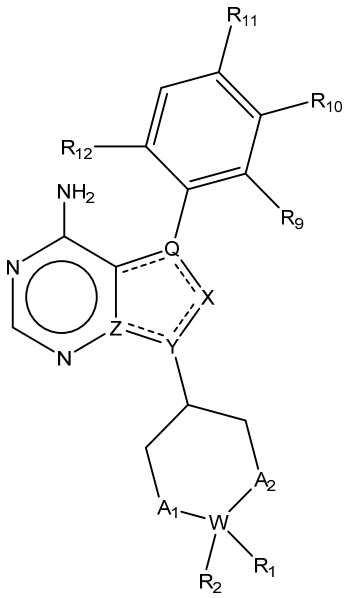
Claims

~~We claim:~~

1. A compound of Formula (I):



(I)

wherein

each Q, Y and Z are independently selected from N and C, and X is N or C-R^a;

provided that at least one of Q, X, Y and Z is N, and

each dashed bond is independently a single or double bond such that the bicycle they form is a heteroaryl;

R_1 is selected from alkyl, alkenyl, alkynyl, amino, acylamino, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, and heteroaralkyl;

either

a) W is N, R_2 is absent, and A_1 and A_2 are each CH_2;

b) W is C, R_2 is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, and amino, and A_1 and A_2 are each independently selected from CH_2 and O; or

c) W is C, and R_1 and R_2 are taken together to form a =CH_2-amido, cycloalkyl, and heterocyclyl, and A_1 and A_2 are each independently selected from CH_2 and O;

R^a is selected from H, halo, CN and alkyl;

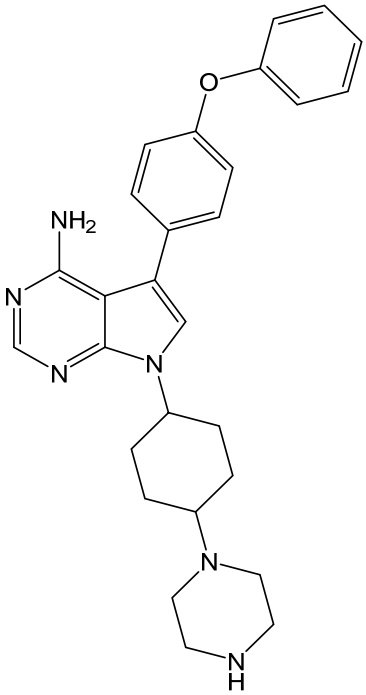
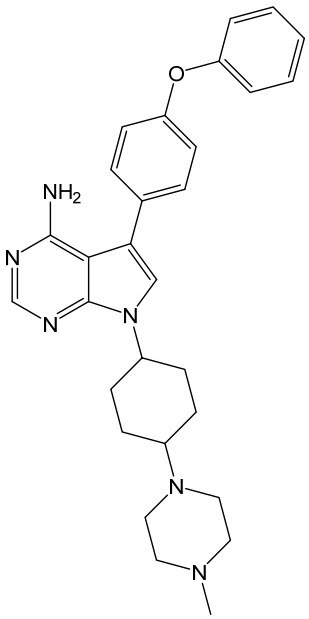
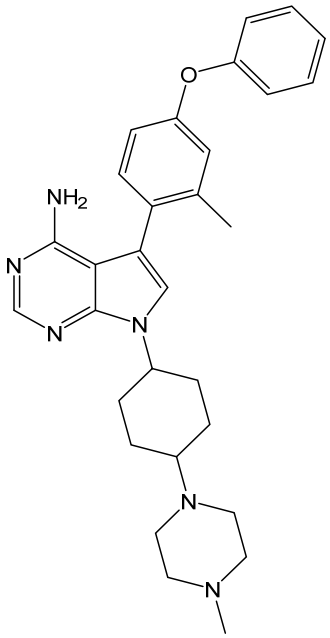
R_9 is selected from H, halo, alkyl, alkoxy, hydroxy, acyloxy, and amino;

R_{10} is H or alkoxy;

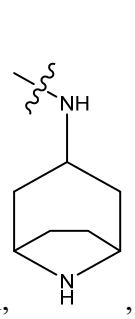
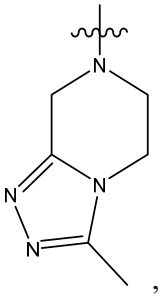
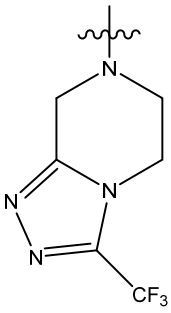
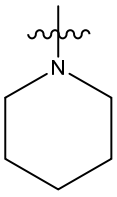
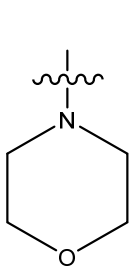
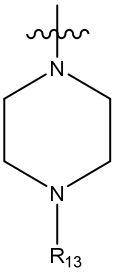
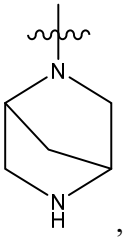
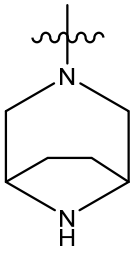
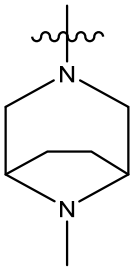
R_{11} is aryloxy, heteroaryloxy, arylalkyl, alkoxycarbonyl, ureido or -C(O)-aryl; and

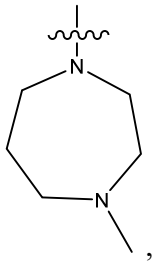
R_{12} is selected from H, halo, CN, alkyl, alkoxy, hydroxy, and acyloxy;

provided that the compound of Formula (I) is not



or

; and

if W is C, R_2, R_9 and R_{12} are each hydrogen, and R_{11} is unsubstituted phenyloxy, then

R_1 is not -$NHCH_2OH$, -$NHCH_2COOH$, -$NHCH_2CONH_2$, -$NHCH_2CH_2NH_2$, -$NH(CH_2)_2N(Me)_2$, -$NHCH_2$-pyridinyl, -NHCO-pyridyl, -C(O)OEt, -NH-tetrahydropyran, -$NHCH_2$pyrrolidinyl, -$NH(CH_2)_3$imidazolyl, -NHpyrrolidinonyl, , , , , , , , , , or

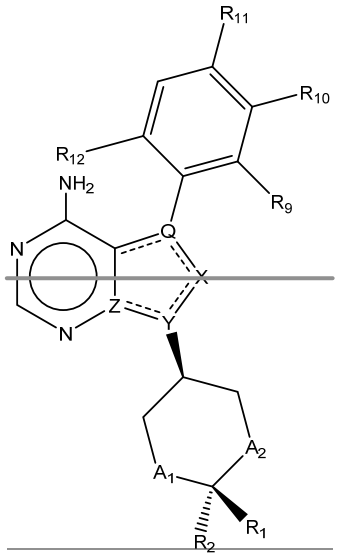


,

wherein R_{13} is selected from H, ethyl, isopropyl, t-butyl, $-CH_2OCH_3$, $-CH_2CH_2OH$ and $-CH_2CH_2OCH_3$; and

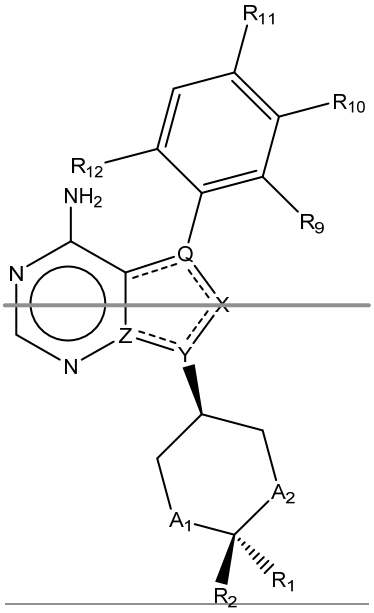
if W is N, R_9 and R_{12} are each hydrogen, and R_{11} is unsubstituted phenyloxy, then R_1 is not piperidinyl.

~~2. The compound of claim 1, having the structure:~~



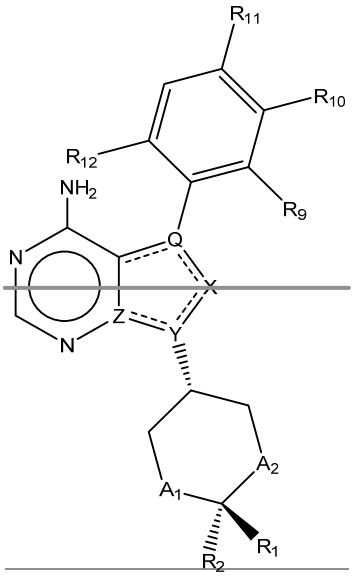
~~wherein R_2 is H.~~

~~3. The compound of claim 1, having the structure:~~



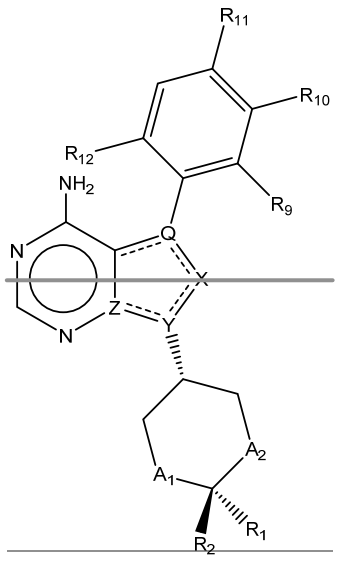
~~wherein R_2 is H.~~

~~4. The compound of claim 1, having the structure:~~

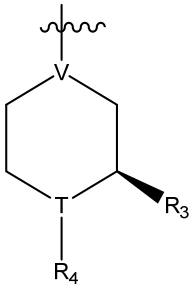


~~wherein R_2 is H.~~

~~5. The compound of claim 1, having the structure:~~



~~wherein R_2 is H.~~

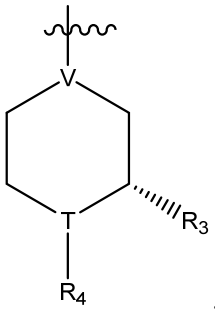


~~6~~2. The compound of any one of claims 1-5, wherein R_1 is , V is N or CH;

T is N or CH;

R_3 is alkyl; and

R_4 is H or alkyl.



~~7~~3. The compound of any one of claims 1-5, wherein R_1 is , V is N or CH;

T is N or CH;

R_3 is alkyl; and

R_4 is H or alkyl.

~~8~~4. The compound of any one of claims 1-~~7~~3, wherein

Q is C, X is C-R^a, R^a is H, Y is N and Z is C;

Q is C, X is C-R^a, R^a is halo, Y is N and Z is C;

Q is C, X is N, Y is C and Z is N;

Q is C, X is N, Y is N and Z is C;

Q is N, X is C-R^a, R^a is H, Y is C and Z is C;

Q is C, X is C-R^a, R^a is H, Y is C and Z is N; or

Q is C, X is C-R^a, R^a is H, Y is N and Z is C.

~~9. The compound of any one of claims 1-8, wherein~~

~~Q is C, X is N, Y is C and Z is N;~~

~~Q is C, X is C-R^a, R^a is H, Y is N and Z is C; or~~

~~Q is C, X is N, Y is N and Z is C.~~

~~10~~5. The compound of any one of claims 1-~~9~~4, wherein A_1 and A_2 are both CH_2.

~~11~~6. The compound of any one of claims 1-~~9~~4, wherein A_1 and A_2 are both O.

~~12. The compound of any one of claims 1-11, wherein W is N and R_2 is absent.~~

~~13. The compound of any one of claims 1-11, wherein W is C.~~

~~14~~7. The compound of claim ~~13~~1, wherein R_2 is selected from H, hydroxy and amino.

