[0015] Figure 5: A) Compound 1 expands mobilized peripheral blood-derived CD34+ and CD34+CD45RA- cell populations ex vivo. Although the total cell count was the same in DMSO and compound 1 treated cells, CD34+ population was more than twice that of DMSO. Similarly, CD34+CD45RA- population was more than three times in the compound 1 treated group vs. DMSO. This observation was enhanced with the co-treatment with SR1. B) Compound 1 enhances expansion of the cord blood-derived CD34+ and CD34+CD45RA- cells during 7-day incubation. C) Compound 1 exerts the positive effect on the in vitro expansion of the cord blood-derived CD34+ and CD34+CD45RA- cells during 12-day incubation.

[0016] Figure 6: CD34+ mPB cells were cultured for ten days in the presence of the vehicle (DMSO), SR1, compound 1, and a combination of compound1 and SR1. The outcome of 50,000 and 500,000 treated cells were transplanted in NSG mice and the bone marrow analysis was performed after 13 week post-transplantation to evaluate the human hematopoietic engraftment. At any give cell dose, CD34+ mPB cells treated with Compound 1 engrafted better than that of DMSO. Interestingly, the percentage of the human CD45+ cells in the BM was highest in NSG mice which received cells treated with the combination (compound 1+SR1) compared to the individual compounds.

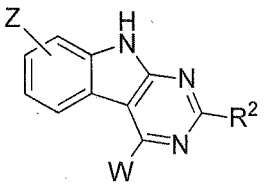
[0017] Figure 7: A) Compound 1 expanded cells are capable of reconstituting human hematopoietic cells in NSG mice. The outcome of 5,000 CD34+ CB Cells treated with vehicle (DMSO), SR1, compound1 and combination were transplanted in immunocompromised NSG mice. After 8- weeks post transplantation, the bone marrow analysis showed a human CD45+ engraftment in all treatment groups except DMSO. The cells treated with the combination (compound1+SR1) showed the highest engraftment levels. B) During 12-day in vitro incubation Compound 40 prevents the loss of human hemopoietic cells with ability to engraft NSG mouse bone marrow.

[0018] Figure 8: Expansion of primitive cell phenotypes ($CD34^+$, $CD34^+CD90^+$, and $CD34^+CD45RA^+$) in bioreactor using the fed-batch approach as measured by flow cytometry. FB control =fed-batch without Compound 40, Cpd 40= fed-batch with Ccompound 40.

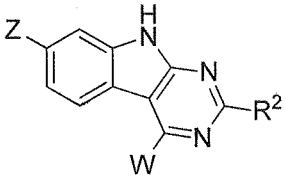
SUMMARY OF THE DISCLOSUREINVENTION

[0019] The inventors have discovered certain pyrimido[4,5-b]indole derivatives. These compounds are useful to expand hematopoietic stem cell populations, particularly, human hematopoietic stem cell populations. The compounds are also useful in the medical treatment of diseases that involve hematopoietic stem cells.

[0020] According to an aspect, the disclosure ~~invention~~ provides for compounds of the following general formulas I, II, III, IV, V and VI:



I



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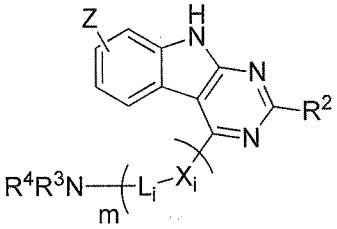

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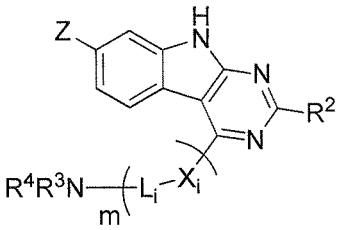

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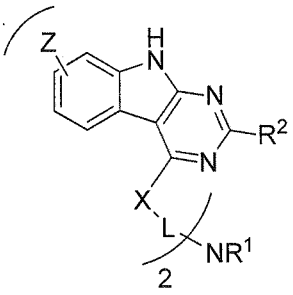
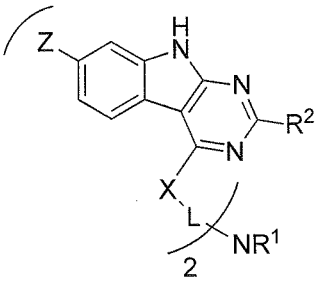
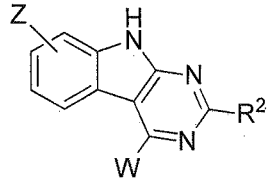


V

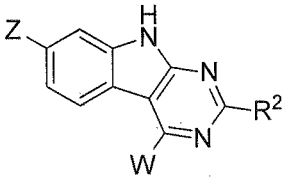


VI

[0020a] According to an aspect, the disclosure provides for a compound of general formula I or II



I



II

or a salt thereof.

wherein:

Z is

1) -P(O) (OR^1) (OR^1),

2) -C(O)OR^1,

3) -C(O)NHR^1,

4) -C(O)$N(R^1)R^1$,

5) -C(O)R^1,

6) -CN,

7) -SR^1,

8) -$S(O)_2NH_2$,

9) -$S(O)_2NHR^1$,

10) -$S(O)_2N(R^1)R^1$,

11) -S(O)R^1,

12) -$S(O)_2R^1$,

13) -L,

14) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

15) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

16) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

17) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

18) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

19) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the is substituted with one or more R^1 or R^A;

W is

1) -OR^1, wherein R^1 is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl,-C_{3-7} cycloalkyl, -C_{3-7} cycloalkenyl, -C_{1-5} perfluorinated, -heterocyclyl, -aryl, -heteroaryl, -benzyl, or 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl, wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

2) -L-OH,

3) -L-OR^1,

4) -SR^1,

5) -CN,

6) -P(O)(OR^1)(OR^1),

7) -NHR^1,

8) –N(R^1)R^1,

9) -L-NH_2,

10) -L-NHR^1,

11) -L-N(R^1)R^1,

12) -L-SR^1,

13) -L-S(O)R^1,

14) -L-$S(O)_2R^1$,

15) -L-P(O)(OR^1)(OR^1),

16) -C(O)OR^1,

17) -C(O)NH_2,

18) -C(O)NHR^1,

19) -C(O)N(R^1)R^1,

20) -NHC(O)R^1,

21) -NR^1C(O)R^1,

22) -NHC(O)OR^1,

23) -NR^1C(O)OR^1,

24) -OC(O)NH_2,

25) -OC(O)NHR^1,

26) -OC(O)N(R^1)R^1,

27) -$OC(O)R^1$,

28) -$C(O)R^1$,

29) -$NHC(O)NH_2$,

30) -$NHC(O)NHR^1$,

31) -$NHC(O)N(R^1)R^1$,

32) -$NR^1C(O)NH_2$,

33) -$NR^1C(O)NHR^1$,

34) -$NR^1C(O)N(R^1)R^1$,

35) -$NHS(O)_2R^1$,

36) -$NR^1S(O)_2R^1$,

37) -$S(O)_2NH_2$,

38) -$S(O)_2NHR^1$,

39) -$S(O)_2N(R^1)R^1$,

40) -$S(O)R^1$,

41) -$S(O)_2R^1$,

42) -$OS(O)_2R^1$,

43) -$S(O)_2OR^1$,

44) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

45) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

46) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heterocyclyl groups,

47) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

48) -L-$NR^1(R^1)$,

49) –$(L\text{-})_2$ NR^1,

50) -L-$(N(R^1)\text{-}L)_n$ – $N(R^1)R^1$,

51) -L-$(N(R^1)\text{-}L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

52) -L-$(N(R^1)\text{-}L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

53) -L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

54) -O-L-N(R^1)R^1,

55) -O-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

56) -O-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

57) -O-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

58) –(O-L)$_2$-NR^1,

59) -O-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

60) -O-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

61) -O-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

62) -O-L-(N(R^1)-L)$_n$- aryl optionally substituted with one or more R^A or R^1 substituents,

63) -S-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents,

64) -S-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

65) -S-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

66) –(S-L)$_2$ NR^1,

67) -S-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

68) -S-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A substituents,

69) -S-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A substituents,

70) -S-L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A substituents,

71) -NR^1(R^1),

72) -(N(R^1)-L)$_n$ – N(R^1)R^1,

73) –(N(R^1)L)$_2$ –NR^1,

74) -(N(R^1)-L)$_n$ – N(R^1)R^A,

75) -(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents,

76) -(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

77) -(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents,

78) -heteroaryl optionally substituted with one or more R^A substituents, or

79) -aryl optionally substituted with one or more R^A substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein when two R^1 substituents are present on the same nitrogen atom, then each R^1 substituent is independently selected from the list of R^1 values described thereafter,

and wherein n is an integer equal to either 0, 1, 2, 3, 4, or 5,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A;

L is

1) -C_{1-6} alkyl,

2) -C_{2-6} alkenyl,

3) -C_{2-6} alkynyl,

4) -C_{3-7} cycloalkyl,

5) -C_{3-7} cycloalkenyl,

6) heterocyclyl,

7) -C_{1-6} alkyl-C_{3-7} cycloalkyl,

8) -C_{1-6} alkyl-heterocyclyl,

9) aryl, or

10) heteroaryl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkyl, the cycloalkenyl, the heterocyclyl, the aryl and the heteroaryl groups are each independently optionally substituted with one or two R^A substituent;

R^1 is

1) –H,

2) -C_{1-6} alkyl,

3) -C_{2-6} alkenyl,

4) -C_{2-6} alkynyl,

5) -C_{3-7} cycloalkyl,

6) -C_{3-7} cycloalkenyl,

7) -C_{1-5} perfluorinated,

8) -heterocyclyl,

9) -aryl,

10) -heteroaryl,

11) -benzyl, or

12) 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

R^2 is

1) -H,

2) $-C_{1-6}$ alkyl,

3) $-SR^1$,

4) $-C(O)R^1$,

5) $-S(O)R^1$,

6) $-S(O)_2R^1$,

7) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

8) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heteroaryl groups,

9) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

10) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the aryl groups,

11) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

12) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present;

