted with 1 to 4 C_{1-3}-alkyl optionally substituted with 1 to 3 F, and

is optionally substituted with 1 to 2 substituents selected from Cl, -CN, -$CONH_2$, -CONH(C_{1-4}-alkyl), -CON(C_{1-4}-alkyl)$_2$, -COOH, -COO-C_{1-4}-alkyl, HO-C_{1-3}-alkylene-, C_{1-3}-alkyl-O-C_{1-3}-alkylene-, C_{1-3}-alkyl-CO-NH-, C_{1-3}-alkyl-S(=O)$_2$-NH-, OH, and C_{1-3}-alkyl-O- optionally substituted with 1 to 3 F;

or a salt thereof.

2. The compound according to claim 1, wherein

R^3 and R^4, together with the amide N atom they are attached to, form a heterocyclyl selected from the group consisting of



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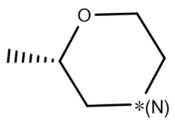

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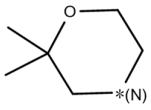

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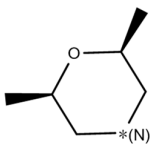

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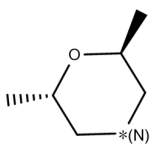

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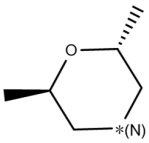

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or a salt thereof.

3. The compound according to claim 1 or 2, wherein

R^1 is selected from the group consisting of CH_3, CH_2CH_3, $CH_2CH_2CH_3$, CHF_2, CF_3, and cyclopropyl;

or a salt thereof.

4. The compound according to claim 1 or 2, wherein

R^1 is selected from the group consisting of CH_3, CH_2CH_3, $CH_2CH_2CH_3$, and cyclopropyl;

or a salt thereof.

5. The compound according to claim 1 or 2, wherein

R^1 is CH_3;

or a salt thereof.

6. The compound according to any of claims 1 to 5, wherein

R^2 is selected from the group consisting of

F, Cl, Br, C_{1-3}-alkyl optionally substituted with 2 or 3 F, further consisting of cyclopropyl, -CN, -C_{1-3}-alkylene-OH, -C_{1-2}-alkylene-O-C_{1-2}-alkyl, OH, -O-C_{1-3}-alkyl optionally substituted with 2 or 3 F, and consisting of -S-C_{1-3}-alkyl; and

n is selected from the group consisting of 0, 1, and 2;

or a salt thereof.

7. The compound according to any of claims 1 to 5, wherein

R^2 is selected from the group consisting of

F, Cl, Br, CH_3, CH_2CH_3, cyclopropyl, CF_3, CH_2OH, OH, OCH_3, and S-CH_3; and

n is selected from the group consisting of 0, 1, and 2;

or a salt thereof.

8. The compound according to claim 2, wherein

R^1 is CH_3 ;

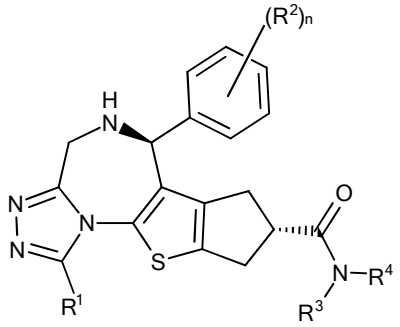
R^2 is Cl;

n is 1;

or a salt thereof.

9. The compound according to any of claims 1 to 8, wherein

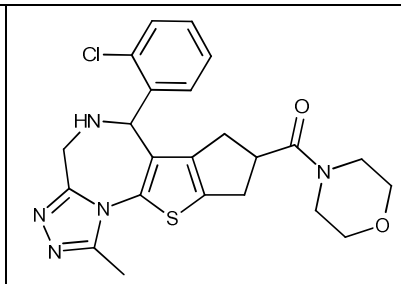
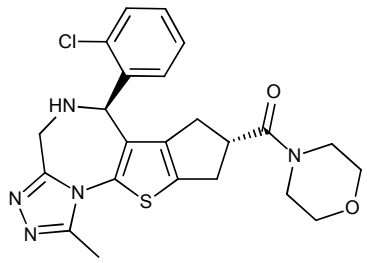
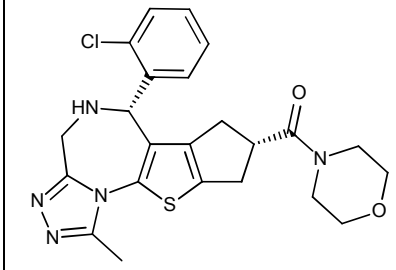
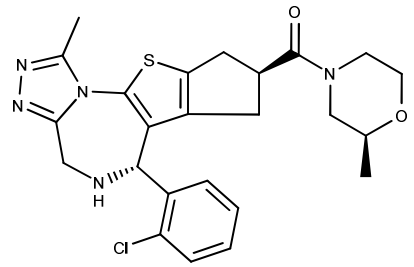
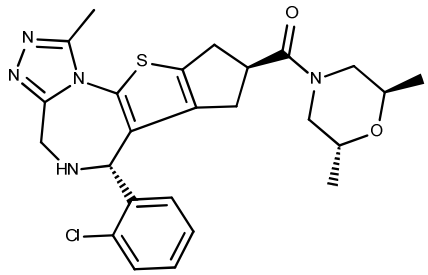
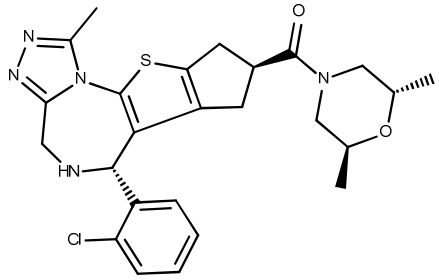
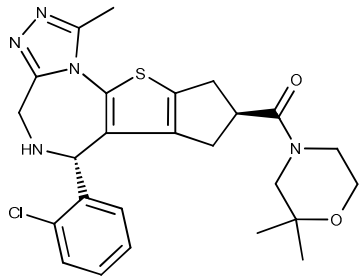
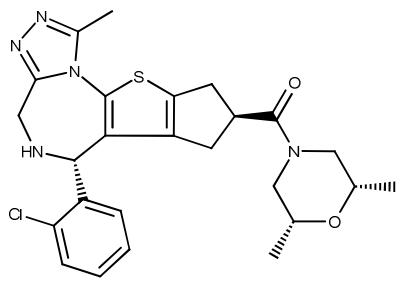
the stereochemistry of the compound is according to formula (I.1)