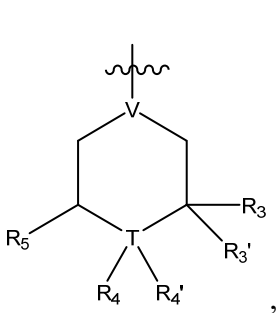
~~15~~8. The compound of any one of claims 1-~~14~~7, wherein R_1 is selected from alkyl, amino, cycloalkyl, heterocyclyl, heterocyclylalkyl, and heteroaryl.

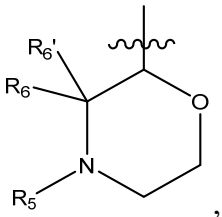
~~16. The compound of any one of claims 1-15, wherein R_1 is a 6-membered heterocyclyl.~~

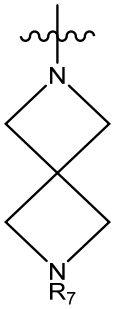
~~17. The compound of claim 16, wherein the 6-membered heterocyclyl comprises 2 nitrogen ring atoms.~~

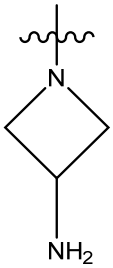
~~18. The compound of claim 17, wherein R_1 is a 1,4-piperazinyl ring.~~

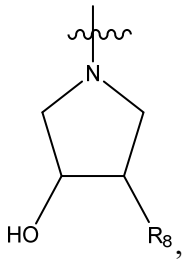
~~19~~. The compound of any one of claims 1-~~15~~8, wherein R_1 is selected from

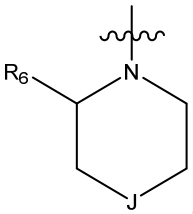


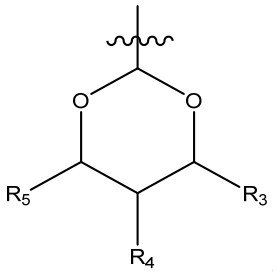
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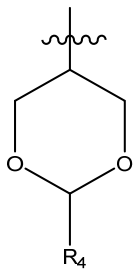
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,


,


,


,


, and


;

V is N or CH;

either T is N and R_4' is absent, or T is C;

J is selected from sulfonyl, C(H)sulfonamido, and >P(=O)-alkyl;

R_3 is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, amino, amido, cycloalkyl, heterocyclyl, carboxy, and alkoxycarbonyl;

R_3' is H or alkyl, or

R_3 and R_3' taken together with the carbon atom to which they are attached form a cycloalkyl;

R_4 is selected from H, halo, CN, alkyl, alkoxy, acyloxy, amino, and amido;

R_4' is H or alkyl;

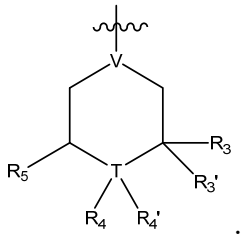
R_5 is H or alkyl;

R_6 and R_6' are each H;

R_6 and R_6' together with the carbon atom to which they are attached form an oxo;

R_7 is H or alkyl; and

R_8 is H, hydroxy, acyloxy, or amino.

2010. The compound of claim 199, wherein R_1 is 

.

21. The compound of claim 20, wherein V is N.

22. The compound of claim 20, wherein V is CH.

23. The compound of any one of claims 20-22, wherein T is N.

24. The compound of any one of claims 20-22, wherein T is C.

25. The compound of claim 19 or 20, wherein
W is C,
R_2 is H,
V is CH, and
T is N.

26. The compound of claim 19 or 20, wherein
W is C,
R_2 is H,
V is N and
T is C.

27. The compound of claim 19 or 20, wherein
W is C,
R_2 is H,
V is N and
T is N.

28. The compound of claim 19 or 20, wherein
W is N,

~~R_2 is absent,~~

~~V is CH and~~

~~T is N.~~

~~29~~11. The compound of any one of claim ~~19~~-~~28~~10, wherein R_3 is selected from H, alkyl, amino, cycloalkyl, heterocyclyl, carboxy, and alkoxycarbonyl.

~~30. The compound of any one of claims 19-29, wherein R_3 is H.~~

~~31. The compound of any one of claims 19-29, wherein R_3 is alkyl.~~

~~32. The compound of claim 31, wherein R_3 is methyl.~~

~~33. The compound of any one of claim 19-32, wherein each R_4 is independently selected from H, alkyl, amino, and amido.~~

~~34. The compound of any one of claim 19-33, wherein R_4 is H.~~

~~35. The compound of any one of claim 19-33, wherein R_4 is alkyl.~~

~~36. The compound of claim 35, wherein R_4 is methyl.~~

~~37. The compound of any one of claim 19-36, wherein R_5 is H.~~

~~38. The compound of any one of claims 19-37, wherein R_9 is H or halo.~~

~~39. The compound of any one of claims 19-38, wherein R_9 is H.~~

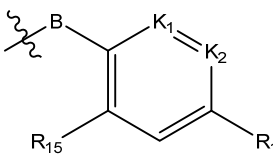
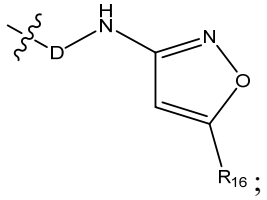
~~40~~12. The compound of any one of claims ~~19~~-~~37~~11, wherein R_9 is selected from halo, alkyl, alkoxy, hydroxy, acyloxy, and amino.

~~41. The compound of any one of claims 19-38, wherein R_9 is halo.~~

~~42. The compound of any one of claims 19-38, wherein R_9 is F.~~

~~43. The compound of any one of claims 19-42, wherein R_{12} is H or halo.~~

4413. The compound of any one of claims ~~19~~9-~~43~~12, wherein

R_{11} is selected from amido, , and ;

B is selected from -O-, CH_2, CHOH, NH, N(C_{1-6}alkyl) and carbonyl;

K_1 and K_2 are independently selected from N and CR_{13};

D is selected from -CH_2-C(O)-, -NH-C(O)-, N(C_{1-6}alkyl)-C(O), and -$CH_2S(O)_2$-;

R_{13} is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, alkoxycarbonyl, amino, amido, and alkoxycarbonyl;

R_{14} is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, alkoxycarbonyl, amino, amido, and alkoxycarbonyl;

R_{15} is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, alkoxycarbonyl, amino, amido, and alkoxycarbonyl; and

R_{16} is selected from H, halo, CN, alkyl, alkoxy, hydroxy, acyloxy, amino, amido, and alkoxycarbonyl.

~~45. The compound of claim 44, wherein B is -O-.~~

~~46. The compound of claim 44 or 45, wherein K_1 is CR_{13}.~~

~~47. The compound of any one of claims 44-46, wherein R_{13} is selected from H, halo, CN, and alkyl.~~

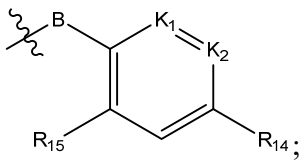
~~48. The compound of any one of claims 44-46, wherein R_{13} is H or F.~~

~~49. The compound of any one of claims 44-48, wherein R_{14} is H or alkyl.~~

~~50. The compound of any one of claims 44-49, wherein R_{15} is H or halo.~~

~~51. The compound of any one of claims 44-50, wherein D is -NHC(O)-.~~

~~52. The compound of any one of claims 44-51, wherein R_{16} is H or alkyl.~~



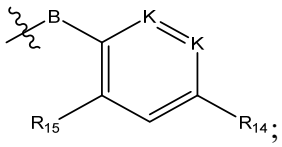
~~53~~14. The compound of claim ~~44~~13, wherein R_{11} is

B is O;

K_1 and K_2 are each CH;

R_{14} is H; and

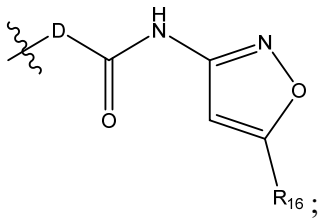
R_{15} is H.



~~54~~15. The compound of claim ~~44~~13, wherein R_{11} is

K_1 and K_2 are each N; and

R_{14} and R_{15} are each H.



~~55~~16. The compound of claim ~~44~~13, wherein R_{11} is

D is NH; and

R_{16} is alkyl.

~~56. A method of co-inhibiting HCK and BCL-2 in a cell, comprising contacting the cell with a compound of formula (I) according to any one of claims 1-55 and a BCL-2 inhibitor.~~

~~57. A method of killing a cell having an FLT3-ITD mutation, comprising contacting the cell with a compound of formula (I) according to any one of claims 1-55 and a BCL-2 inhibitor.~~

~~58. The method of claim 56 or 57, wherein the compound of formula (I) is a HCK inhibitor~~.

~~59. The method of any one of claims 56-58, further comprising contacting the cell with an FLT3-ITD inhibitor.~~

~~60. The method of claim 58, wherein the HCK inhibitor is a dual HCK/FLT3-ITD inhibitor.~~

~~61~~17. Use of a compound of formula (I) according to any one of claims 1-16 in the manufacture of a medicament for ~~A method of~~ treating acute myeloid leukemia, ~~comprising~~ wherein the compound of formula (I) is to be administered conjointly ~~administering to a subject a compound of formula (I) according to any one of claims 1-55 and~~ with a BCL-2 inhibitor.

~~62~~18. The use~~method~~ of claim ~~61~~17, wherein the subject has FLT3-ITD+ acute myeloid leukemia.

~~63. The method of claim 61 or 62, wherein the subject has malignant hematopoiesis and/or non-malignant multilineage hematopoiesis characterized by cells having one or more mutations in a gene selected from DNMT3A, IDH2, IDH1, NPM1, TET2, CEBPA, ASXL1, EZH2, SETBP1, SMC3, KIT, NRAS, and WT1.~~

~~64~~19. The use~~method~~ of any one of claims 17-18~~any one of claims 61-63~~, wherein the compound of formula (I) is a HCK inhibitor.

~~65~~20. The use~~method~~ of any one of claims ~~61-64~~17-19, wherein the medicament is for ~~further comprising~~ conjoint~~ly~~ administ~~ering~~ration with a FLT3-ITD inhibitor.

~~66~~21. The use~~method~~ of claim ~~64~~19, wherein the HCK inhibitor is a dual HCK/FLT3-ITD inhibitor.

~~67. The method of claim 65 or 66, wherein the HCK inhibitor, the FLT3-ITD inhibitor, and the BCL-2 inhibitor are administered simultaneously or sequentially in separate unit dosage forms.~~

~~68. The method of claim 64, comprising administering a single unit dosage form comprising an HCK inhibitor, a BCL-2 inhibitor, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.~~

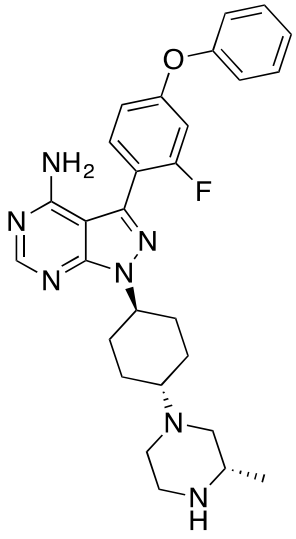
~~69. The method of claim 68, wherein the single unit dosage form further comprises an FLT3-ITD inhibitor, or wherein the HCK inhibitor is a dual HCK/FLT3-ITD inhibitor.~~

~~70~~22. The use~~method~~ of ~~any one of~~ claim~~s 59, 65, 67, and 69,~~20 ~~wherein~~ the FLT3-ITD inhibitor is selected from AC220, sorafenib, PKC412, CEP-701, UNC2025, MLN518, KW-2449 and AMG-925, sunitinib, SU5614, AC2206, crenolanib, and PLX3397.