R^A is

1) -halogen,

2) $-CF_3$,

3) -OH,

4) $-OR^1$,

5) -L-OH,

6) $-L-OR^1$,

7) $-OCF_3$,

8) -SH,

9) -SR1,

10) -CN,

11) $-NO_2$,

12) $-NH_2$,

13) $-NHR^1$,

14) $-NR^1R^1$,

15) $-L-NH_2$,

16) $-L-NHR^1$,

17) $-L-SR^1$,

18) $-L-S(O)R^1$,

19) $-L-S(O)_2R^1$,

20) -C(O)OH,

21) $-C(O)OR^1$,

22) $-C(O)NH_2$,

23) $-C(O)NHR^1$,

24) $-C(O)N(R^1)R^1$,

25) $-NHC(O)R^1$,

26) $-NR^1C(O)R^1$,

27) $-NHC(O)OR^1$,

28) $-NR^1C(O)OR^1$,

29) $-OC(O)NH_2$,

30) $-OC(O)NHR^1$,

31) $-OC(O)N(R^1)R^1$,

32) $-OC(O)R^1$,

33) $-C(O)R^1$,

34) $-NHC(O)NH_2$,

35) $-NHC(O)NHR^1$,

36) $-NHC(O)N(R^1)R^1$,

37) $-NR^1C(O)NH_2$,

38) $-NR^1C(O)NHR^1$,

39) -$NR^1C(O)N(R^1)R^1$,

40) -$NHS(O)_2R^1$,

41) -$NR^1S(O)_2R^1$,

42) -$S(O)_2NH_2$,

43) -$S(O)_2NHR^1$,

44) -$S(O)_2N(R^1)R^1$,

45) -$S(O)R^1$,

46) -$S(O)_2R^1$,

47) -$OS(O)_2R^1$,

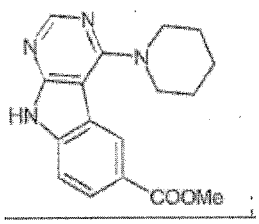
48) -$S(O)_2OR^1$,

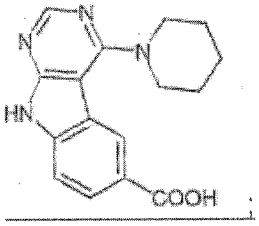
49) -benzyl,

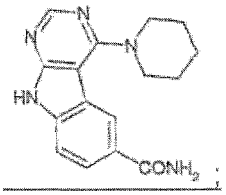
50) -N_3, or

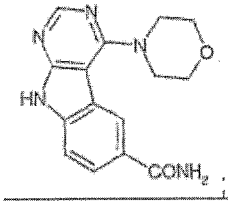
51) -C(-N=N-)(CF_3),

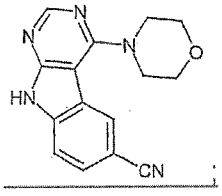
and wherein the benzyl group is optionally substituted with 1, 2 or 3 R^A or R^1 substituents provided that the compound of Formula (I) is other than