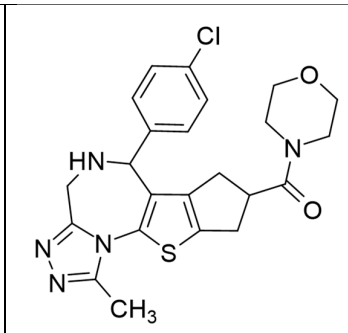
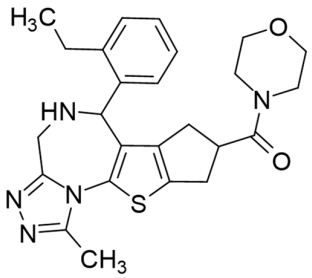
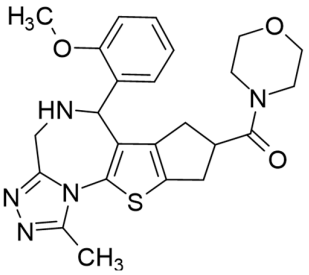
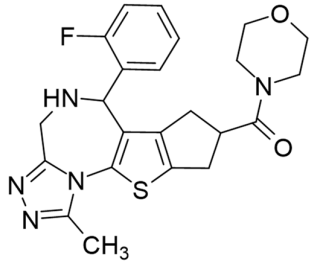
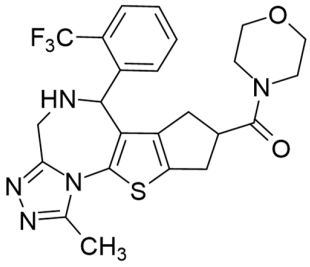
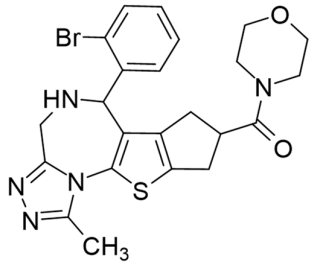
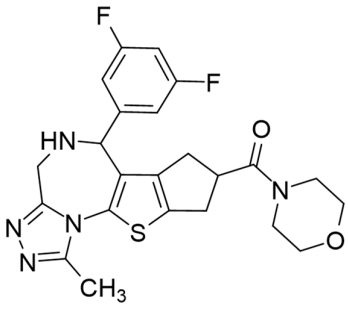
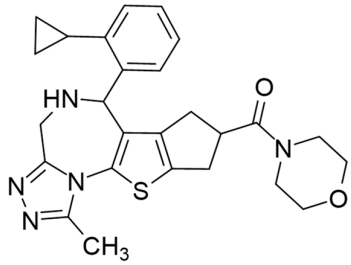
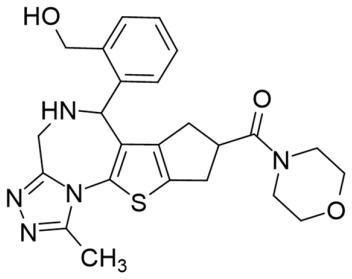
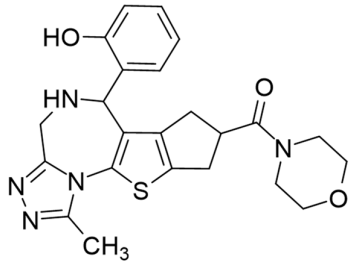


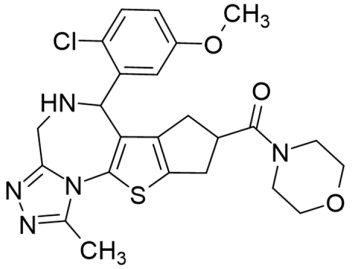
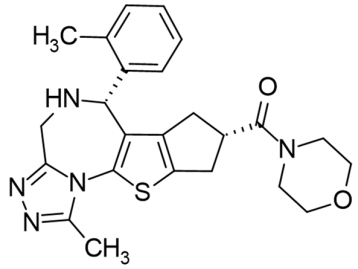
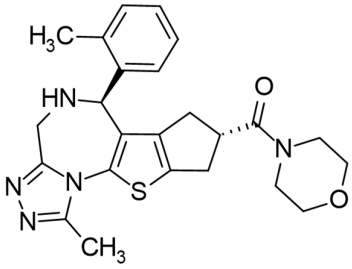
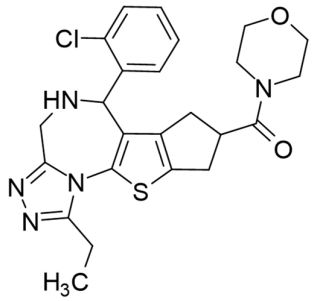
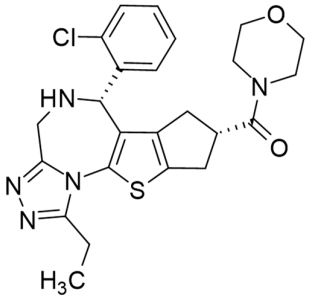
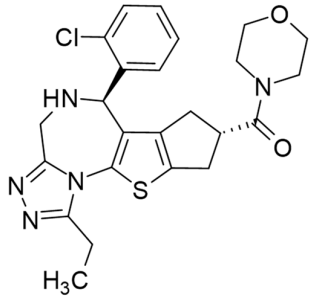
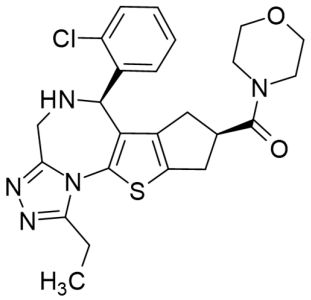
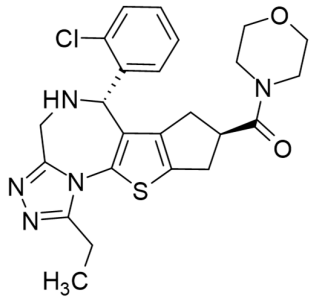
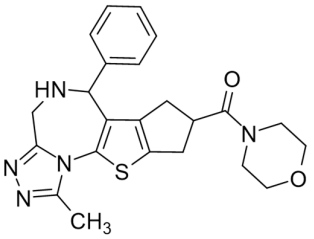
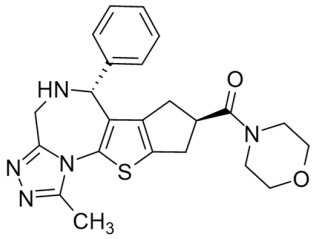
(I.1)