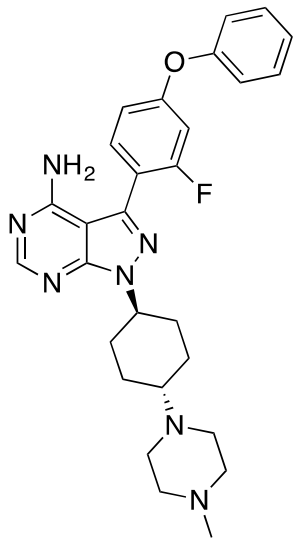
~~71~~23. The use~~method~~ of any one of ~~preceding~~ claims 17-22, wherein the BCL-2 inhibitor is selected from AT-101, TW-37, TM-1206, gossypolic acid, gossypolonic acid, apogossypol, apogossypolone, A385358, ABT-737, ABT-263, ABT-199, WEHI-539, BXI-61, BXI-72, obatoclax, JY-1-106, and SAHB peptides.

~~72. The method of claim 71, wherein the BCL-2 inhibitor is selected from gossypol, obatoclax, ABT-737, ABT-199, and ABT-263.~~

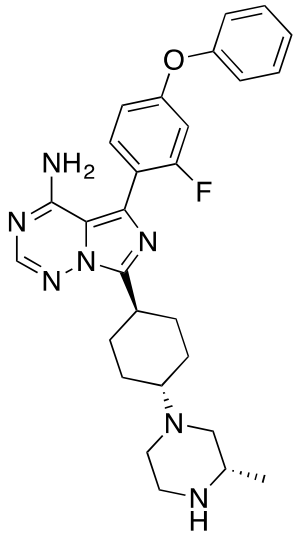
~~73~~24. The use~~method~~ of claim ~~72~~23, wherein the BCL-2 inhibitor is ABT-199.



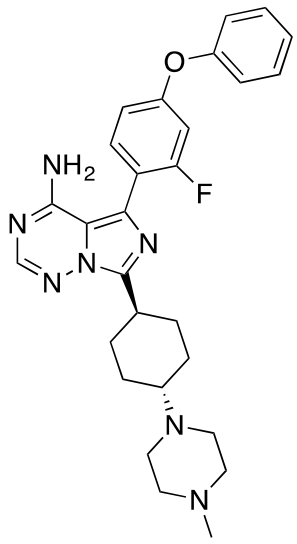
~~74~~25. The use ~~method~~ of claim ~~73~~19, wherein the HCK inhibitor is and the BCL-2 inhibitor is ABT-199.



~~75~~26. The use~~method~~ of claim ~~73~~19, wherein the HCK inhibitor is and the BCL-2 inhibitor is ABT-199.



~~76~~27. The use~~method~~ of claim ~~73~~19, wherein the HCK inhibitor is and the BCL-2 inhibitor is ABT-199.



~~77~~28. The use~~method~~ of claim ~~73~~19, wherein the HCK inhibitor is and the BCL-2 inhibitor is ABT-199.

~~78. The method of claim 73, wherein the FLT3-ITD inhibitor is AC220 and the BCL-2 inhibitor is ABT-199.~~

~~79. The method of claim 72, wherein the FLT3-ITD inhibitor is SU5614 and the BCL-2 inhibitor is ABT-737.~~

~~80. The method of any preceding claim, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is each present as a pharmaceutically acceptable salt.~~

~~81. The method of any preceding claim, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is each present in a pharmaceutically acceptable composition.~~

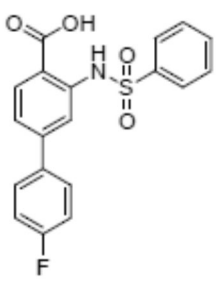
~~82. The method of any preceding claim, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is administered conjointly with dexamethasone.~~

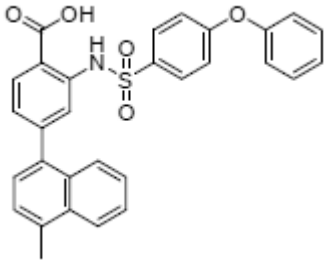
~~83~~29. The use~~method~~ of any ~~preceding~~one of claims 17-28, wherein the ~~HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor~~ medicament is ~~administered~~ for conjoint~~ly~~ administration with an anti-apoptosis agent.

~~84~~30. The use~~method~~ of claim ~~83~~29, wherein the anti-apoptosis agent is tretinoin, GGTI 298 TFA salt, BTSA1, AT406, SM-406, elesclomol, STA-4783, Ganetespib, STA-9090, NQDI-1, or zoledronic acid.

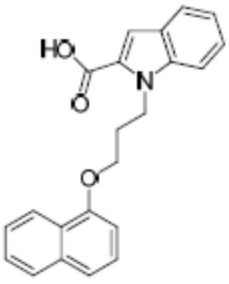
~~85~~31. The use~~method~~ of any ~~preceding~~one of claims 17-30, wherein the ~~HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor~~ medicament is ~~administered~~for conjoint~~ly~~ administration with an Mcl-1 inhibitor.

~~86~~32. The use~~method~~ of claim ~~85~~31, wherein the Mcl-1 inhibitor is

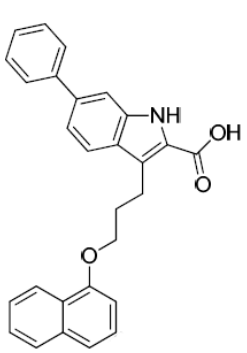
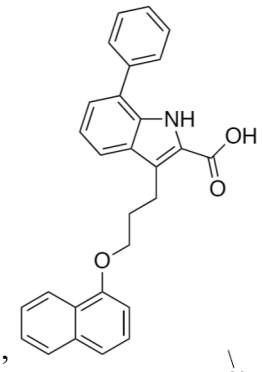
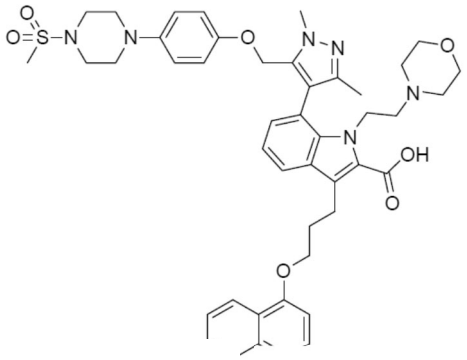
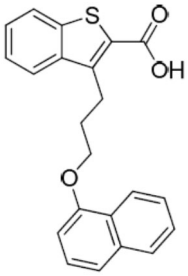
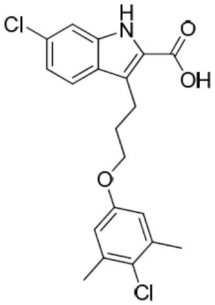
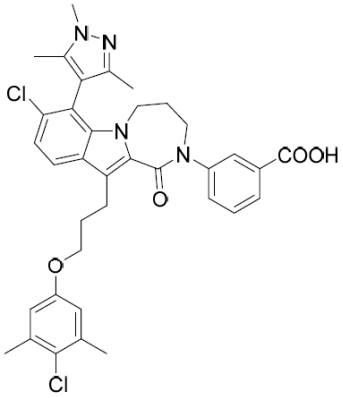
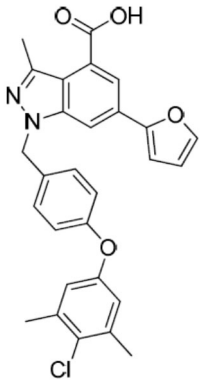
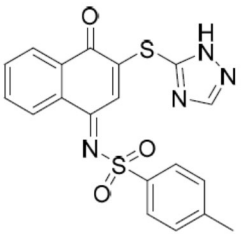
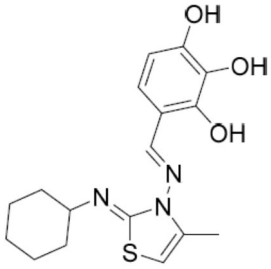
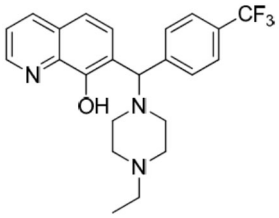
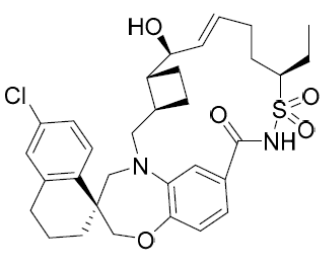
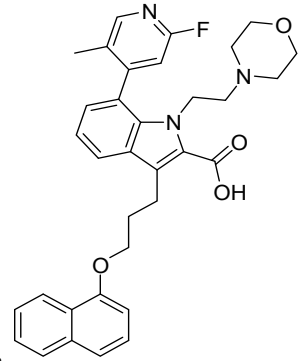