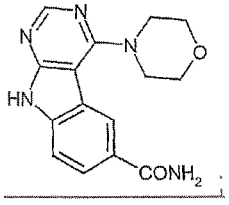


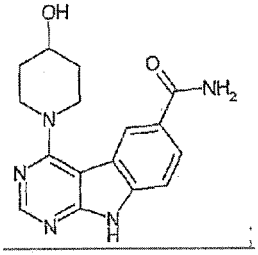


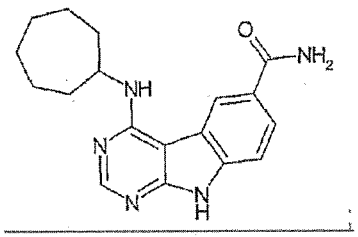


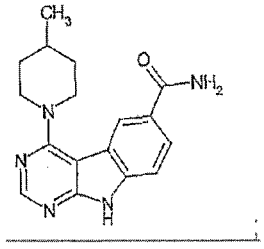


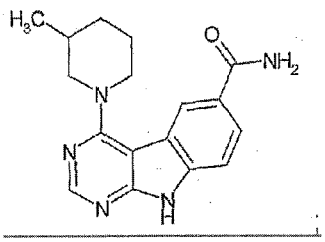


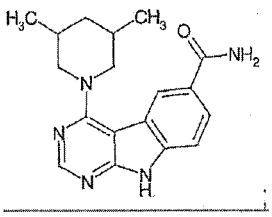


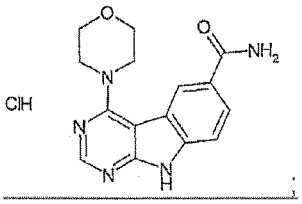


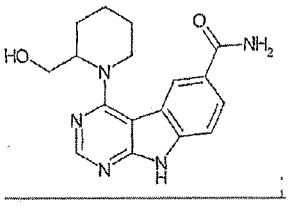


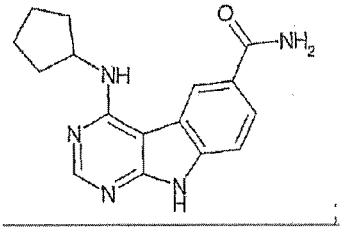


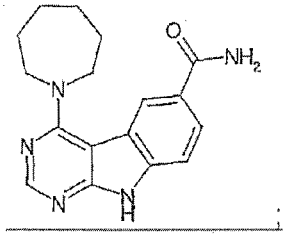


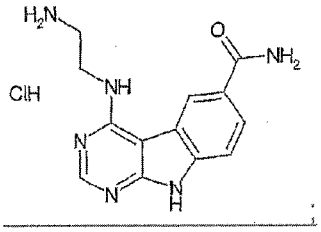


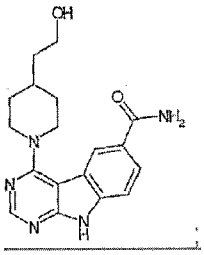


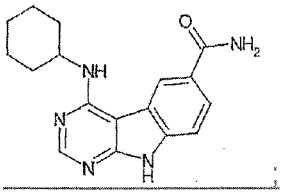


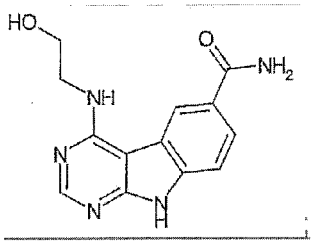


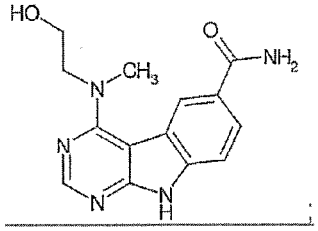


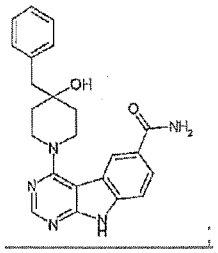


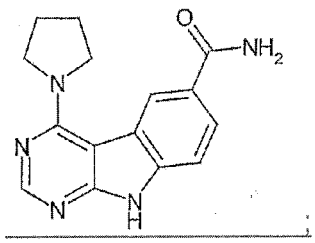


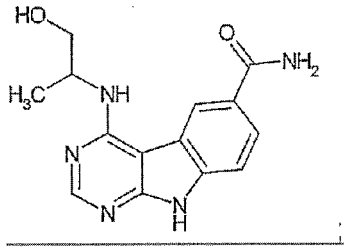


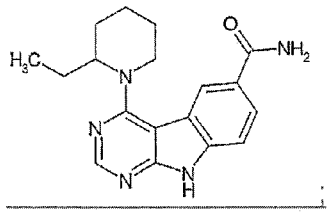


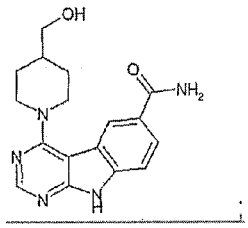


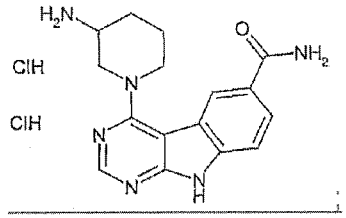


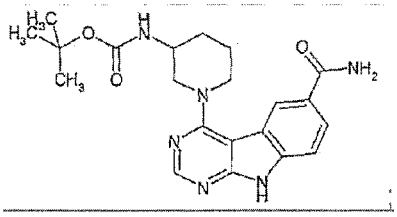


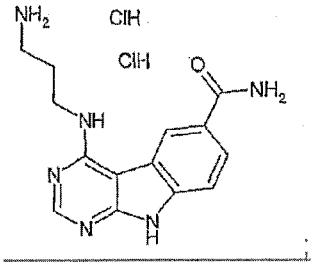


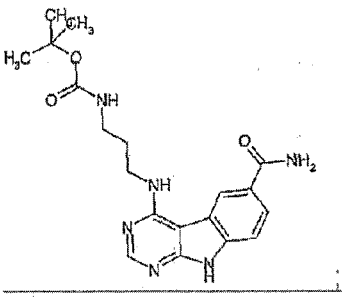


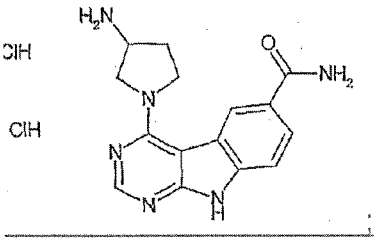


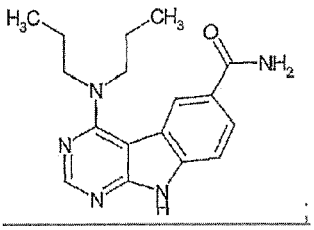


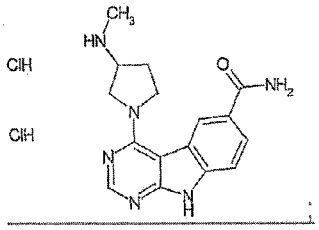


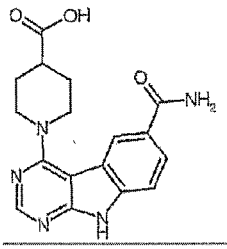


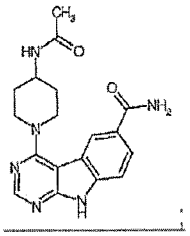


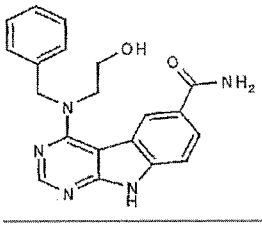


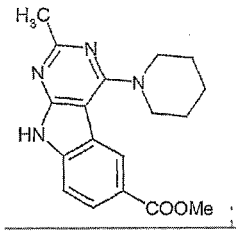


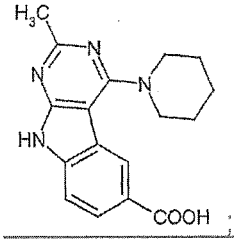


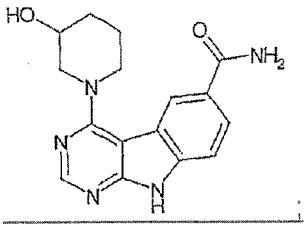


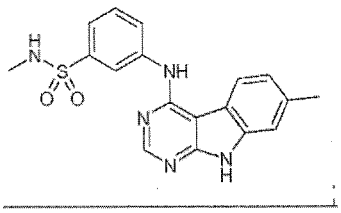


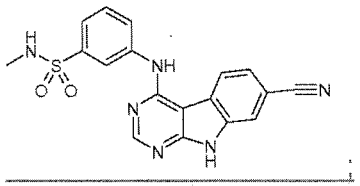


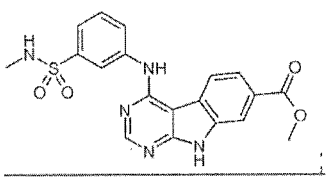


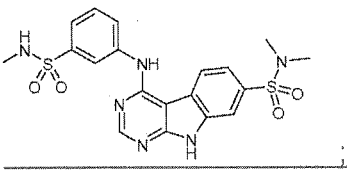


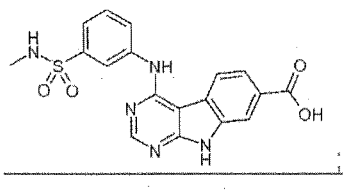


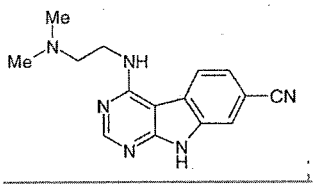


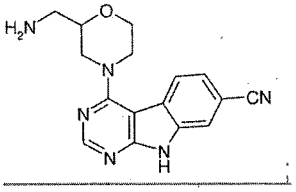


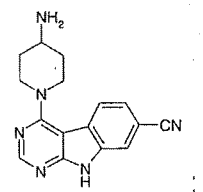


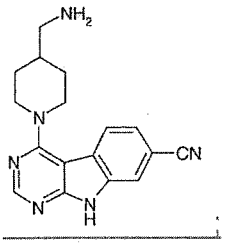


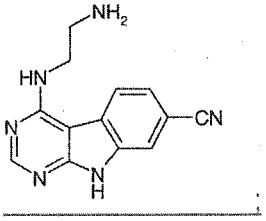


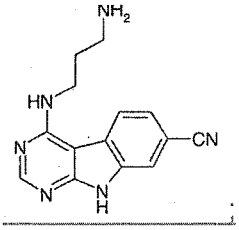


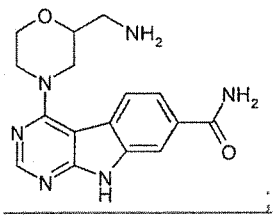


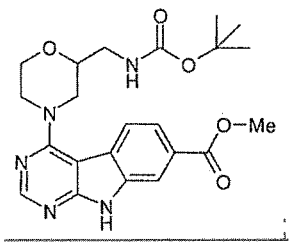


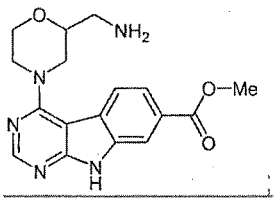


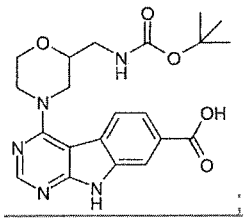


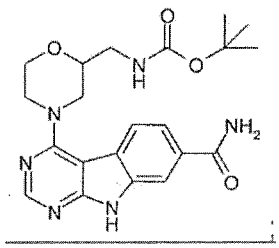


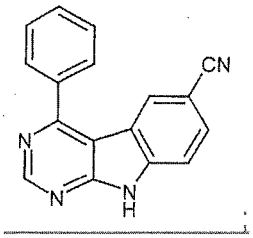


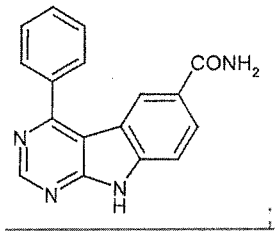


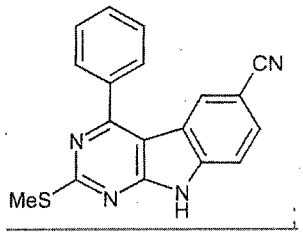


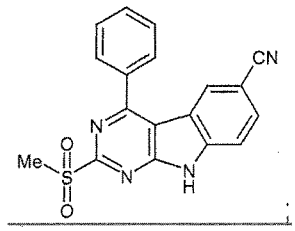


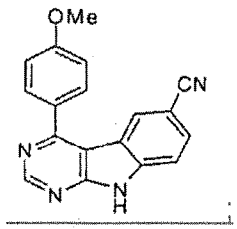


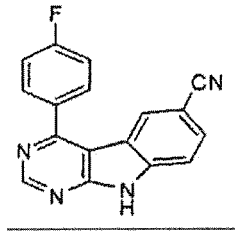


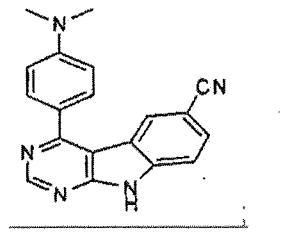


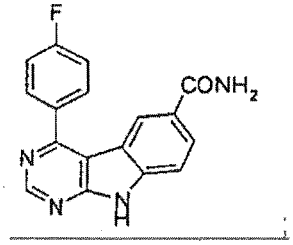


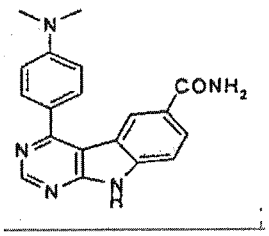


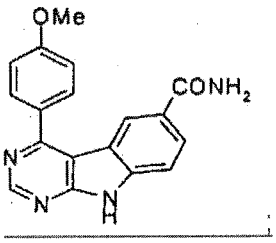


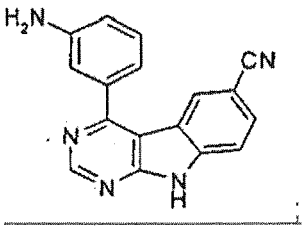


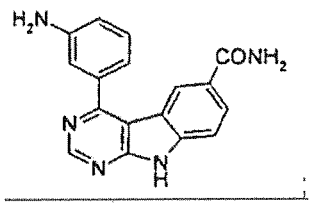




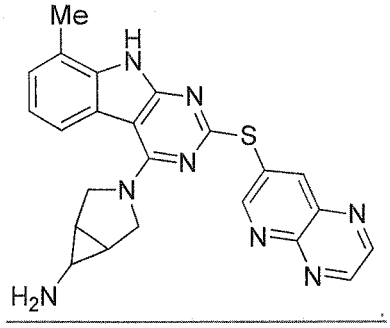








and



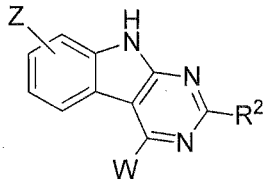
[0021] The substituents in the above general formulas I, II, III, IV, V and VI, namely, Z, W, L, Li, X, X_i, R^1, R^2, R^3, R^4 and m are as defined herein below.

[0022] According to an aspect, the disclosure ~~invention~~ provides for pharmaceutical compositions comprising a compound of general formula I, II, III, IV, V or VI.

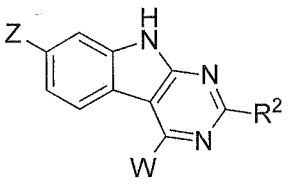
[0023] According to an aspect, the disclosure ~~invention~~ provides for use of a compound of general formula I, II, III, IV, V or VI to expand hematopoietic stem cells. In embodiments of the disclosure~~invention~~, the hematopoietic stem cells are human cells.

[0024] According to an aspect, the disclosure ~~invention~~ provides for a method of increasing hematopoietic stem cells or progenitor cells, the method comprising culturing a starting cell population in the presence of a compound of general formula I, II, III, IV, V or VI. In embodiments of the disclosure~~invention~~, the starting cell population is *in vivo*, *in vitro* or *ex vivo*. Also, in embodiments of the disclosure~~invention~~, the starting cell population comprises CD34+ cells harvested from mobilized peripheral blood (mPB), bone marrow (BM) or umbilical cord blood (UCB). Moreover, in embodiments of the method according to the disclosure~~invention~~, optionally, culture of the starting cell population in the presence of a compound of general formula I, II, III, IV, V or VI in performed together with at least one cell expanding factor which is a biologic or another small molecule.

[0024a] According to an aspect, the disclosure provides a method of increasing stem and progenitor cells, the method comprising; contacting a starting population in the presence of at least one compound, optionally together with at least one cell expanding factor which is a biologic or another small molecule, wherein said compound is of general formula I or II



I



II

or a salt thereof,

wherein:

Z is

1) -P(O) (OR^1) (OR^1),
2) -C(O)OR^1,
3) -C(O)NHR^1,
4) -C(O)N(R^1)R^1,
5) -C(O)R^1,
6) -CN,
7) -SR^1,

8) $-S(O)_2NH_2$,

9) $-S(O)_2NHR^1$,

10) $-S(O)_2N(R^1)R^1$,

11) $-S(O)R^1$,

12) $-S(O)_2R^1$,

13) -L,

14) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

15) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

16) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

17) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

18) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

19) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the is substituted with one or more R^1 or R^A;