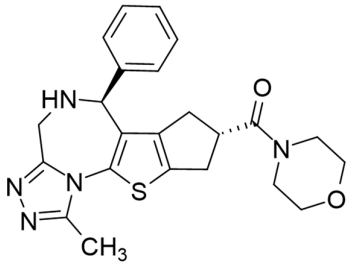
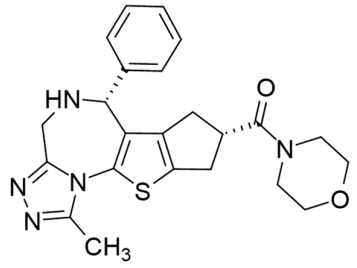
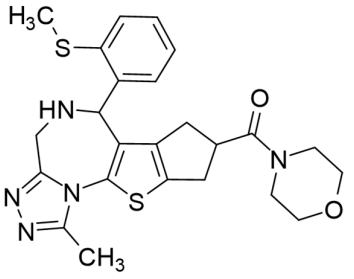
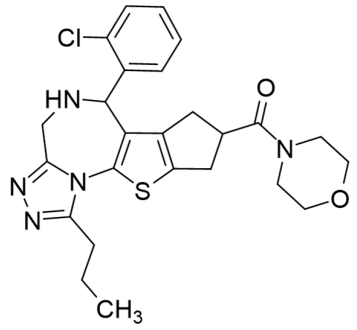
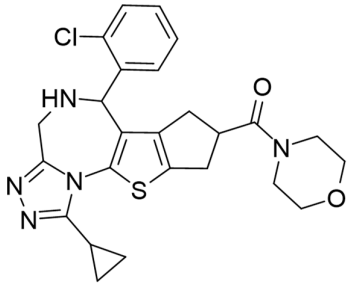
or a salt thereof.

10. The compound according to claim 2, wherein said compound is selected from:

1		2	
3		4	
5		6	
26		27	

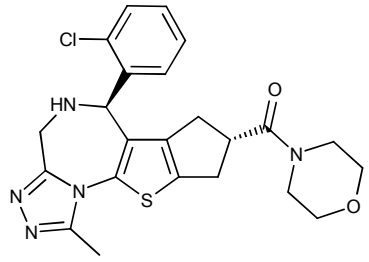
52		53	
54		55	
56		57	
58		59	
60		61	

62		63	
64		67	
68		69	
70		71	
74		75	

76		78	
79		80	
81			

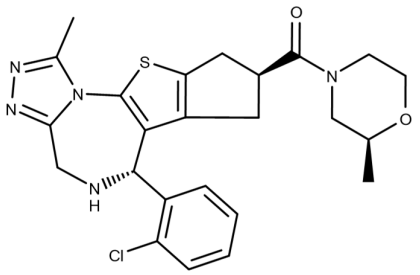
or a salt thereof.

11. The compound according to claim 10, wherein said compound is

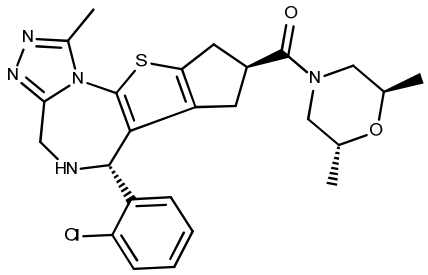


.

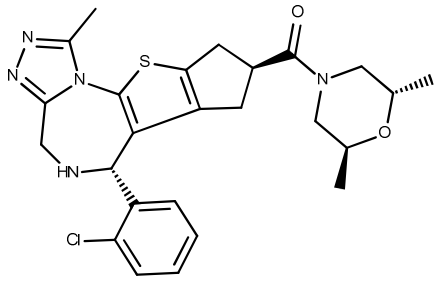
12. The compound according to claim 10, wherein said compound is



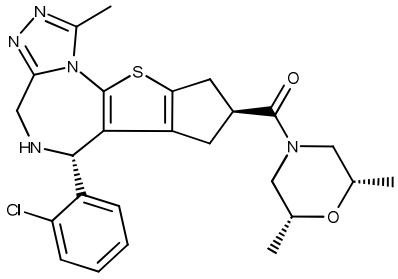
13. The compound according to claim 10, wherein said compound is



14. The compound according to claim 10, wherein said compound is



15. The compound according to claim 10, wherein said compound is



16. The compound according to claim 1, wherein

R^3 is selected from the group consisting of H and C_{1-3}-alkyl optionally substituted with 1 to 3 F; and

R^4 is selected from the group consisting of C_{1-4}-alkyl optionally substituted with 1 substituent selected from F, OH, and OCF_3;

or

R^4 is selected from the group consisting of -C_{0-1}-alkylene-C_{3-6}-cycloalkyl,

wherein said cycloalkyl is a saturated mono- or bicyclic ring system, and

wherein said cycloalkyl is optionally substituted with 1 to 2 F and optionally substituted with 1 CH_3 or CH_2CH_3;

or

R^4 is selected from the group consisting of -C_{0-2}-alkylene-phenyl and -C_{0-2}-alkylene-heteroaryl,

wherein said alkylene is optionally substituted with 1 to 2 CH_3,

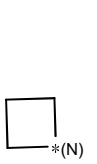
wherein the 2 H atoms of 1 >CH_2 group of said alkylene are optionally replaced by an ethylene (-CH_2-CH_2-) bridge to form a cyclopropylene moiety >C(-CH_2-CH_2-),

wherein said heteroaryl is a 5-membered monocycle containing 1 ring member selected from N, NH, O, and S and optionally further containing 1 ring member N, or a 6-membered monocycle containing 1 to 2 ring members N, and

wherein said phenyl and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from F, Cl, Br, -CN, -O-C_{1-3}-alkyl optionally substituted with 1 to 3 F, and from C_{1-3}-alkyl optionally substituted with 1 to 3 F or with 1 substituent selected from -CN and -O-C_{1-2}-alkyl;

or

R^3 and R^4 are selected from the group in which R^3 and R^4, together with the amide N atom they are attached to, form a heterocyclyl selected from the group consisting of



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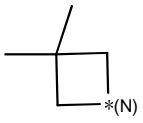

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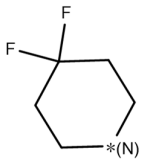

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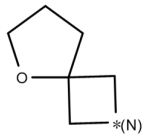

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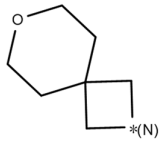

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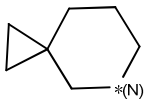

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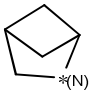

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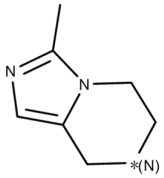


;

or a salt thereof.