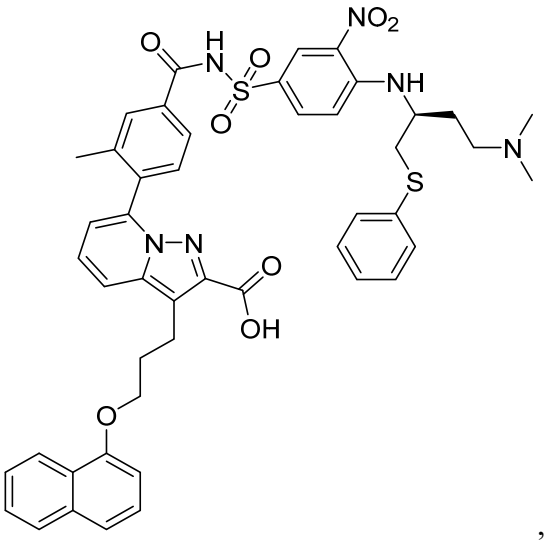
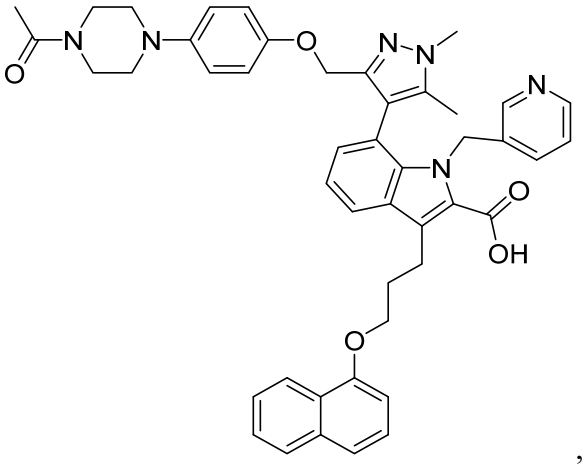
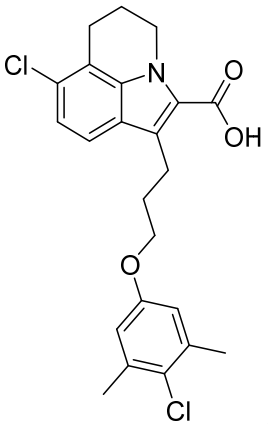
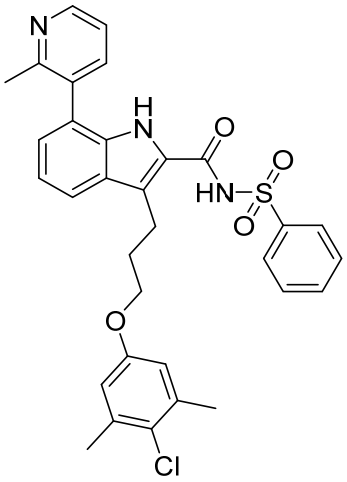
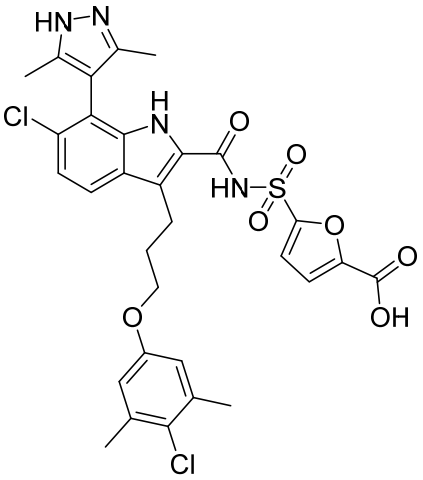
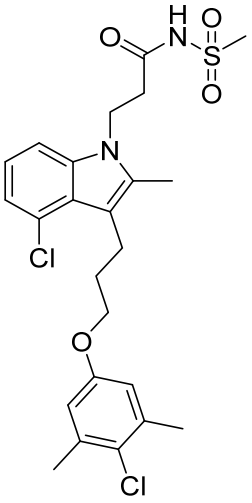
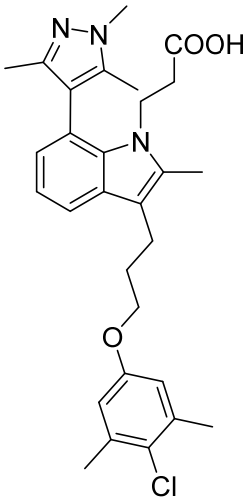
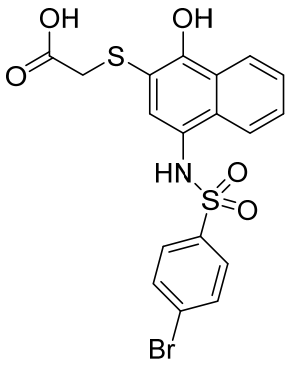
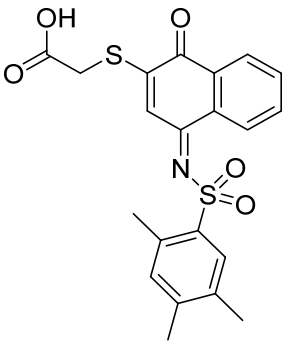
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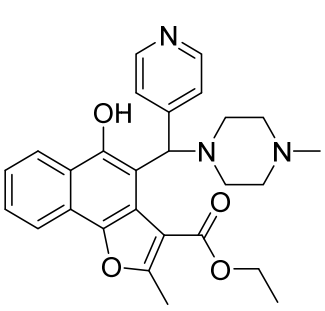
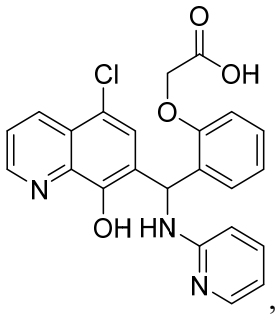
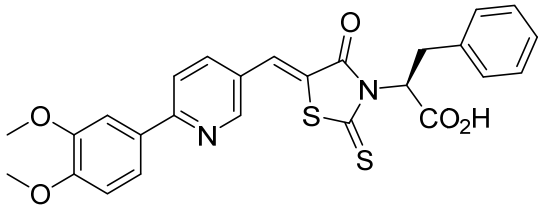
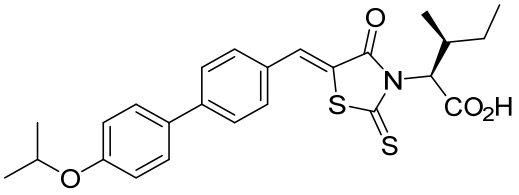
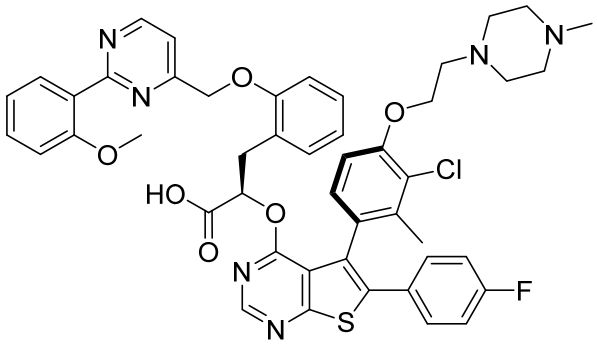
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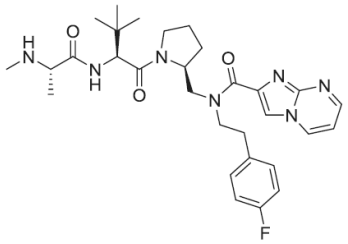
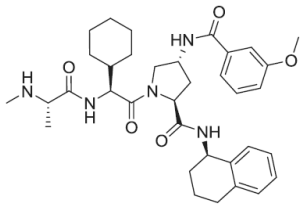
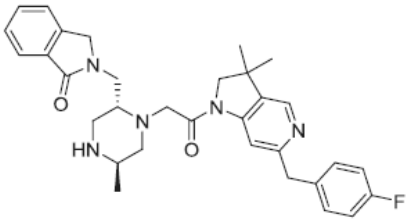
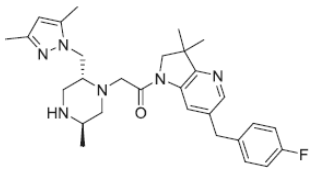
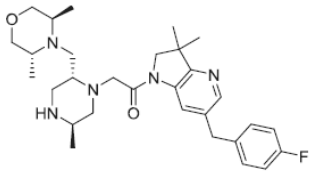













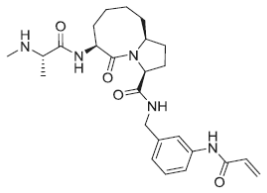
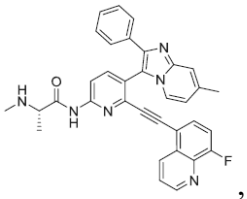
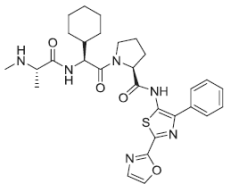
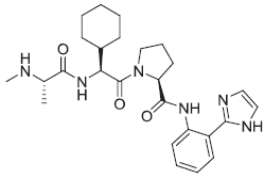
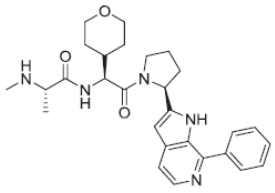
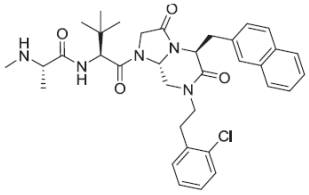
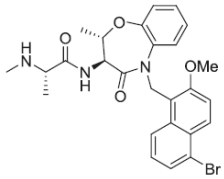
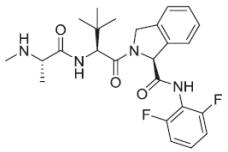
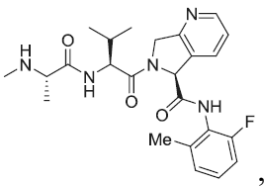
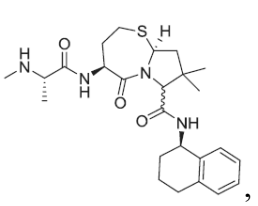
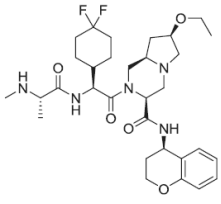
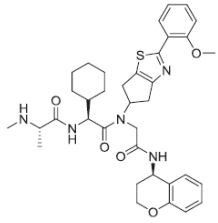
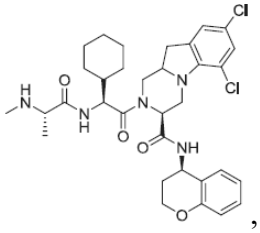
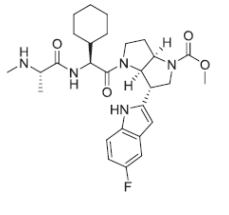
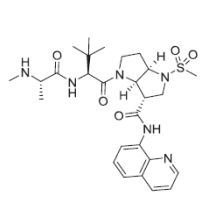
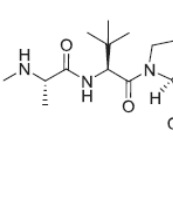

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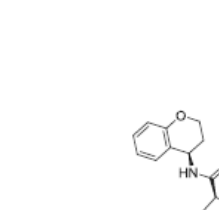
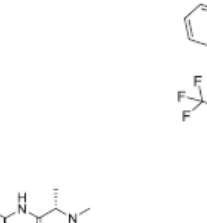
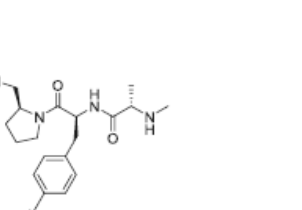
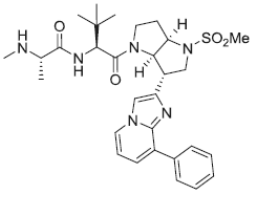
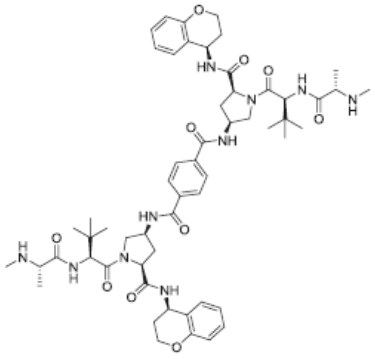






8733. The usemethod of any one of preceding claims 17-33, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor medicament is administeredfor conjointly administration with an IAP antagonist.