W is

1) -H,

2) -halogen,

3) $-OR^1$,

4) -L-OH,

5) $-L-OR^1$,

6) $-SR^1$,

7) -CN,

8) $-P(O)(OR^1)(OR^1)$,

9) $-NHR^1$,

10) $-N(R^1)R^1$,

11) $-L-NH_2$,

12) -L-NHR^1,

13) -L-$N(R^1)R^1$,

14) -L-SR^1,

15) -L-$S(O)R^1$,

16) -L-$S(O)_2R^1$,

17) -L-$P(O)(OR^1)(OR^1)$,

18) -$C(O)OR^1$,

19) -$C(O)NH_2$,

20) -$C(O)NHR^1$,

21) -$C(O)N(R^1)R^1$,

22) -$NHC(O)R^1$,

23) -$NR^1C(O)R^1$,

24) -$NHC(O)OR^1$,

25) -$NR^1C(O)OR^1$,

26) -$OC(O)NH_2$,

27) -$OC(O)NHR^1$,

28) -$OC(O)N(R^1)R^1$,

29) -$OC(O)R^1$,

30) -$C(O)R^1$,

31) -$NHC(O)NH_2$,

32) -$NHC(O)NHR^1$,

33) -$NHC(O)N(R^1)R^1$,

34) -$NR^1C(O)NH_2$,

35) -$NR^1C(O)NHR^1$,

36) -$NR^1C(O)N(R^1)R^1$,

37) -$NHS(O)_2R^1$,

38) -$NR^1S(O)_2R^1$,

39) -$S(O)_2NH_2$,

40) -$S(O)_2NHR^1$,

41) -$S(O)_2N(R^1)R^1$,

42) -$S(O)R^1$,

43) $-S(O)_2R^1$,

44) $-OS(O)_2R^1$,

45) $-S(O)_2OR^1$,

46) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

47) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

48) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heterocyclyl groups,

49) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

50) $-L-NR^1(R^1)$,

51) $-(L-)_2\ NR^1$,

52) $-L-(N(R^1)-L)_n - N(R^1)R^1$,

53) $-L-(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

54) $-L-(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

55) $-L-(N(R^1)-L)_n$ – aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

56) $-O-L-N(R^1)R^1$,

57) -O-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

58) -O-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

59) -O-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

60) $-(O-L)_2-NR^1$,

61) $-O-L-(N(R^1)-L)_n - N(R^1)R^1$,

62) $-O-L-(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

63) $-O-L-(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

64) -O-L-$(N(R^1)\text{-}L)_n$- aryl optionally substituted with one or more R^A or R^1 substituents,

65) -S-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents,

66) -S-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

67) -S-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

68) $-(S\text{-}L)_2\ NR^1$,

69) $-S\text{-}L\text{-}(N(R^1)\text{-}L)_n - N(R^1)R^1$,

70) $-S\text{-}L\text{-}(N(R^1)\text{-}L)_n$ – heteroaryl optionally substituted with one or more R^A substituents,

71) $-S\text{-}L\text{-}(N(R^1)\text{-}L)_n$ – heterocyclyl optionally substituted with one or more R^A substituents,

72) $-S\text{-}L\text{-}(N(R^1)\text{-}L)_n$ – aryl optionally substituted with one or more R^A substituents,

73) $-NR^1(R^1)$,

74) $-(N(R^1)\text{-}L)_n - N(R^1)R^1$,

75) $-(N(R^1)L)_2 -NR^1$,

76) $-(N(R^1)\text{-}L)_n - N(R^1)R^A$,

77) $-(N(R^1)\text{-}L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents,

78) $-(N(R^1)\text{-}L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

79) $-(N(R^1)\text{-}L)_n$ – aryl optionally substituted with one or more R^A or R^1 substituents,

80) -heteroaryl optionally substituted with one or more R^A substituents, or

81) -aryl optionally substituted with one or more R^A substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein when two R^1 substituents are present on the same nitrogen atom, then each R^1 substituent is independently selected from the list of R^1 values described thereafter,

and wherein n is an integer equal to either 0, 1, 2, 3, 4, or 5,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A;

L is

1) $-C_{1\text{-}6}$ alkyl,

2) $-C_{2\text{-}6}$ alkenyl,

3) $-C_{2\text{-}6}$ alkynyl,

4) $-C_{3\text{-}7}$ cycloalkyl,

5) $-C_{3\text{-}7}$ cycloalkenyl,

6) heterocyclyl,

7) -C_{1-6} alkyl-C_{3-7} cycloalkyl,

8) -C_{1-6} alkyl-heterocyclyl,

9) aryl, or

10) heteroaryl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkyl, the cycloalkenyl, the heterocyclyl, the aryl and the heteroaryl groups are each independently optionally substituted with one or two R^A substituent;

R^1 is

1) –H,

2) -C_{1-6} alkyl,

3) -C_{2-6} alkenyl,

4) -C_{2-6} alkynyl,

5) -C_{3-7} cycloalkyl,

6) -C_{3-7} cycloalkenyl,

7) -C_{1-5} perfluorinated,

8) -heterocyclyl,

9) -aryl,

10) -heteroaryl,

11) -benzyl, or

12) 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

R^2 is

1) -H,

2) -C_{1-6} alkyl,

3) -SR^1,

4) -$C(O)R^1$,

5) -$S(O)R^1$,

6) -$S(O)_2R^1$,

7) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

8) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heteroaryl groups,

9) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

10) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the aryl groups,

11) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

12) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present;

R^A is

1) -halogen,

2) $-CF_3$,

3) -OH,

4) $-OR^1$,

5) -L-OH,

6) $-L-OR^1$,

7) $-OCF_3$,

8) -SH,

9) -SR1,

10) -CN,

11) $-NO_2$,

12) $-NH_2$,

13) $-NHR^1$,

14) $-NR^1R^1$,

15) $-L-NH_2$,

16) $-L-NHR^1$,

17) $-L-SR^1$,

18) $-L-S(O)R^1$,

19) $-L-S(O)_2R^1$,

20) -C(O)OH,

21) $-C(O)OR^1$,

22) $-C(O)NH_2$,

23) $-C(O)NHR^1$,

24) $-C(O)N(R^1)R^1$,

25) $-NHC(O)R^1$,

26) $-NR^1C(O)R^1$,

27) $-NHC(O)OR^1$,

28) $-NR^1C(O)OR^1$,

29) $-OC(O)NH_2$,

30) $-OC(O)NHR^1$,

31) $-OC(O)N(R^1)R^1$,

32) $-OC(O)R^1$,

33) $-C(O)R^1$,

34) $-NHC(O)NH_2$,

35) $-NHC(O)NHR^1$,

36) $-NHC(O)N(R^1)R^1$,

37) $-NR^1C(O)NH_2$,

38) $-NR^1C(O)NHR^1$,

39) $-NR^1C(O)N(R^1)R^1$,

40) $-NHS(O)_2R^1$,

41) $-NR^1S(O)_2R^1$,

42) $-S(O)_2NH_2$,

43) $-S(O)_2NHR^1$,

44) $-S(O)_2N(R^1)R^1$,

45) $-S(O)R^1$,

46) $-S(O)_2R^1$,

47) $-OS(O)_2R^1$,

48) $-S(O)_2OR^1$,

49) -benzyl,

50) $-N_3$, or

51) $-C(-N=N-)(CF_3)$,

and wherein the benzyl group is optionally substituted with 1, 2 or 3 R^A or R^1 substituents.

[0025] According to an aspect, the disclosure ~~invention~~ provides for a cell population expanded according to the method of the disclosure~~invention~~, more specifically, a cell population expanded using a compound according to the disclosure~~invention~~. In embodiments, the disclosure ~~invention~~ provides for hematopoietic stems cells expanded according to the method of the disclosure~~invention~~, more specifically, hematopoietic stems cells expanded using a compound according to the disclosure~~invention~~.

[0026] According to an aspect, the disclosure ~~invention~~ provides for a method of treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject, the method comprising administering to the subject in need of such treatment hematopoietic stem cells expanded using a compound of general formula I, II, III, IV, V or VI, or a compound of general formula I, II, III, IV, V or VI.

[0027] In embodiments of the disclosure~~invention~~, the hematopoietic disorder/malignancy, the autoimmune disease and/or the inherited immunodeficient disease comprise bone marrow failure conditions, a variety of congenital diseases of global concern (e.g. sickle cell anemia and thalassemia), lupus, acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, myeloproliferative disorders, myelodysplastic syndromes, multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's disease, aplastic anemia, pure red cell aplasia, hemoglobinuria, Fanconi anemia, thalassemia, sickle cell anemia, Wiskott-Aldrich syndrome, inborn errors of metabolism (such as Gaucher disease among others).

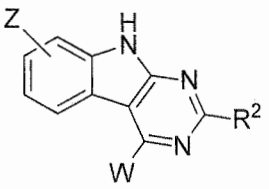
[0028] According to an aspect, the disclosure ~~invention~~ provides for a kit for use in increasing stem or progenitor cells or in expanding hematopoietic stem cells, the kit comprising a compound of general formula I, II,

III, IV, V or VI, and instructions for use. In embodiments of the disclosure~~invention~~, the kit comprises at least one cell expanding factor which is a biologic or another small molecule.

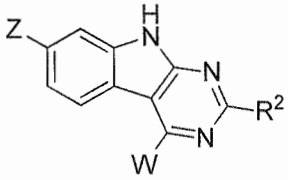
DETAILED DESCRIPTION OF THE INVENTION

[0029] The inventors have discovered certain pyrimido[4,5-b]indole derivatives. These compounds are useful to expand hematopoietic stem cell populations, particularly, human hematopoietic stem cell populations. The compounds are also useful in the medical treatment of diseases that involve hematopoietic stem cells.

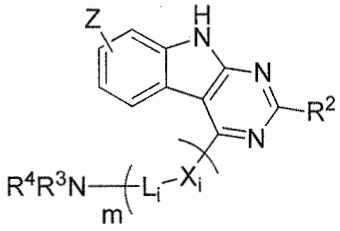
[0030] The compounds according the invention have the general Formula I, II, III, IV, V or IV shown below. Salts or prodrugs of such compounds are also within the scope of the compounds according to the invention.



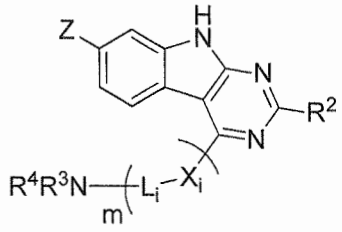
I



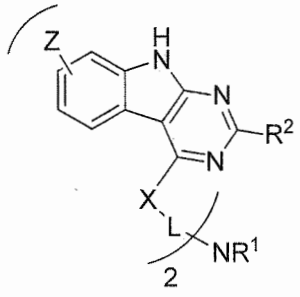
II



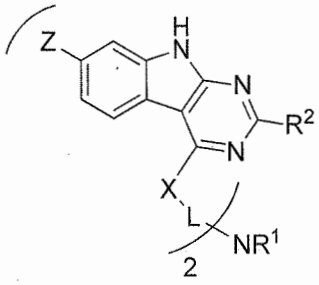
III



IV



V

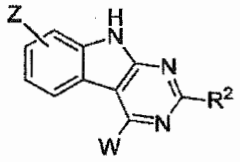


VI

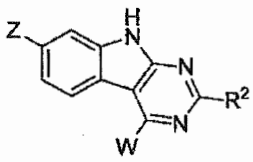
[0031] In formulas I, II, III, IV, V and VI, the substituents are defined as outlined below.