17. The compound according to claim 16, wherein

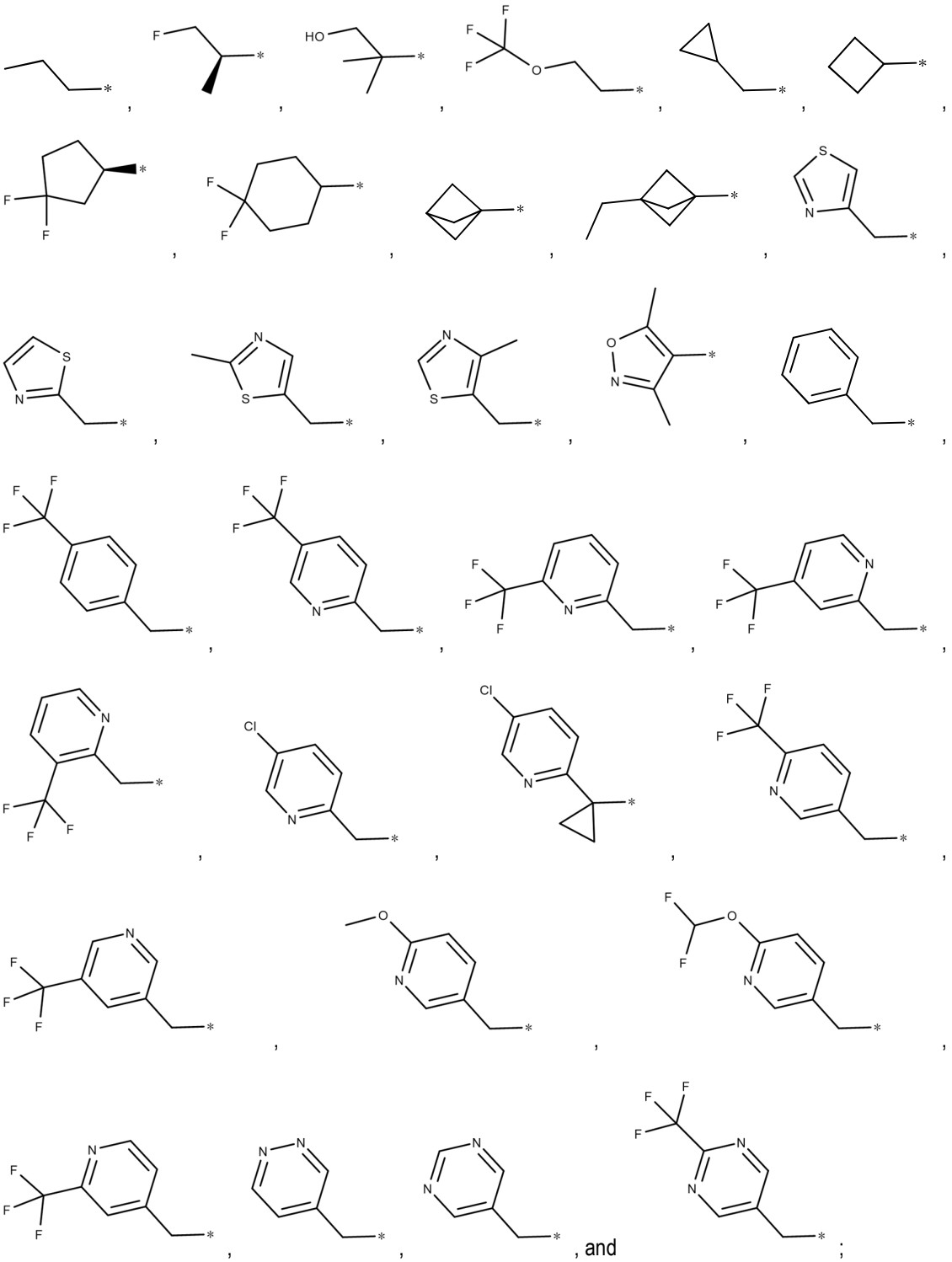
R^1 is CH_3;

R^2 is selected from the group consisting of F, Cl, and Br;

n is 1;

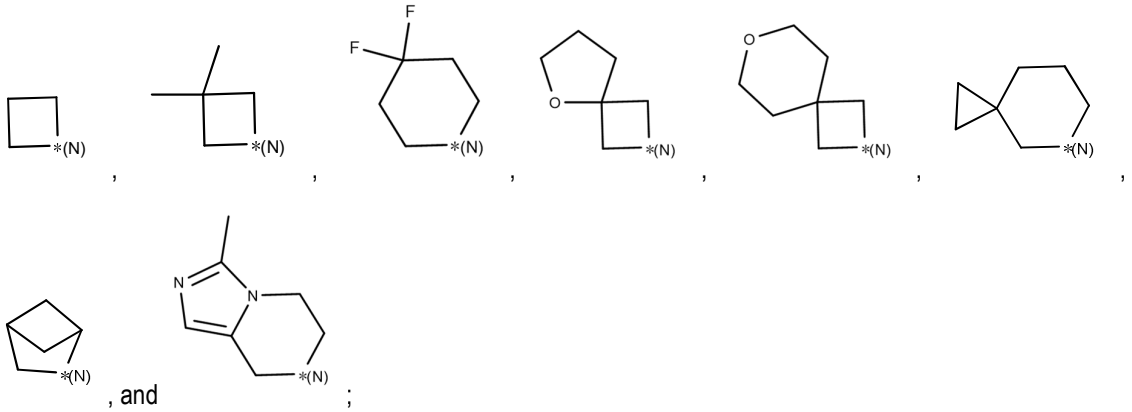
R^3 is selected from the group consisting of H, CH_3, and $CH_2CH_2CH_3$; and

R^4 is selected from the group consisting of



or

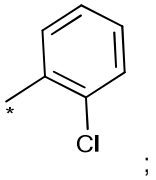
R^3 and R^4 are selected from the group in which R^3 and R^4, together with the amide N atom they are attached to, form a heterocyclyl selected from the group consisting of



or a salt thereof.