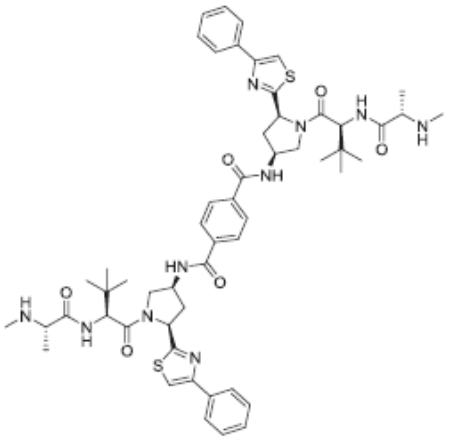
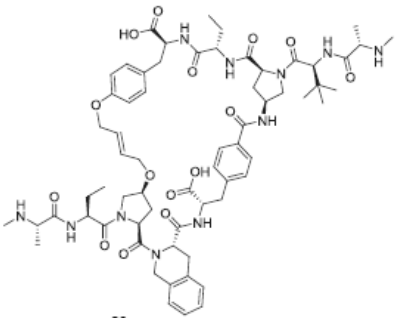
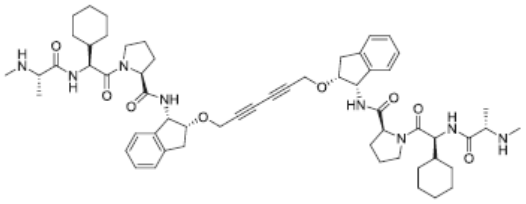
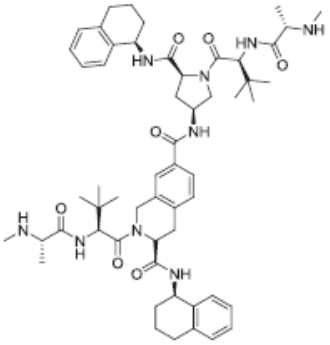
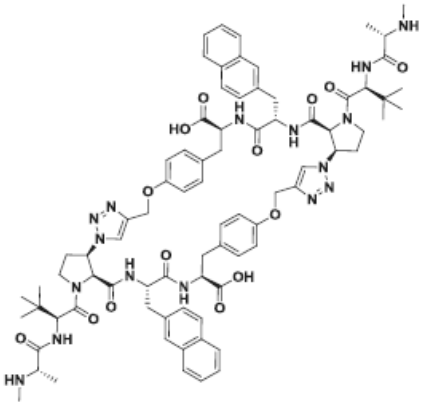
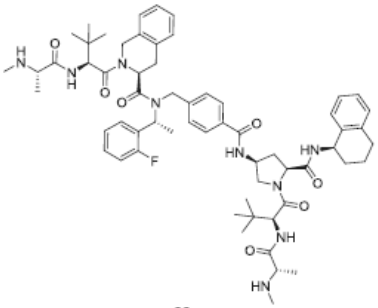
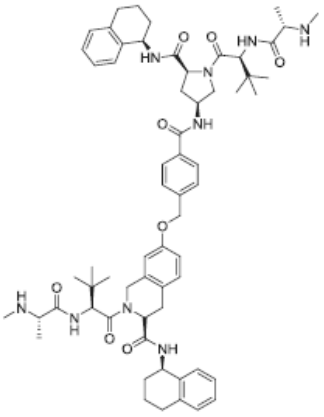
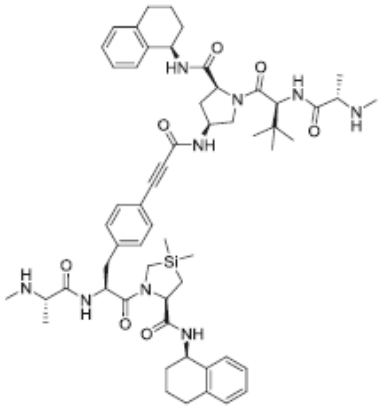
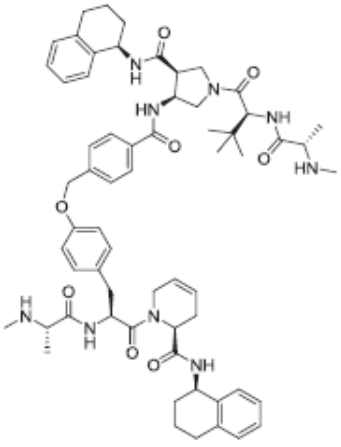
8834. The usemethod of claim 33, wherein the IAP antagonist is

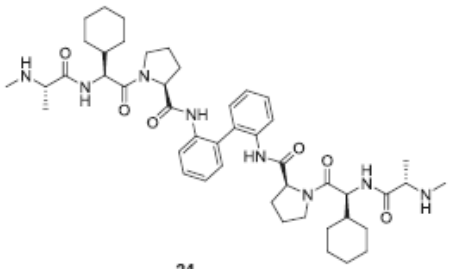
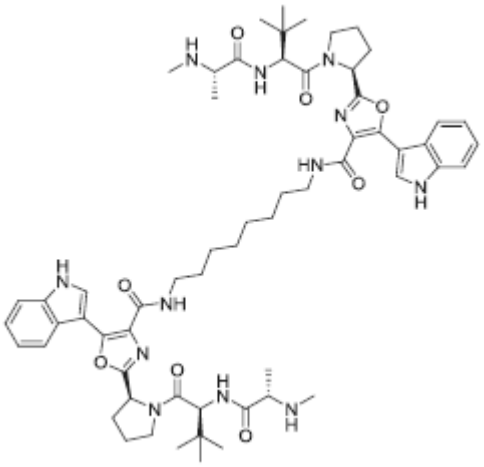
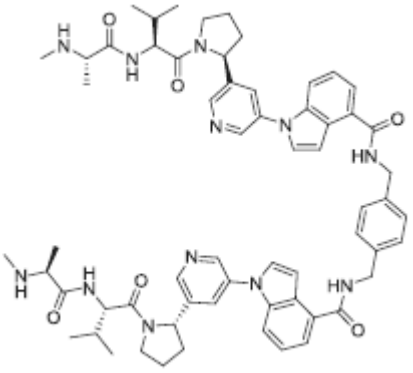
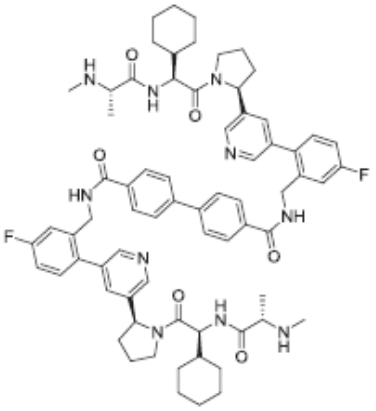
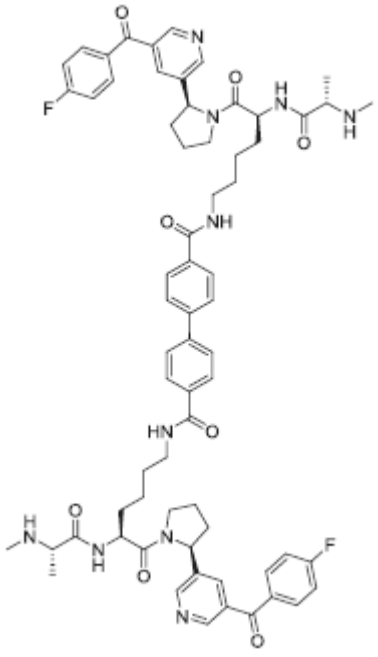
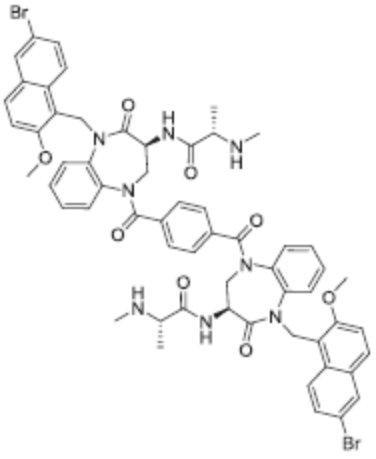






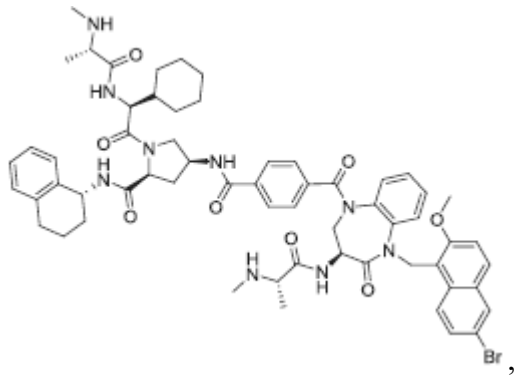
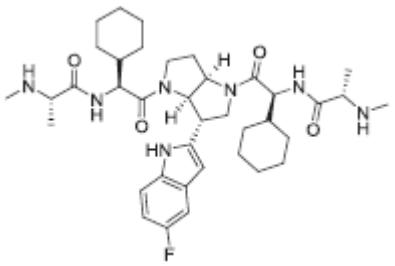
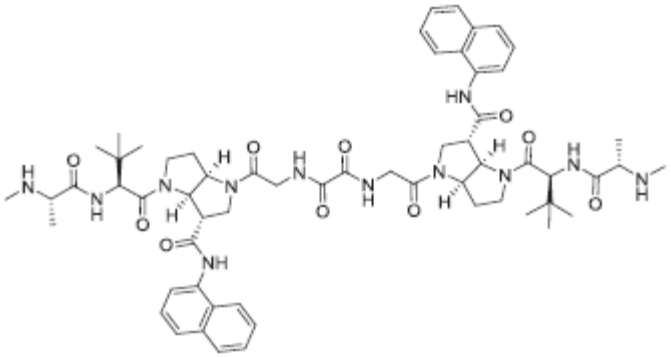
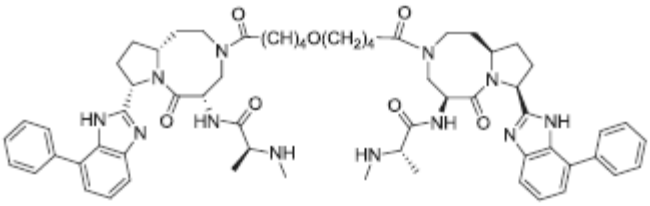
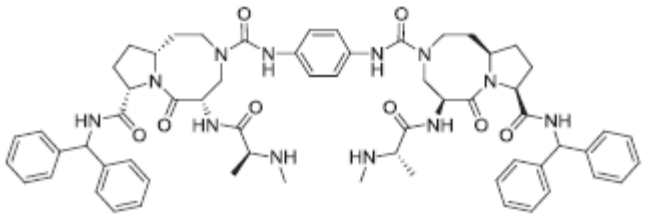
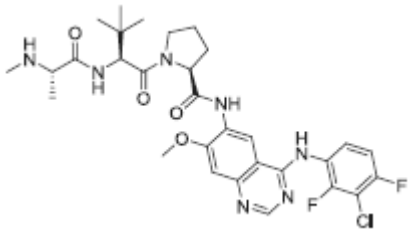
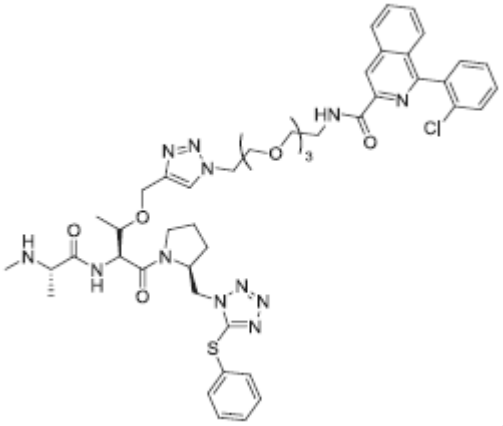
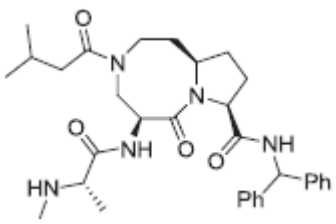

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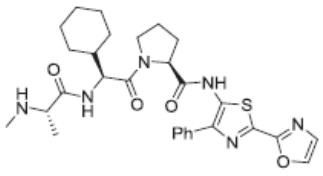
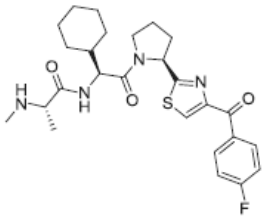
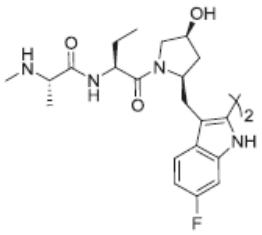
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~~89~~35. The use~~method~~ of any one of ~~preceding~~ claims 17-34, wherein the medicament is for conjoint administration with ~~wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is administered conjointly~~ with a cell-cycle inhibitor.

~~90~~36. The use~~method~~ of claim ~~89~~35, wherein the cell cycle inhibitor is selected from palbociclib, ribociclib, abemaciclib, flavopiridol, AT9283, alisertib, and MK-1775.

37. A compound of formula (I) according to any one of claims 1-15 for use in treating treating acute myeloid leukemia conjointly with a BCL-2 inhibitor.

38. The compound for use of claim 37, wherein the subject has FLT3-ITD+ acute myeloid leukemia.

39. The compound for use of any one of claims 37-38, wherein the compound of formula (I) is a HCK inhibitor.

40. The compound for use of any one of claims 36-37, wherein the compound of formula (I) is for conjoint administration with a FLT3-ITD inhibitor.

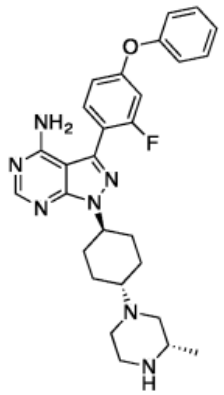
41. The compound for use of claim 39, wherein the HCK inhibitor is a dual HCK/FLT3-ITD inhibitor.