CLAIMS

1. A compound of general formula I or II



I



II

or a salt or a prodrug thereof,

wherein:

Z is

1) -P(O) (OR^1) (OR^1),
2) -C(O)OR^1,
3) -C(O)NHR^1,
4) -C(O)$N(R^1)R^1$,
5) -C(O)R^1,
6) -CN,
7) -SR^1,
8) -$S(O)_2NH_2$,
9) -$S(O)_2NHR^1$,
10) -$S(O)_2N(R^1)R^1$,
11) -S(O)R^1,
12) -$S(O)_2R^1$,
13) -L,
14) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,
15) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,
16) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

17) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

18) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

19) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present, and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the is substituted with one or more R^1 or R^A;

W is

1) -H,
2) -halogen,
3) $-OR^1$,
4) -L-OH,
5) $-L-OR^1$,
6) $-SR^1$,
7) -CN,
8) $-P(O)(OR^1)(OR^1)$,
9) $-NHR^1$,
10) $-N(R^1)R^1$,
11) $-L-NH_2$,
12) $-L-NHR^1$,
13) $-L-N(R^1)R^1$,
14) $-L-SR^1$,
15) $-L-S(O)R^1$,
16) $-L-S(O)_2R^1$,
17) $-L-P(O)(OR^1)(OR^1)$,
18) $-C(O)OR^1$,
19) $-C(O)NH_2$,
20) $-C(O)NHR^1$,
21) $-C(O)N(R^1)R^1$,
22) $-NHC(O)R^1$,
23) $-NR^1C(O)R^1$,

24) -NHC(O)OR^1,

25) -NR^{1}C(O)OR^1,

26) -OC(O)NH$_2$,

27) -OC(O)NHR^1,

28) -OC(O)N(R^1)R^1,

29) -OC(O)R^1,

30) -C(O)R^1,

31) -NHC(O)NH$_2$,

32) -NHC(O)NHR^1,

33) -NHC(O)N(R^1)R^1,

34) -NR^{1}C(O)NH$_2$,

35) -NR^{1}C(O)NHR^1,

36) -NR^{1}C(O)N(R^1)R^1,

37) -NHS(O)$_2$R^1,

38) -NR^{1}S(O)$_2$R^1,

39) -S(O)$_2$NH$_2$,

40) -S(O)$_2$NHR^1,

41) -S(O)$_2$N(R^1)R^1,

42) -S(O)R^1,

43) -S(O)$_2$R^1,

44) -OS(O)$_2$R^1,

45) -S(O)$_2$OR^1,

46) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

47) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

48) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heterocyclyl goups,

49) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

50) -L-NR^1(R^1),

51) -L-)$_2$ NR^1,

52) -L-(N(R^1)-L)$_n$ – N(R^1)R^1,

53) -L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

54) -L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

55) -L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

56) -O-L-N(R^1)R^1,

57) -O-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

58) -O-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

59) -O-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

60) -O-L)$_2$-NR^1,

61) -O-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

62) -O-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

63) -O-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

64) -O-L-(N(R^1)-L)$_n$- aryl optionally substituted with one or more R^A or R^1 substituents,

65) -S-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents,

66) -S-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

67) -S-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

68) -S-L)$_2$ NR^1,

69) -S-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

70) -S-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A substituents,

71) -S-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A substituents,

72) -S-L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A substituents,

73) -NR^1(R^1),

74) -(N(R^1)-L)$_n$ – N(R^1)R^1,

75) -N(R^1)L)$_2$ –NR^1,

76) -(N(R^1)-L)$_n$ – N(R^1)R^A,

77) -(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents,

78) -(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

79) -(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents,

80) -heteroaryl optionally substituted with one or more R^A substituents, or

81) -aryl optionally substituted with one or more R^A substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein when two R^1 substituents are present on the same nitrogen atom, then each R^1 substituent is independently selected from the list of R^1 values described thereafter,

and wherein n is an integer equal to either 0, 1, 2, 3, 4, or 5,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A;

L is

1) -C_{1-6} alkyl,
2) -C_{2-6} alkenyl,
3) -C_{2-6} alkynyl,
4) -C_{3-7} cycloalkyl,
5) -C_{3-7} cycloalkenyl,
6) heterocyclyl,
7) -C_{1-6} alkyl-C_{3-7} cycloalkyl,
8) -C_{1-6} alkyl-heterocyclyl,
9) aryl, or
10) heteroaryl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkyl, the cycloalkenyl, the heterocyclyl, the aryl and the heteroaryl groups are each independently optionally substituted with one or two R^A substituent;

R^1 is

1) –H,
2) -C_{1-6} alkyl,
3) -C_{2-6} alkenyl,
4) -C_{2-6} alkynyl,

5) -C_{3-7} cycloalkyl,
6) -C_{3-7} cycloalkenyl,
7) -C_{1-5} perfluorinated,
8) -heterocyclyl,
9) -aryl,
10) -heteroaryl,
11) -benzyl, or
12) 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

R^2 is

1) -H,
2) -C_{1-6} alkyl,
3) -SR^1,
4) -$C(O)R^1$,
5) -$S(O)R^1$,
6) -$S(O)_2R^1$,
7) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,
8) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heteroaryl groups,
9) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,
10) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the aryl groups,
11) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or
12) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present;

R^A is

1) -halogen,
2) -CF_3,

3) -OH,
4) -OR^1,
5) -L-OH,
6) -L-OR^1,
7) -OCF_3,
8) -SH,
9) -SR1,
10) -CN,
11) -NO_2,
12) -NH_2,
13) -NHR^1,
14) -NR^1R^1,
15) -L-NH_2,
16) -L-NHR^1,
17) -L-NR^4R^1,
18) -L-SR^1,
19) -L-$S(O)R^1$,
20) -L-$S(O)_2R^1$,
21) -C(O)OH,
22) -$C(O)OR^1$,
23) -$C(O)NH_2$,
24) -$C(O)NHR^1$,
25) -$C(O)N(R^1)R^1$,
26) -$NHC(O)R^1$,
27) -$NR^1C(O)R^1$,
28) -$NHC(O)OR^1$,
29) -$NR^1C(O)OR^1$,
30) -$OC(O)NH_2$,
31) -$OC(O)NHR^1$,
32) -$OC(O)N(R^1)R^1$,
33) -$OC(O)R^1$,
34) -$C(O)R^1$,

35) -NHC(O)NH_2,

36) -NHC(O)NHR^1,

37) -NHC(O)$N(R^1)R^1$,

38) -$NR^1C(O)NH_2$,

39) -$NR^1C(O)NHR^1$,

40) -$NR^1C(O)N(R^1)R^1$,

41) -$NHS(O)_2R^1$,

42) -$NR^1S(O)_2R^1$,

43) -$S(O)_2NH_2$,

44) -$S(O)_2NHR^1$,

45) -$S(O)_2N(R^1)R^1$,

46) -$S(O)R^1$,

47) -$S(O)_2R^1$,

48) -$OS(O)_2R^1$,

49) -$S(O)_2OR^1$,

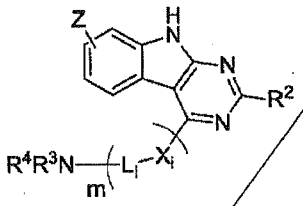
50) -benzyl,

51) -N_3, or

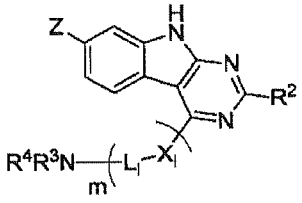
52) -C(-N=N-)(CF_3),

and wherein the benzyl group is optionally substituted with 1, 2 or 3 R^A or R^1 substituents.

2. A compound of general formula III or IV,



III



IV

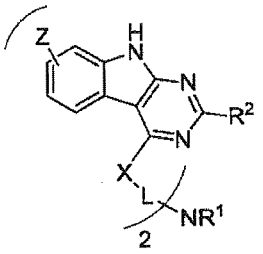
or a salt or a prodrug thereof,

wherein Z and R^2 are each as defined in claim 1, and m is an integer from 1 to 6,

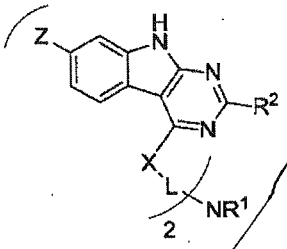
and wherein when m is 2 or more, X_i are the same or different and are each independently NR^1, CH_2, O or S, wherein R^1 is as defined in claim 1, and L_i are the same or different and are each independently L as defined in claim 1,

and wherein R^3 and R^4 are the same or different and are each independently H, R^1 as defined in claim 1, or they join together with N to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

3. A compound of general formula V or VI,



V

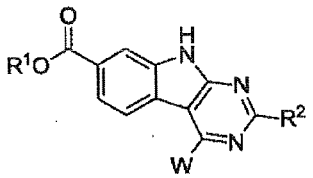


VI

or a salt or a prodrug thereof,

wherein Z, L, R^1 and R^2 are each as defined in claim 1.

4. A compound of formula IIA

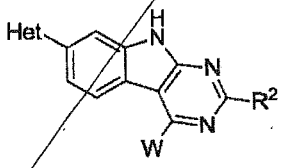


IIA

or a salt or a prodrug thereof,

wherein R^1, W and R^2 are each as defined in claim 1.

5. A compound of formula IIB

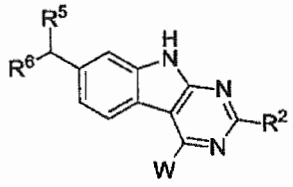


IIB

or a salt or a prodrug thereof,

wherein W and R^2 are each as defined in claim 1, and Het is a 3 to 7-membered heterocycle, optionally substituted with one or more R^1 or R^A as defined in claim 1.

6. A compound of formula IIC



IIC

or a salt or a prodrug thereof,

wherein W and R^2 are each as defined in claim 1,

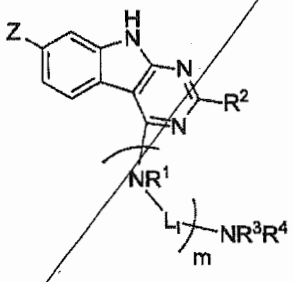
and wherein R^5 and R^6 are the same or different and are each independently L as defined in claim 1, or they join together with C to form a 5 to 7-membered ring which optionally includes one or more heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

7. A compound according to claim 6, wherein the ring is a 5-membered ring, and the heteroatom is N.

8. A compound according to claim 6 or 7, wherein the ring includes four N.

9. A compound according to any one of claims 6 to 8, wherein R^2 is benzyl.

10. A compound of formula IVA

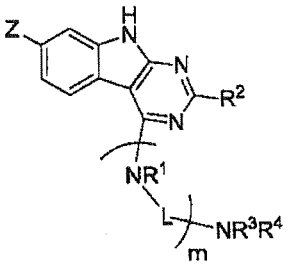


IVA

or a salt or a prodrug thereof,

wherein W, L, R^1 and R^2 are each as defined in claim 1,
and wherein m, Li, R^3 and R^4 are each as defined in claim 2.