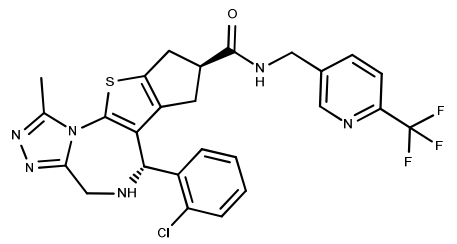
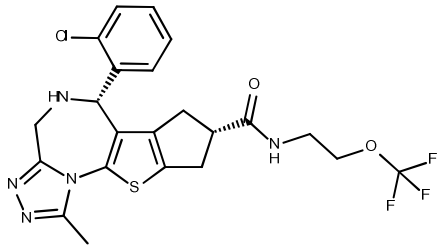
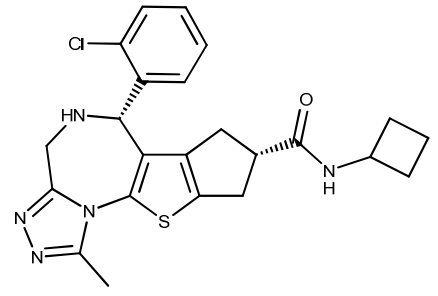
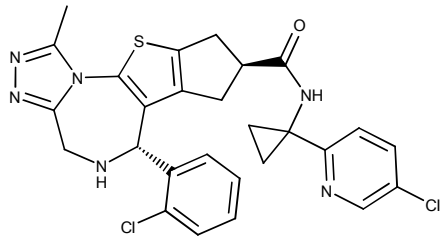
18. The compound according to claim 17, wherein

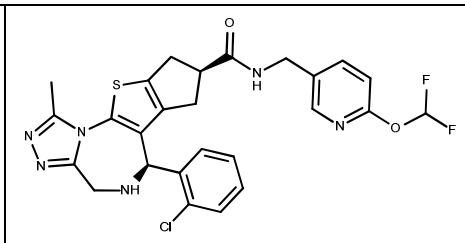
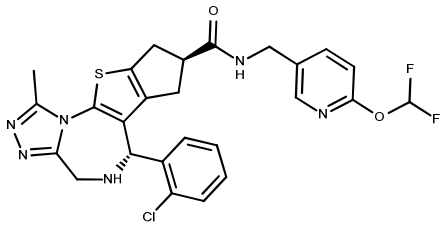
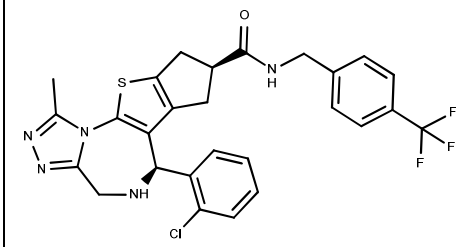
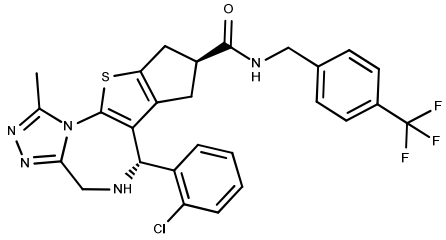
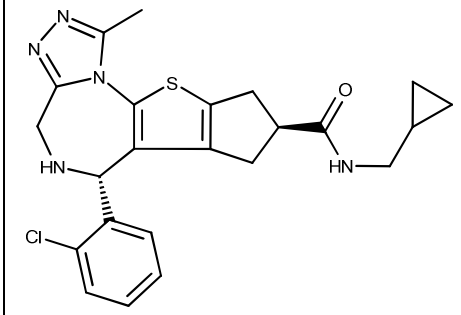
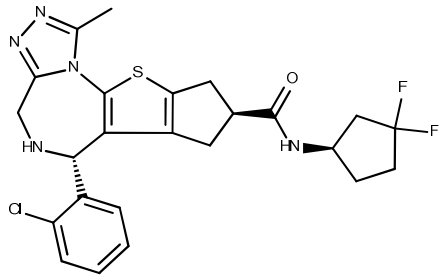
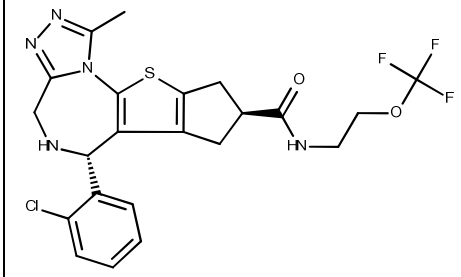
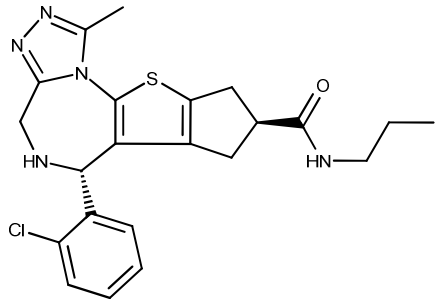
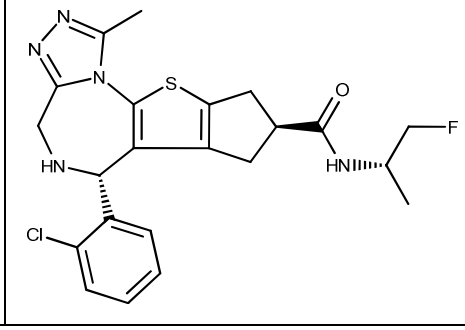
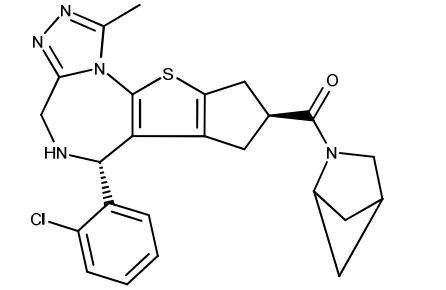
R^2, n, and the phenyl substitution pattern are selected such that the resulting substituted phenyl ring shown in formula (I.0) is selected from the group consisting of