42. The compound for use of claim 40, wherein the FLT3-ITD inhibitor is selected from AC220, sorafenib, PKC412, CEP-701, UNC2025, MLN518, KW-2449 and AMG-925, sunitinib, SU5614, AC2206, crenolanib, and PLX3397.

43. The compound for use of any one of claims 37-42, wherein the BCL-2 inhibitor is selected from AT-101, TW-37, TM-1206, gossypolic acid, gossypolonic acid, apogossypol, apogossypolone, A385358, ABT-737, ABT-263, ABT-199, WEHI-539, BXI-61, BXI-72, obatoclax, JY-1-106, and SAHB peptides.

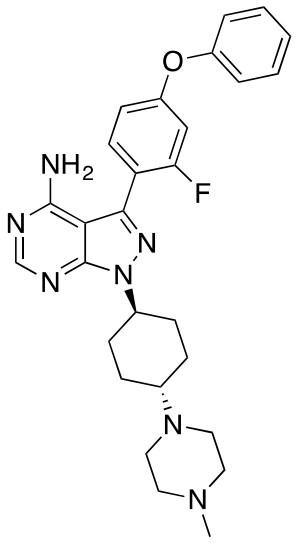
44. The compound for use of claim 43, wherein the BCL-2 inhibitor is ABT-199.

45. The compound for use of claim 39, wherein the HCK inhibitor is



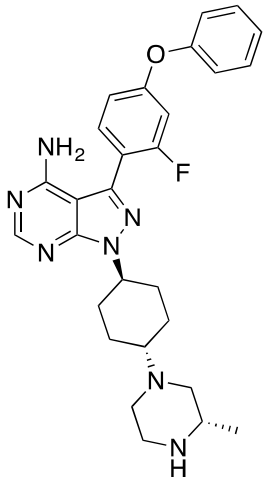
and the BCL-2 inhibitor is ABT-199.

46. The compound for use of claim 39, wherein the HCK inhibitor is



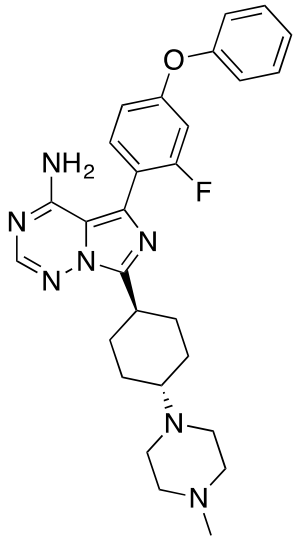
and the BCL-2 inhibitor is ABT-199.

47. The compound for use of claim 39, wherein the HCK inhibitor is



and the BCL-2 inhibitor is ABT-199.

48. The compound for use of claim 39, wherein the HCK inhibitor is

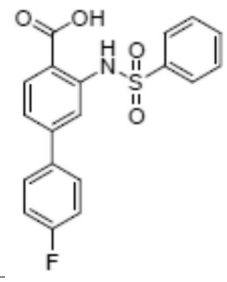


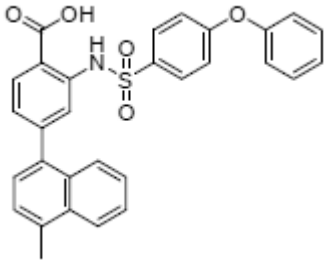
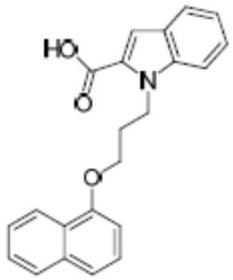
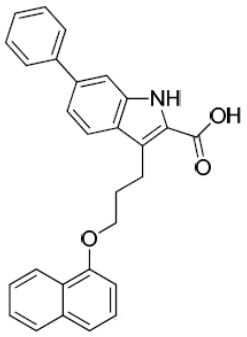
and the BCL-2 inhibitor is ABT-199.

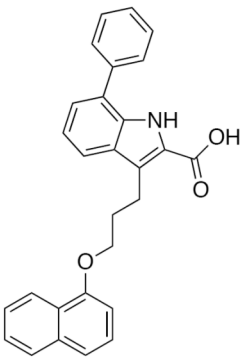
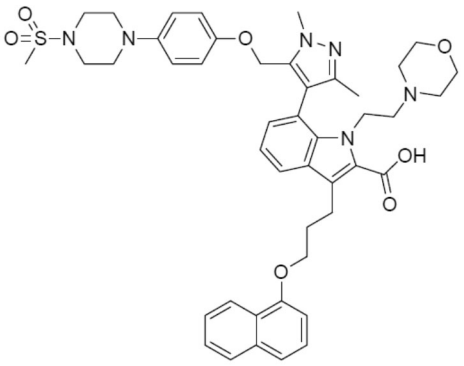
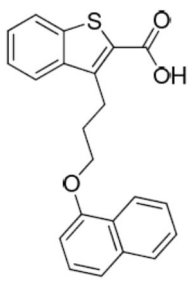
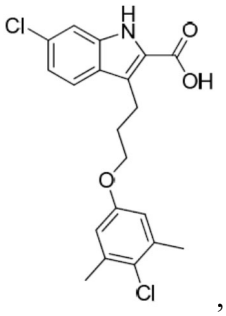
49. The compound for use of any one of claims 37-48, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is for conjoint administration with an anti-apoptosis agent.

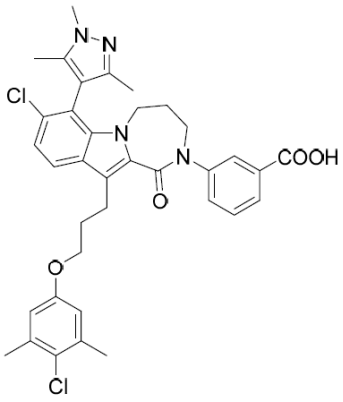
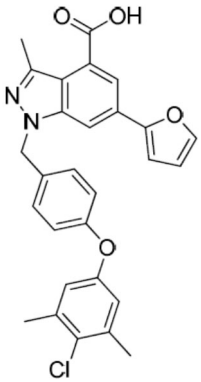
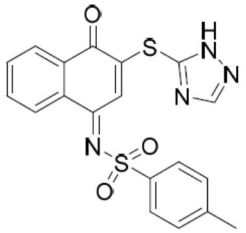
50. The compound for use of claim 49, wherein the anti-apoptosis agent is tretinoin, GGTI 298 TFA salt, BTSA1, AT406, SM-406, elesclomol, STA-4783, Ganetespib, STA-9090, NQDI-1, or zoledronic acid.

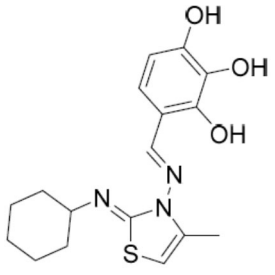
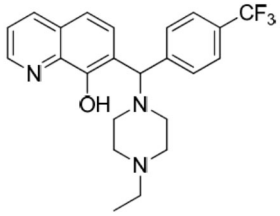
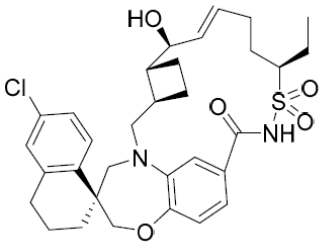
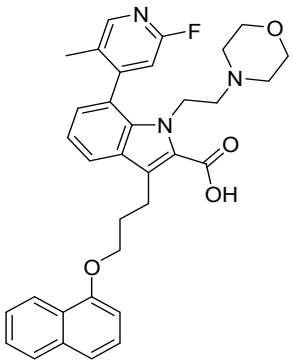
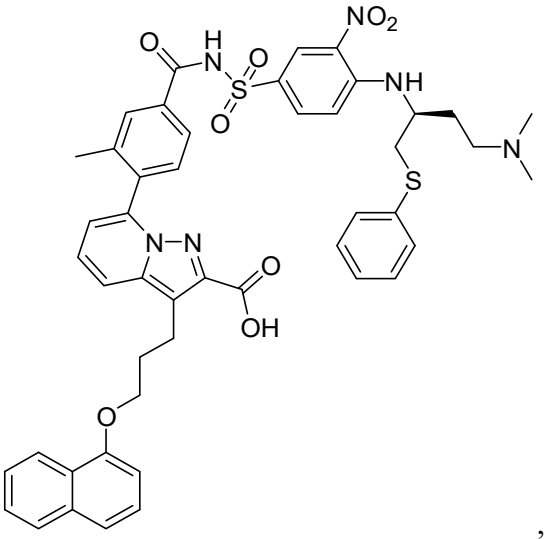
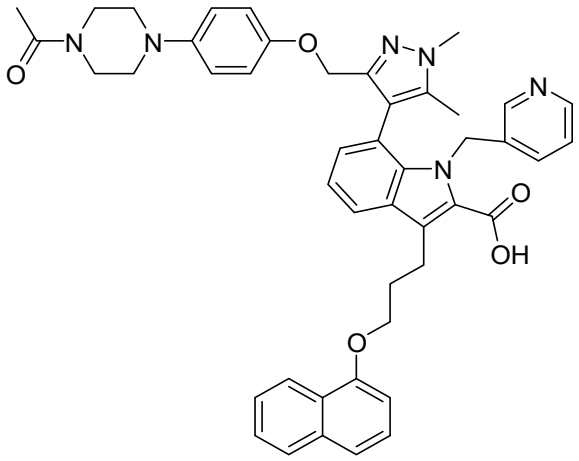
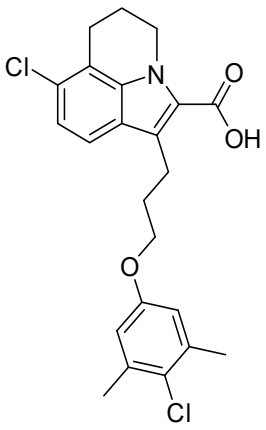
51. The compound for use of any one of -claims 37-50, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is for conjoint administration with an Mcl-1 inhibitor.