11. A compound of formula VIA

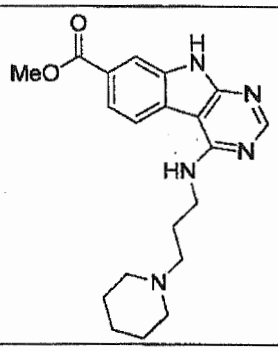
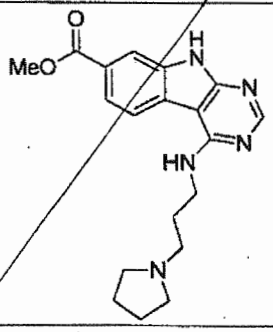
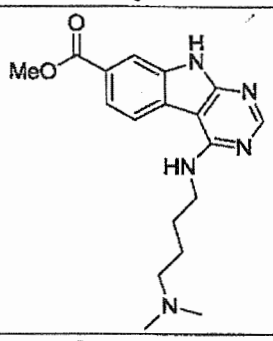
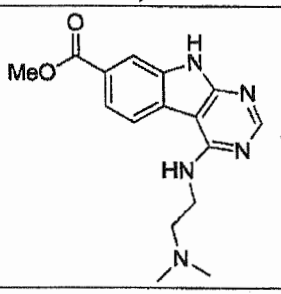


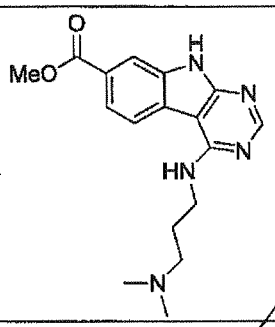
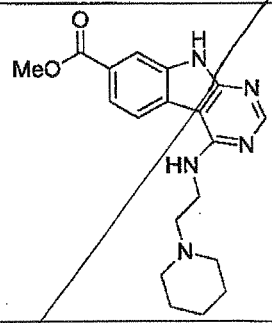
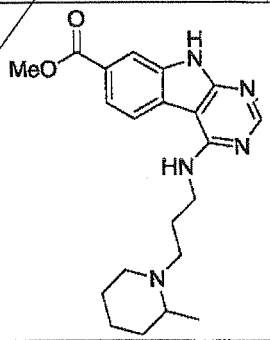
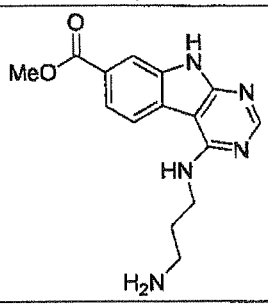
VIA

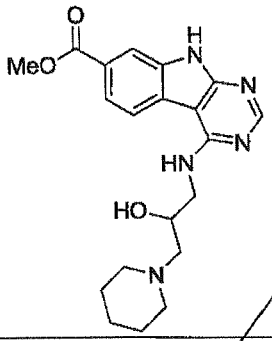
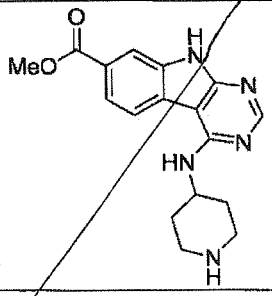
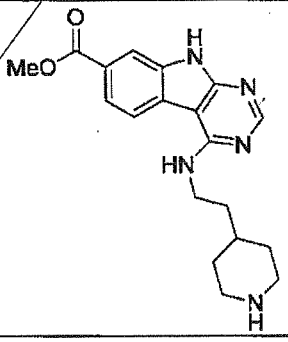
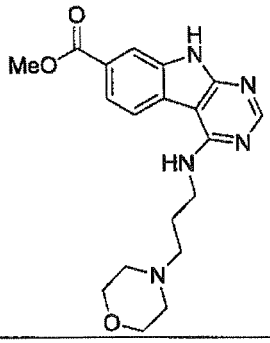
or a salt or a prodrug thereof,
wherein Z, L, R^1 and R^2 are each as defined in claim 1,
and wherein R^3 and R^4 are each as defined in claim 2.

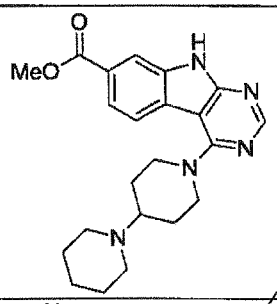
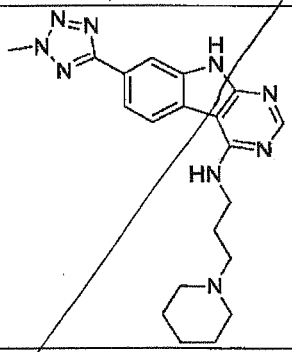
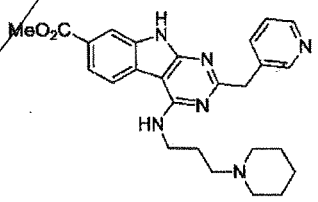
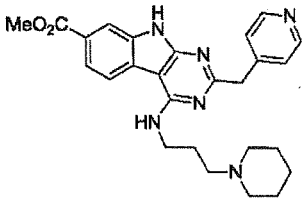
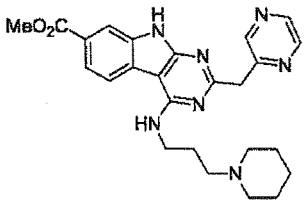
12. A compound according to claim 1, wherein:
Z is CO_2Me or 2-methyl-2H-tetrazol-5-yl;
R^2 is benzyl, 3-thienylmethyl or 3-pyridinyl methyl; and
W is NH-L-N(R^1)R^1 wherein L is C_{2-4} alkyl and R^1 is C_{1-4} alkyl or (R^1) and R^1 join together with the nitrogen atom to which they are attached to form a 3 to 7-membered ring, which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

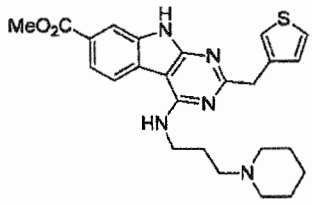
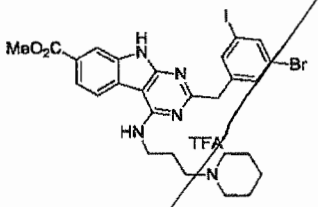
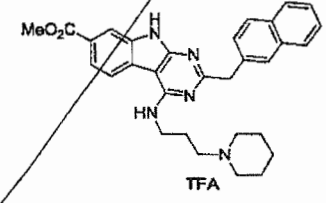
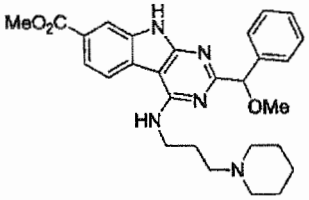
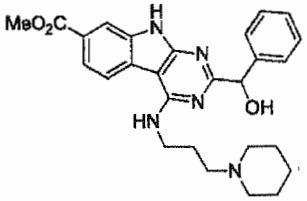
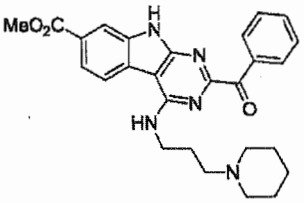
13. A compound which is:

Compound number	Structure
1	
2	
3	
4	

Compound number	Structure
5	
6	
7	
8	

Compound number	Structure
9	
10	
11	
12	

Compound number	Structure
13	
14	
15	
16	
17	

Compound number	Structure
18	
19	
20	
21	
22	
23	

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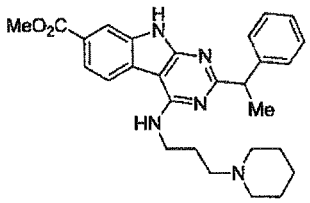
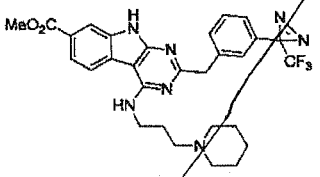
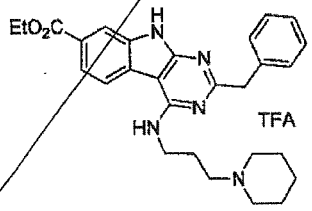
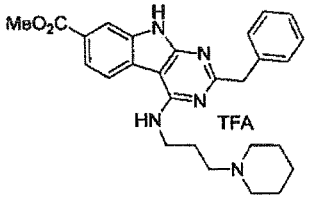
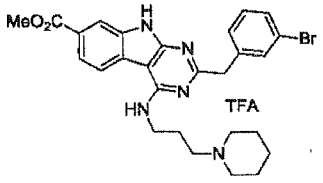
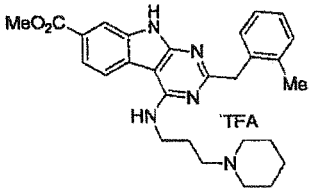
24	
25	
26	
27	
28	
29	