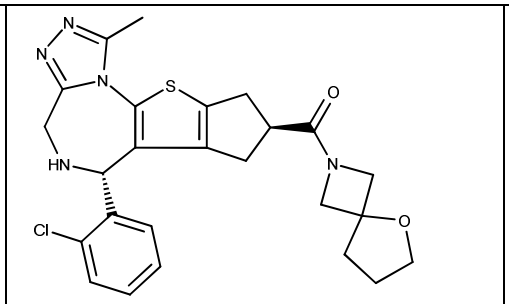
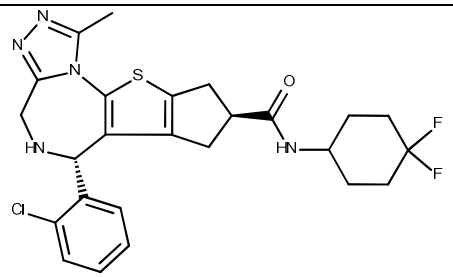
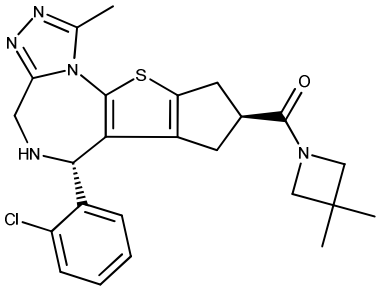
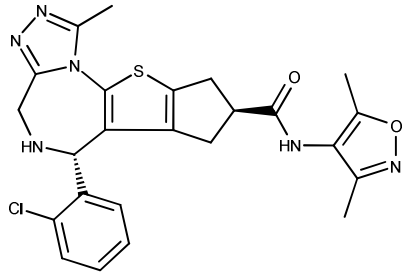
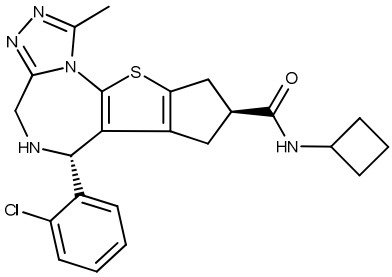
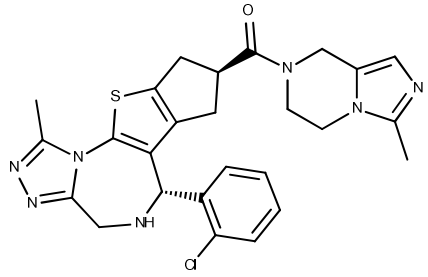
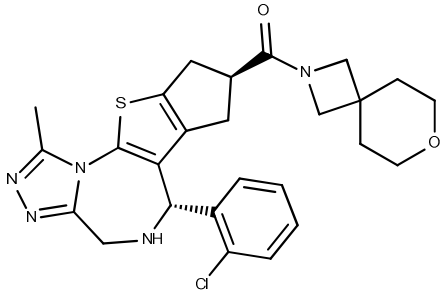
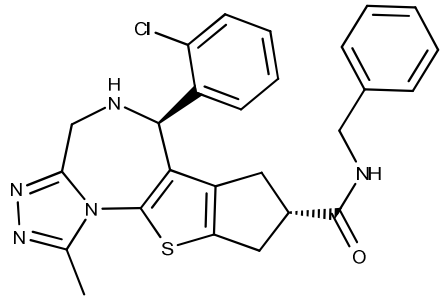
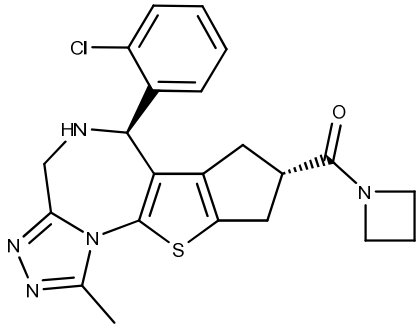
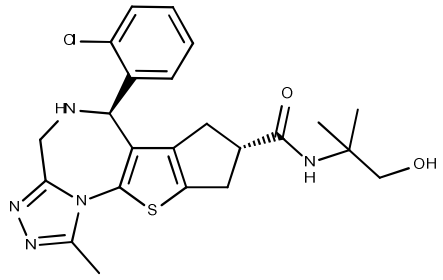


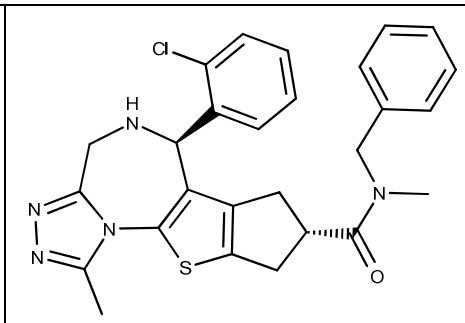
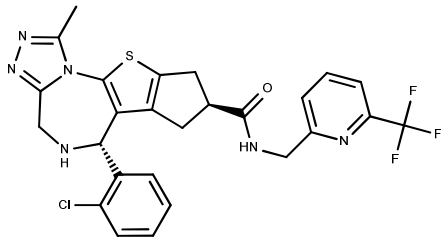
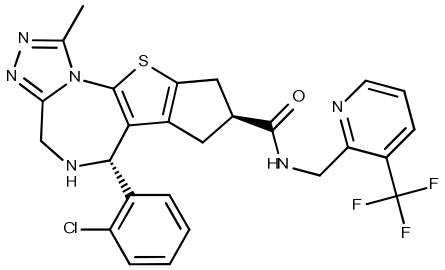
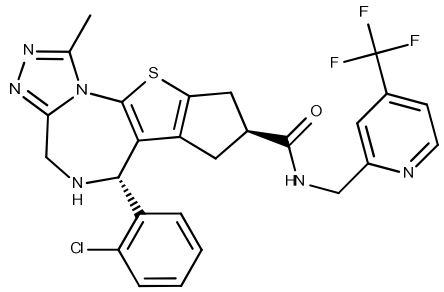
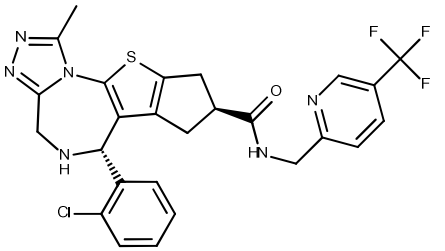
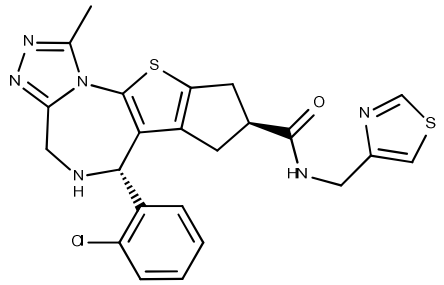
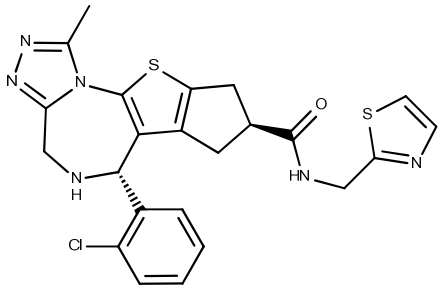
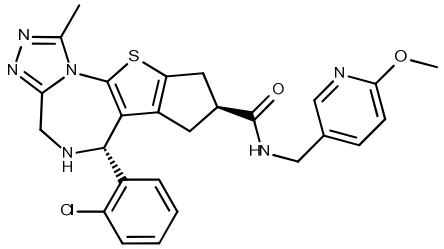
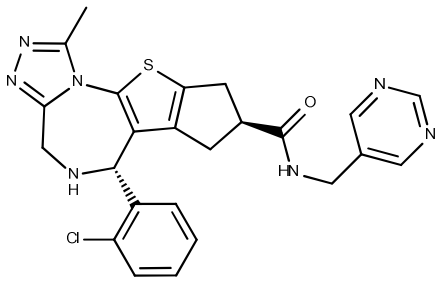
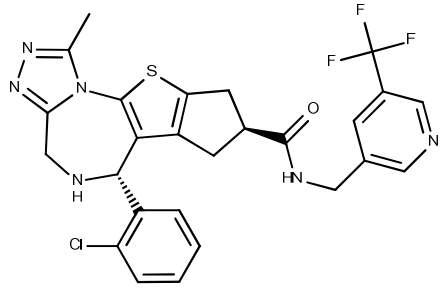
or a salt thereof.