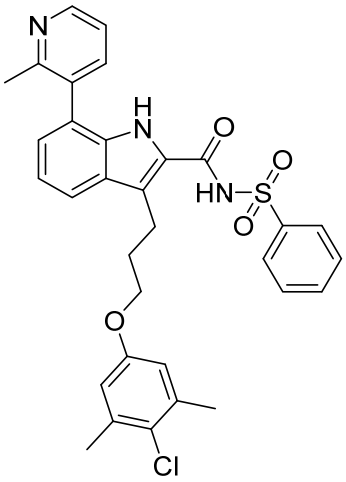
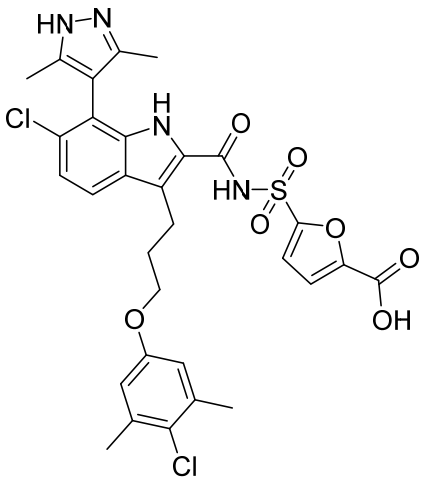
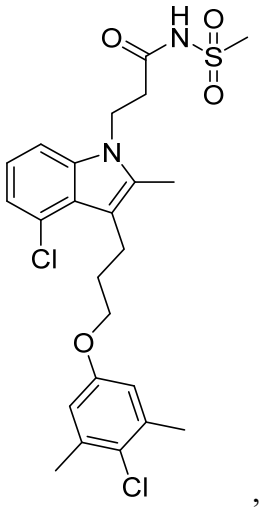
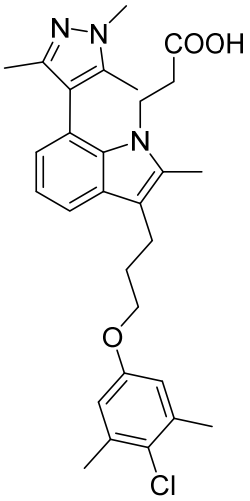
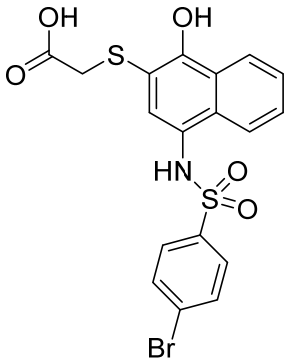
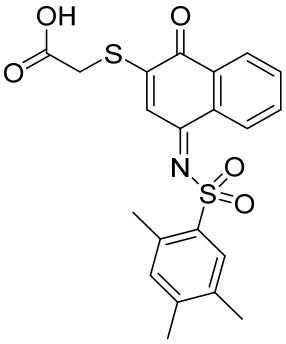
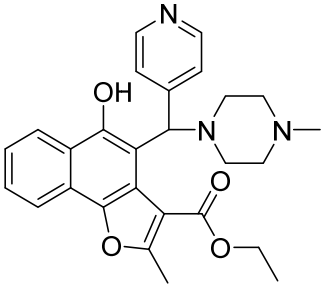
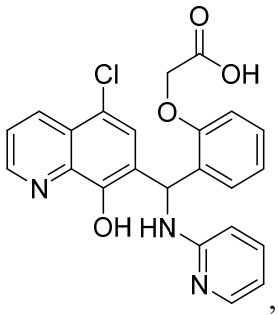
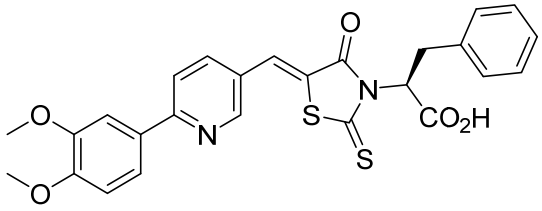
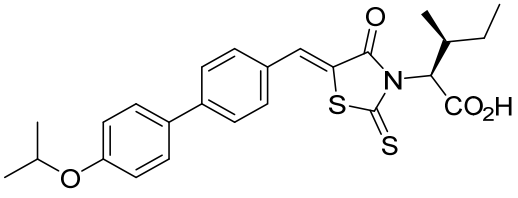
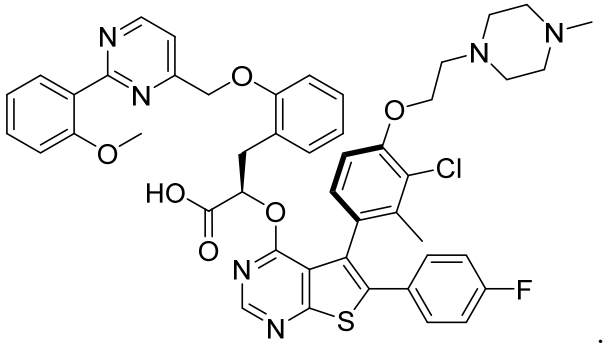
52. The compound for use of claim 51, wherein the Mcl-1 inhibitor is ,

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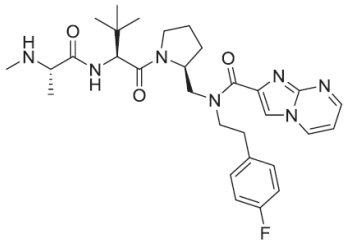
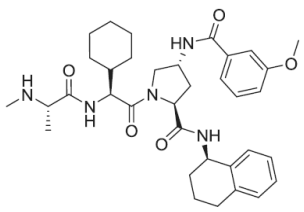
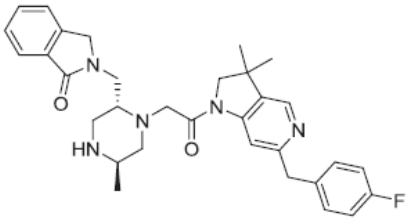
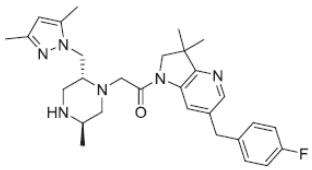
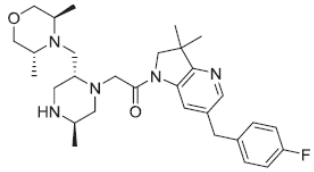
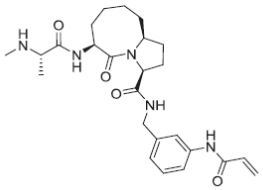
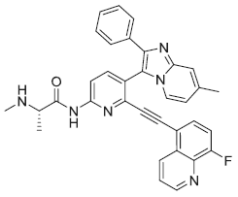
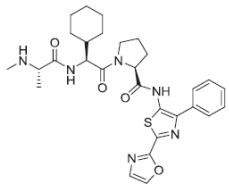
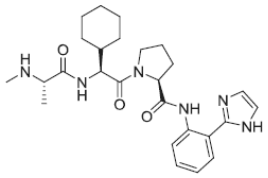
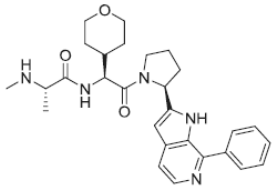
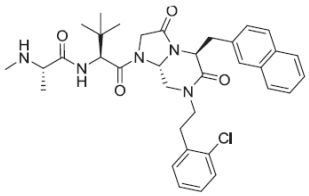
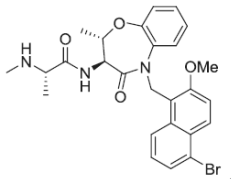
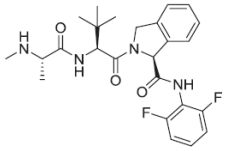
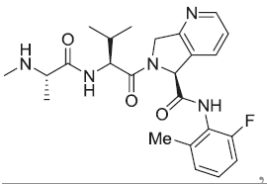
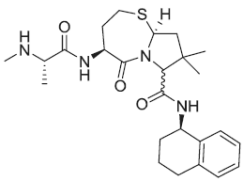
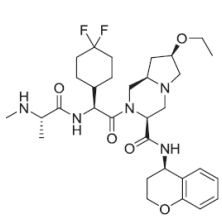
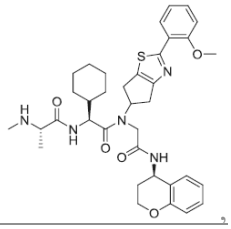
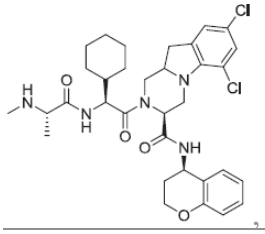
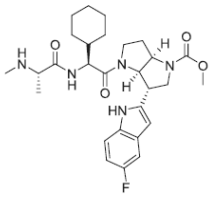
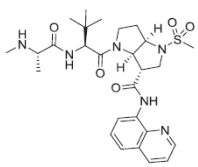
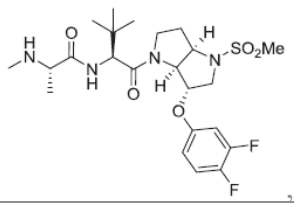
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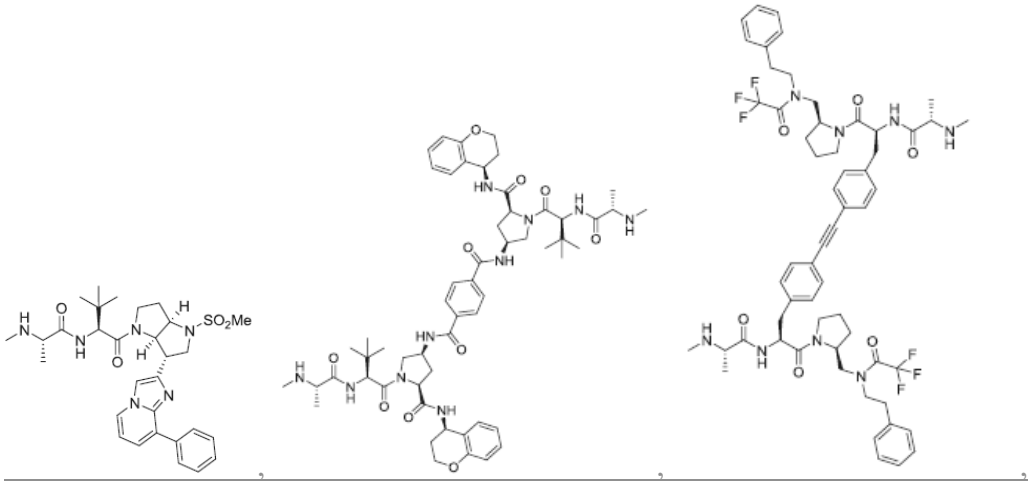

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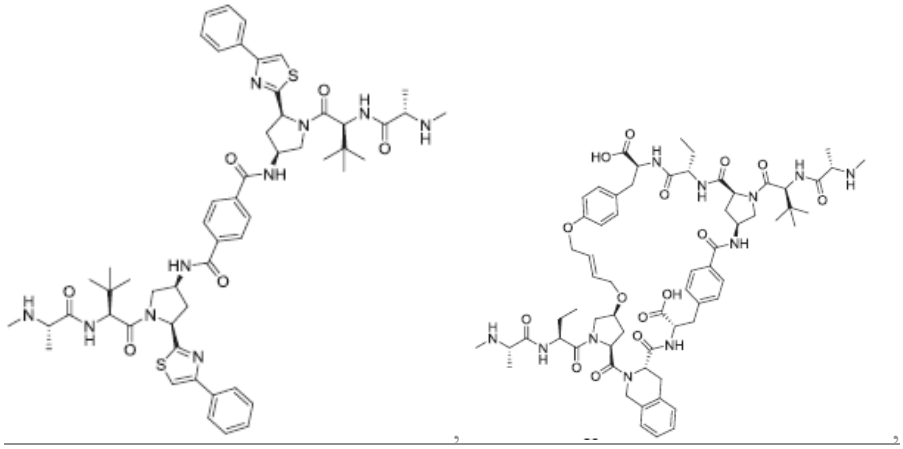

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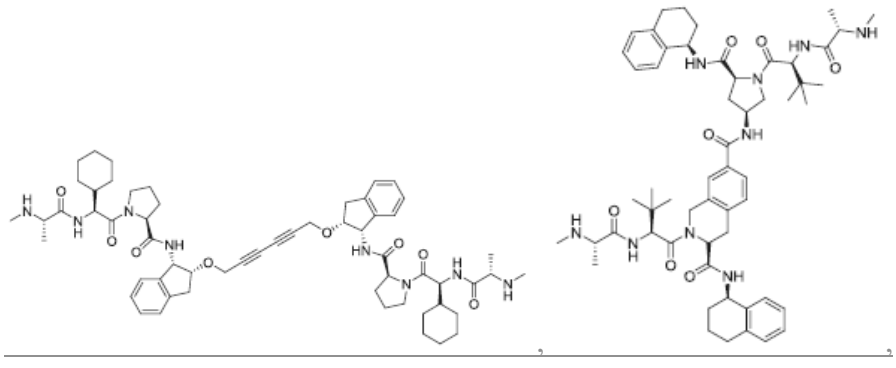
53. The compound for use of any one of- claims 37-52, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is for conjoint administration with an IAP antagonist.