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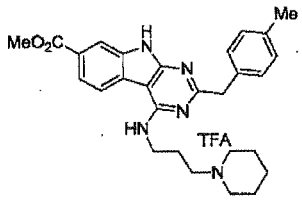
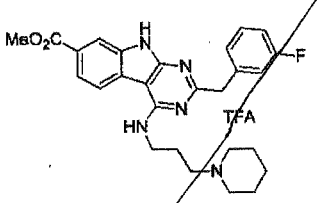
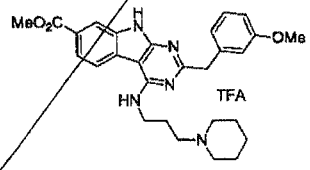
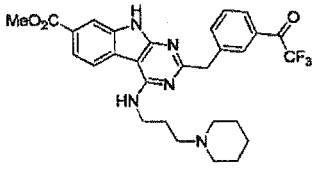
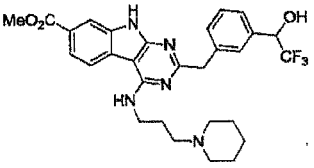
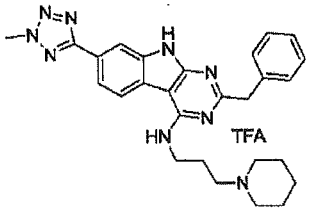
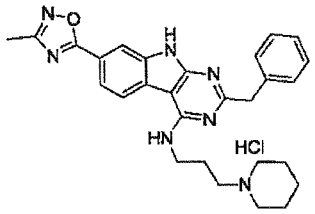
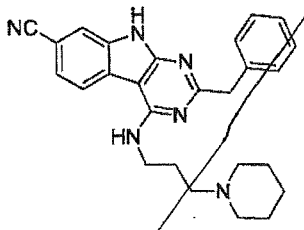
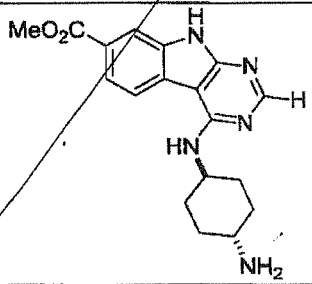
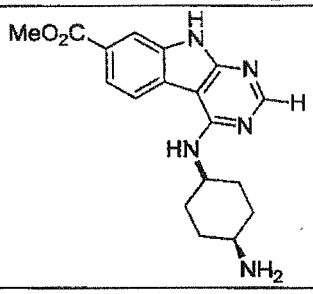
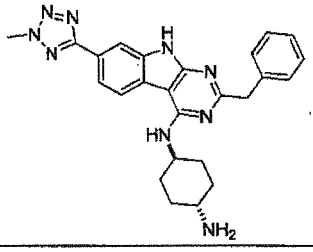
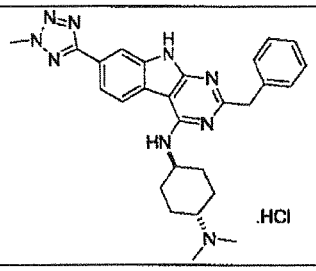
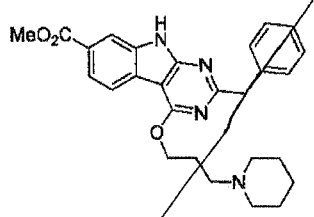
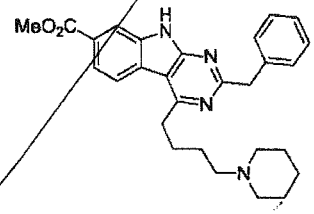
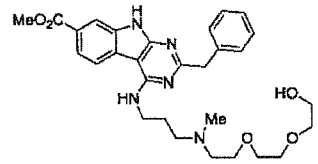
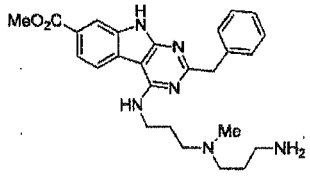
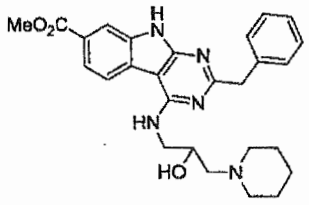
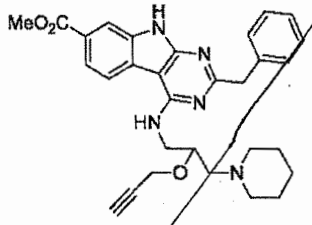
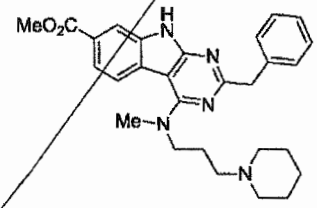
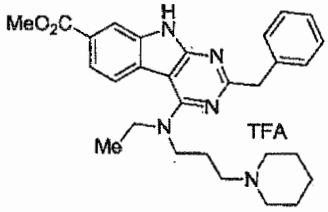
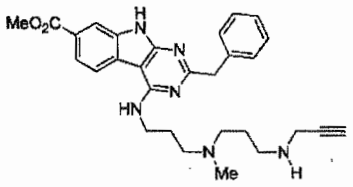
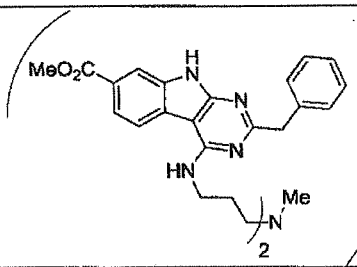
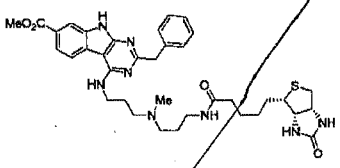
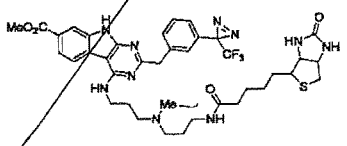
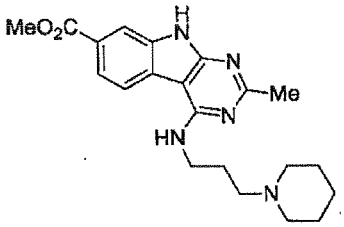
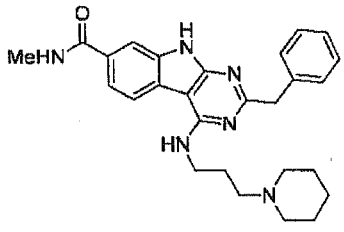
30	
31	
32	
33	
34	
35	

Compound number	Structure
36	
37	
38	
39	
40	

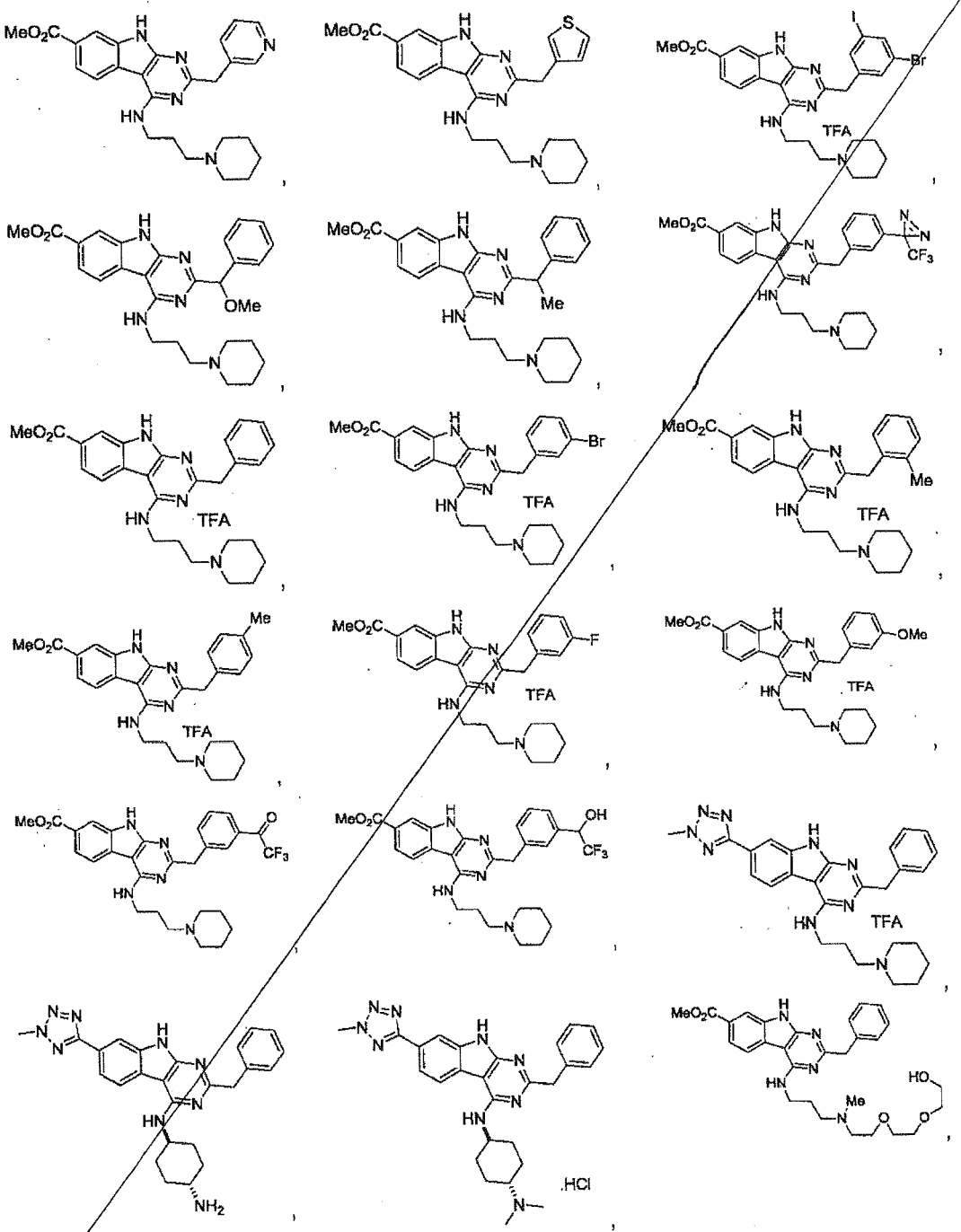
Compound number	Structure
41	
42	
43	
44	
45	

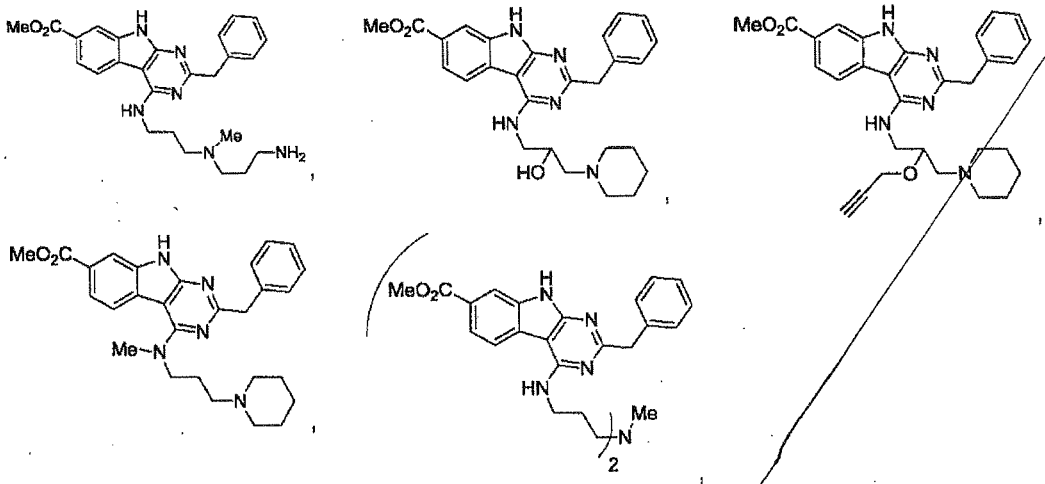
Compound number	Structure
46	
47	
48	
49	
50	

Compound number	Structure
51	
52	
53	
54	
55	

or a salt or a prodrug thereof.