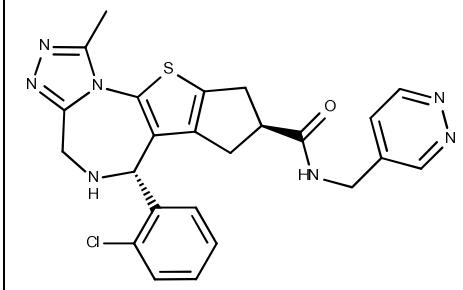
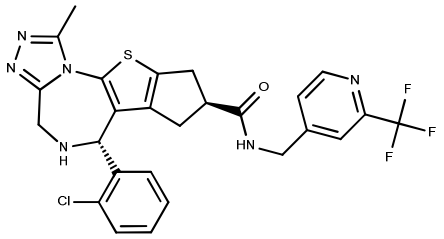
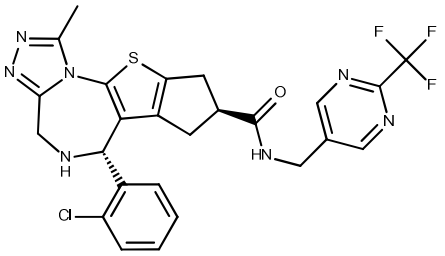
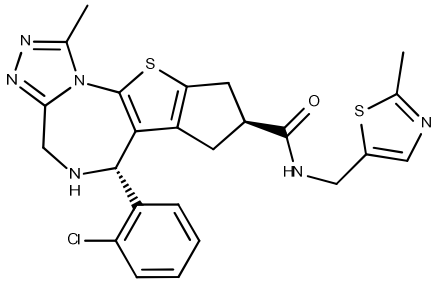
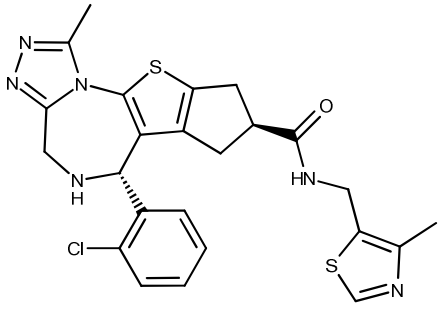
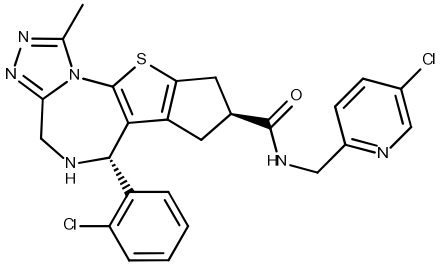
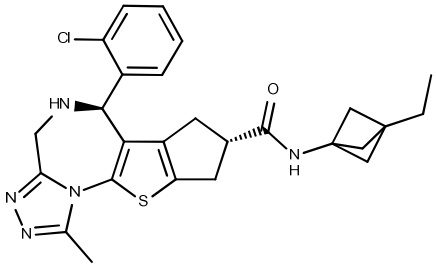
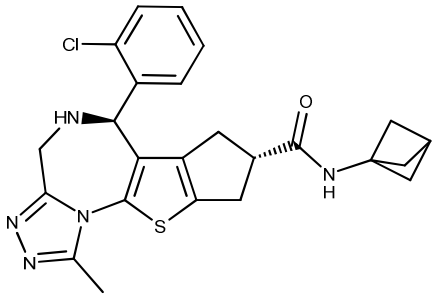
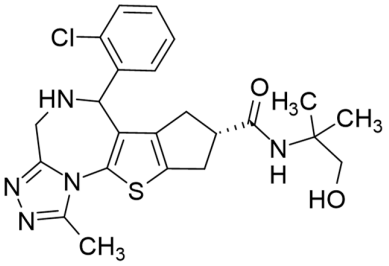
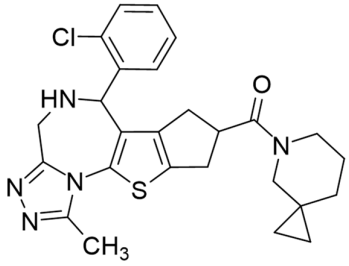
19. The compound according to claim 16, wherein said compound is selected from:

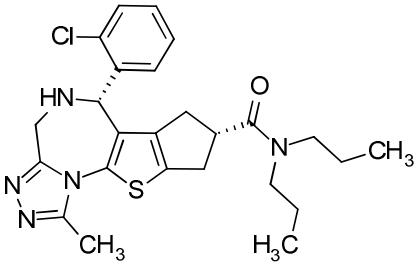
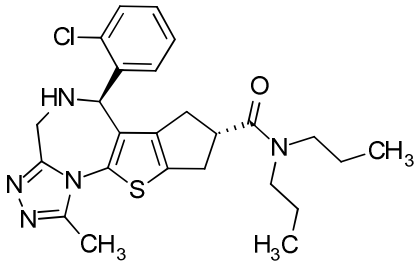
7		8	
9		10	

11		12	
13		14	
15		16	
17		19	
20		21	

22		23	
24		25	
28		29	
30		31	
32		33	

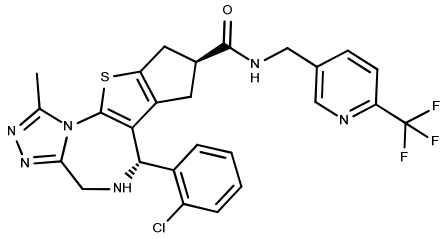
34		35	
36		37	
38		39	
40		41	
42		43	

44		45	
46		47	
48		49	
50		51	
65		66	

72		73	

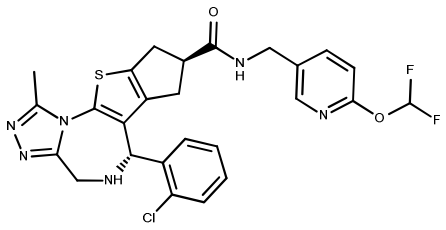
or a salt thereof.

20. The compound according to claim 19, wherein said compound is



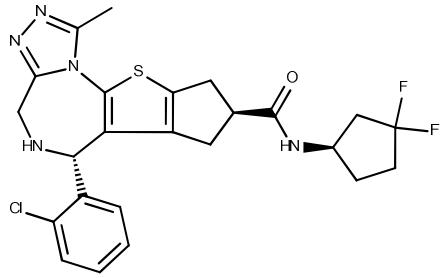
.

21. The compound according to claim 19, wherein said compound is



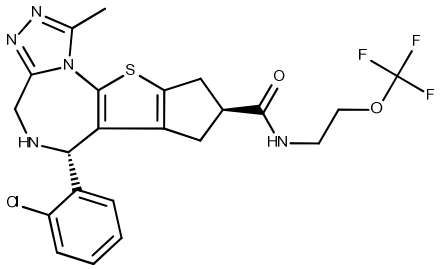
.

22. The compound according to claim 19, wherein said compound is



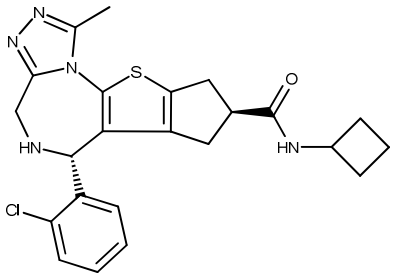
.

23. The compound according to claim 19, wherein said compound is



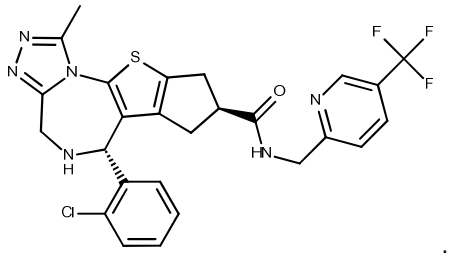
.

24. The compound according to claim 19, wherein said compound is



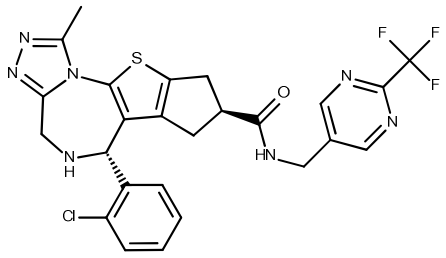
.

25. The compound according to claim 19, wherein said compound is



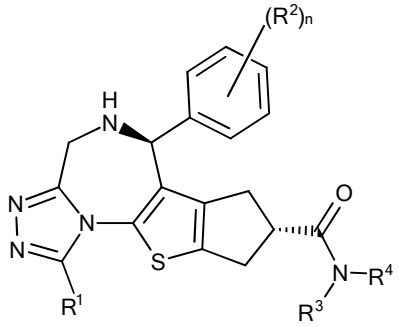
.

26. The compound according to claim 19, wherein said compound is



.

27. The compound according to one or more of claims 1 to 26, wherein the stereochemistry of the compound is according to formula (I.1)



(I.1)

or a salt thereof.

28. A pharmaceutically acceptable salt of the compound according to one or more of claims 1 to 27.

29. A pharmaceutical composition comprising one or more compounds according to one or more of claims 1 to 27, or pharmaceutically acceptable salts thereof, optionally together with one or more inert carriers and/or diluents.

30. A pharmaceutical composition comprising one or more compounds according to one or more of claims 1 to 27, or pharmaceutically acceptable salts thereof, and one or more additional therapeutic agents, optionally together with one or more inert carriers and/or diluents.

31. The pharmaceutical composition according to claim 30,
wherein the one or more additional therapeutic agents are selected from the group consisting of antidiabetic agents, agents for the treatment of overweight and/or obesity, agents for the treatment of high blood pressure, heart failure and/or atherosclerosis, agents for the treatment of ocular diseases, and agents for the treatment of allergies and inflammation-related conditions and diseases.

32. The compound according to one or more of claims 1 to 27 or a pharmaceutically acceptable salt thereof, for use as a medicament.

33. The compound according to one or more of claims 1 to 27 or a pharmaceutically acceptable salt thereof for use in the treatment of ocular diseases, preferably diabetic macular edema, dry and wet age-related macular degeneration, geographic atrophy and non-exudative choroidal neovascularization, and for the treatment of allergies and inflammation-related conditions and diseases, preferably urticaria and NASH.

34. Use of the compound according to one or more of claims 1 to 27 or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of ocular diseases, preferably diabetic macular edema, dry and wet age-related macular degeneration, geographic atrophy and non-exudative choroidal neovascularization, and for the treatment of allergies and inflammation-related conditions and diseases, preferably urticaria and NASH.