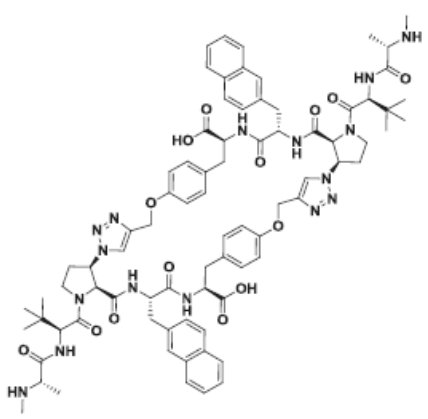
54. The compound for use of claim 53, wherein the IAP antagonist is

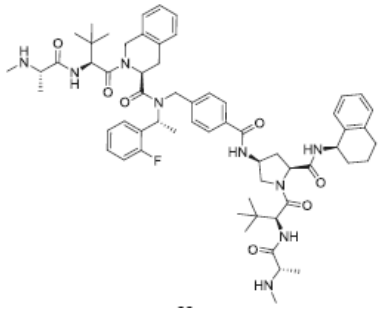






















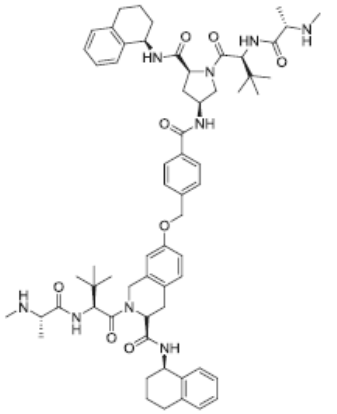


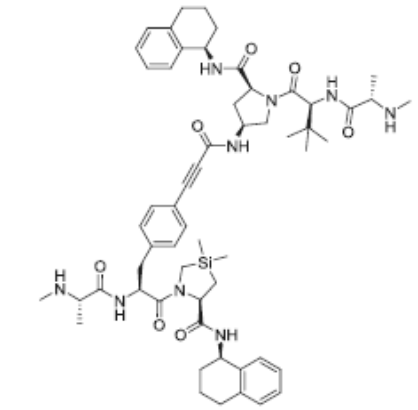


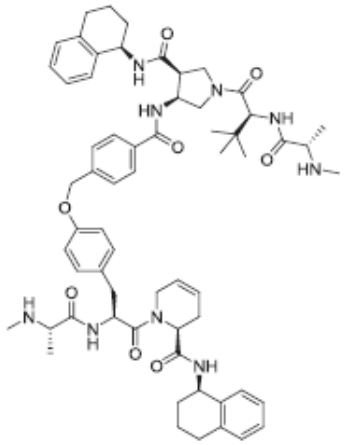


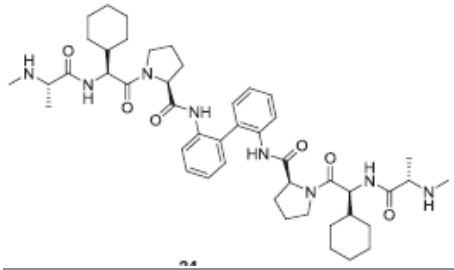


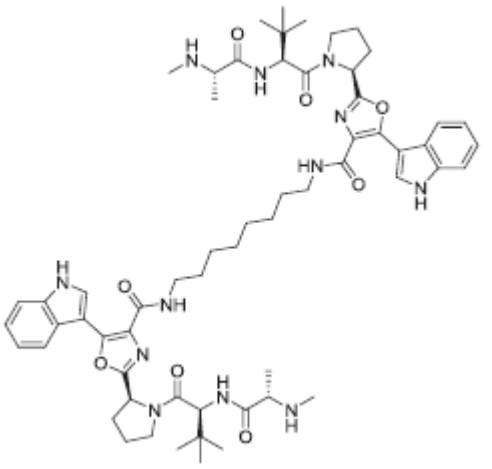


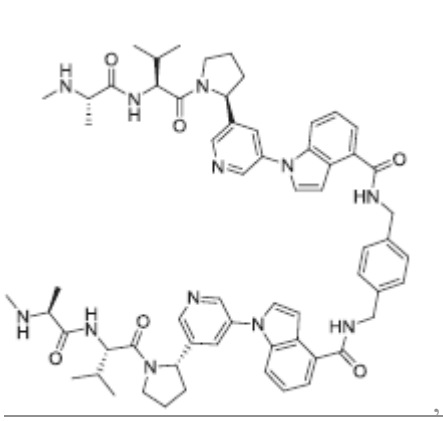


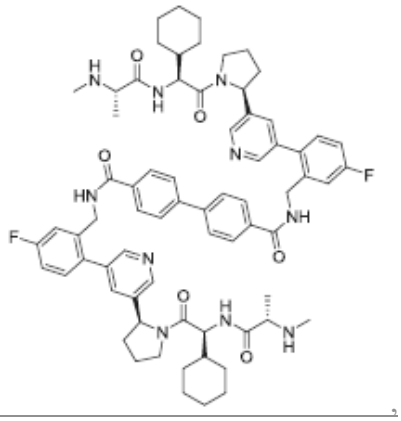


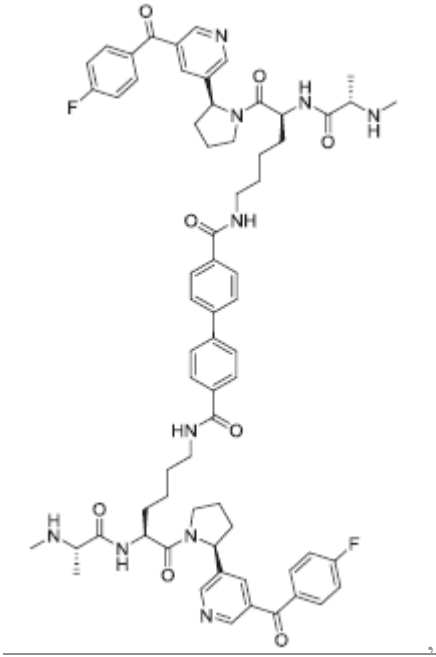


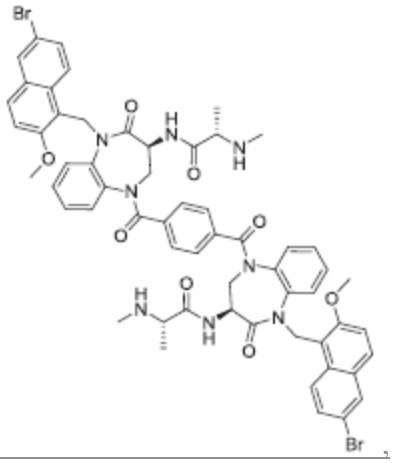


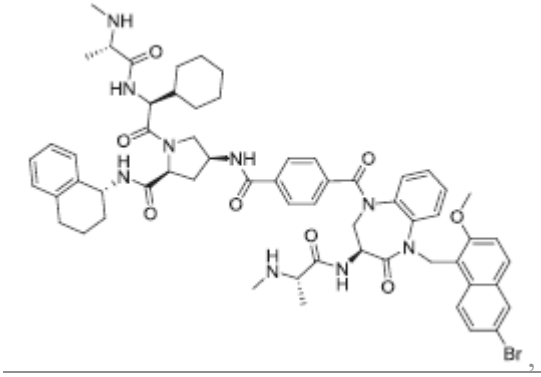


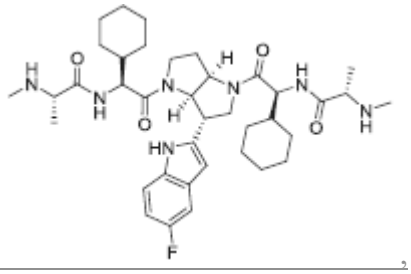


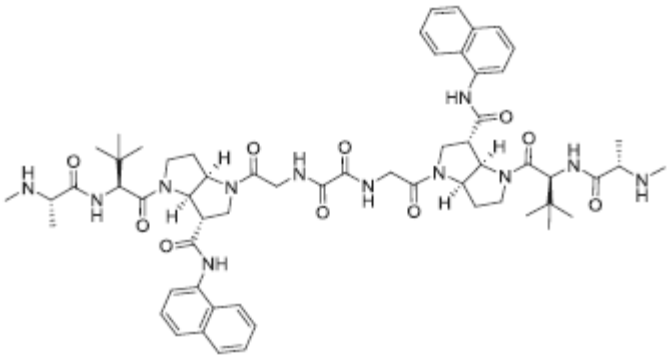
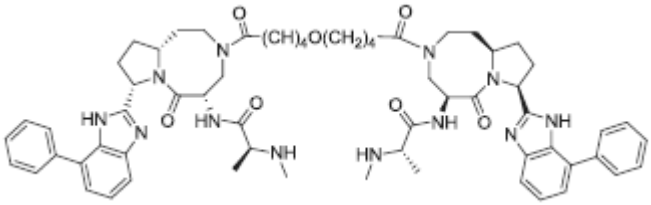
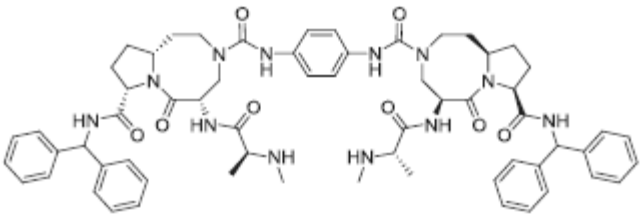
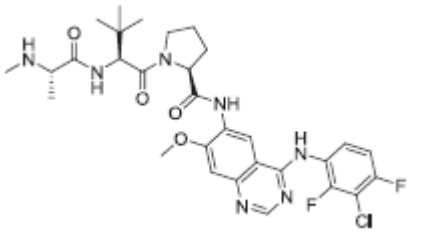
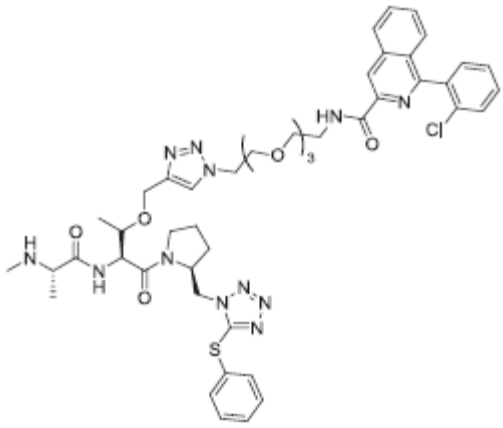
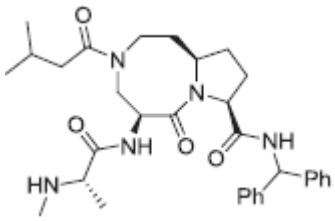
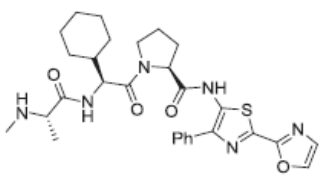
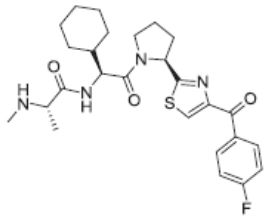
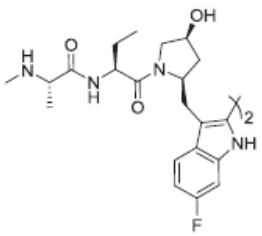











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55. The compound for use of any one of claims 37-34, wherein the HCK inhibitor, and/or FLT3-ITD inhibitor, and/or the BCL-2 inhibitor is for conjoint administration with a cell-cycle inhibitor.

56. The compound for use of claim 55, wherein the cell--cycle inhibitor is selected from palbociclib, ribociclib, abemaciclib, flavopiridol, AT9283, alisertib, and MK-1775.