14. A compound which is:





or a salt or a prodrug thereof.

15. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 14 or a salt or a prodrug thereof, and a pharmaceutically acceptable carrier.

16. Use of a compound as defined in any one of claims 1 to 14, to expand hematopoietic stem cells.

17. Use according to claim 16, wherein the hematopoietic stem cells are human cells.

18. A method of increasing stem and progenitor cells, the method comprising: culturing a starting population comprising hematopoietic stem cells (HSCs) with an agent capable of increasing the number of HSCs, the agent comprising a compound as defined in any one of claims 1 to 14.

19. A method according to claim 18, which is *in vivo*, *in vitro* or *ex vivo*.

20. A method according to claim 18 or 19, in which the starting cell population includes CD34+ cells harvested from mobilized peripheral blood (mPB), bone marrow (BM) or umbilical cord blood (UCB).

21. A method of expanding hematopoietic stem cells, the method comprising: culturing a starting cell population in the presence of at least one compound as defined in any one of claims 1 to 14, optionally together with at least one cell expanding factor which is a biologic or another small molecule.

22. A cell population as expanded according to a method as defined in any one of claims 18 to 21.

23. A pharmaceutical composition comprising a cell population expanded using a compound as defined in any one of claims 1 to 14.

24. A method of treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject, comprising administering to the subject in need of such treatment hematopoietic stem cells expanded using a compound as defined in any one of claims 1 to 14, or a compound as defined in any one of claims 1 to 14 or a salt or a prodrug thereof.

25. A method according to claim 21, wherein the hematopoietic disorder/malignancy, the autoimmune disease and/or the inherited immunodeficient disease comprise bone marrow failure conditions, a variety of congenital diseases of global concern (e.g. sickle cell anemia and thalassemia), lupus, acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, myeloproliferative disorders, myelodysplastic syndromes, multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's disease, aplastic anemia, pure red cell aplasia, hemoglobinuria, Fanconi anemia, thalassemia, sickle cell anemia, Wiskott-Aldrich syndrome, inborn errors of metabolism (such as Gaucher disease among others.

26. Use of hematopoietic stem cells expanded using a compound as defined in any one of claims 1 to 14, or a compound as defined in any one of claims 1 to 14 or a salt or a prodrug thereof, for treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject.

27. Use of a compound as defined in any one of claims 1 to 14 or a prodrug thereof, in the manufacture of a medicament for treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject.

28. Use of the pharmaceutical composition as defined in claim 15, for treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject.

29. Use according to any one of claims 26 to 28, wherein the hematopoietic disorder/malignancy, the autoimmune disease and/or the inherited immunodeficient disease include bone marrow failure conditions, a variety of congenital diseases of global concern (e.g. sickle cell anemia and thalassemia), lupus, acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, myeloproliferative disorders, myelodysplastic syndromes, multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's disease, aplastic anemia, pure red cell aplasia, hemoglobinuria, Fanconi anemia, thalassemia, sickle cell anemia, Wiskott-Aldrich syndrome, inborn errors of metabolism (such as Gaucher disease among others).

30. Hematopoietic stem cells expanded using a compound as defined in any one of claims 1 to 14, or a compound as defined in any one of claims 1 to 14 or a salt or a prodrug thereof, for treating a hematopoietic disorder/malignancy, an autoimmune disease and/or an inherited immunodeficient disease in a subject.

31. Hematopoietic stem cells or a compound as defined in claim 30, wherein the hematopoietic disorder/malignancy, the autoimmune disease and/or the inherited immunodeficient disease include bone marrow failure conditions, a variety of congenital diseases of global concern (e.g. sickle cell anemia and thalassemia), lupus, acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, myeloproliferative disorders, myelodysplastic syndromes, multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's disease, aplastic anemia, pure red cell aplasia, hemoglobinuria, Fanconi anemia, thalassemia, sickle cell anemia, Wiskott-Aldrich syndrome, inborn errors of metabolism (such as Gaucher disease among others).

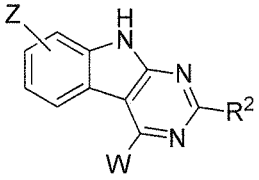
32. A pharmaceutical composition according to claim 15 or 23, which is suitable for intravenous infusion.

33. A kit for use in increasing stem and progenitor cells, comprising a compound as defined in any one of claims 1 to 14, and instructions for use.

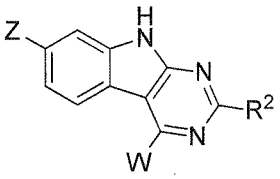
34. A kit for use in expanding hematopoietic stem cells, comprising a compound as defined in any one of claims 1 to 14, and instructions for use, optionally, the kit comprises at least one cell expanding factor which is a biologic or another small molecule.

CLAIMS

1. A compound of general formula I or II



I



II

or a salt thereof,

wherein:

Z is

1) -P(O) (OR^1) (OR^1),
2) -C(O)OR^1,
3) -C(O)NHR^1,
4) -C(O)$N(R^1)R^1$,
5) -C(O)R^1,
6) -CN,
7) -SR^1,
8) -$S(O)_2NH_2$,
9) -$S(O)_2NHR^1$,
10) -$S(O)_2N(R^1)R^1$,
11) -$S(O)R^1$,
12) -$S(O)_2R^1$,
13) -L,
14) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,
15) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,
16) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,
17) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,
18) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or
19) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the is substituted with one or more R^1 or R^A;

W is

1) -OR^1, wherein R^1 is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl,-C_{3-7} cycloalkyl, -C_{3-7} cycloalkenyl, -C_{1-5} perfluorinated, -heterocyclyl, -aryl, -heteroaryl, -benzyl, or 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl, wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;
2) -L-OH,
3) -L-OR^1,
4) -SR^1,
5) -CN,
6) -P(O)(OR^1)(OR^1),
7) -NHR^1,
8) –N(R^1)R^1,
9) -L-NH_2,
10) -L-NHR^1,
11) -L-N(R^1)R^1,
12) -L-SR^1,
13) -L-S(O)R^1,
14) -L-$S(O)_2R^1$,
15) -L-P(O)(OR^1)(OR^1),
16) -C(O)OR^1,
17) -C(O)NH_2,
18) -C(O)NHR^1,
19) -C(O)N(R^1)R^1,
20) -NHC(O)R^1,
21) -NR^1C(O)R^1,
22) -NHC(O)OR^1,
23) -NR^1C(O)OR^1,

24) -$OC(O)NH_2$,

25) -$OC(O)NHR^1$,

26) -$OC(O)N(R^1)R^1$,

27) -$OC(O)R^1$,

28) -$C(O)R^1$,

29) -$NHC(O)NH_2$,

30) -$NHC(O)NHR^1$,

31) -$NHC(O)N(R^1)R^1$,

32) -$NR^1C(O)NH_2$,

33) -$NR^1C(O)NHR^1$,

34) -$NR^1C(O)N(R^1)R^1$,

35) -$NHS(O)_2R^1$,

36) -$NR^1S(O)_2R^1$,

37) -$S(O)_2NH_2$,

38) -$S(O)_2NHR^1$,

39) -$S(O)_2N(R^1)R^1$,

40) -$S(O)R^1$,

41) -$S(O)_2R^1$,

42) -$OS(O)_2R^1$,

43) -$S(O)_2OR^1$,

44) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

45) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

46) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heterocyclyl groups,

47) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

48) -L-$NR^1(R^1)$,

49) –$(L-)_2$ NR^1,

50) -L-$(N(R^1)-L)_n$ – $N(R^1)R^1$,

51) -L-$(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

52) -L-$(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

53) -L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

54) -O-L-N(R^1)R^1,

55) -O-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

56) -O-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

57) -O-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

58) –(O-L)$_2$-NR^1,

59) -O-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

60) -O-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

61) -O-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

62) -O-L-(N(R^1)-L)$_n$- aryl optionally substituted with one or more R^A or R^1 substituents,

63) -S-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents,

64) -S-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

65) -S-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

66) –(S-L)$_2$ NR^1,

67) -S-L-(N(R^1)-L)$_n$ – N(R^1)R^1,

68) -S-L-(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A substituents,

69) -S-L-(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A substituents,

70) -S-L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A substituents,

71) -NR^1(R^1),

72) -(N(R^1)-L)$_n$ – N(R^1)R^1,

73) –(N(R^1)L)$_2$ –NR^1,

74) -(N(R^1)-L)$_n$ – N(R^1)R^A,

75) -(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents,

76) -(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

77) -$(N(R^1)\text{-}L)_n$ – aryl optionally substituted with one or more R^A or R^1 substituents,

78) -heteroaryl optionally substituted with one or more R^A substituents, or

79) -aryl optionally substituted with one or more R^A substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein when two R^1 substituents are present on the same nitrogen atom, then each R^1 substituent is independently selected from the list of R^1 values described thereafter,

and wherein n is an integer equal to either 0, 1, 2, 3, 4, or 5,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A;

L is

1) -$C_{1\text{-}6}$ alkyl,
2) -$C_{2\text{-}6}$ alkenyl,
3) -$C_{2\text{-}6}$ alkynyl,
4) -$C_{3\text{-}7}$ cycloalkyl,
5) -$C_{3\text{-}7}$ cycloalkenyl,
6) heterocyclyl,
7) -$C_{1\text{-}6}$ alkyl-$C_{3\text{-}7}$ cycloalkyl,
8) -$C_{1\text{-}6}$ alkyl-heterocyclyl,
9) aryl, or
10) heteroaryl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkyl, the cycloalkenyl, the heterocyclyl, the aryl and the heteroaryl groups are each independently optionally substituted with one or two R^A substituent;

R^1 is

1) –H,
2) -$C_{1\text{-}6}$ alkyl,
3) -$C_{2\text{-}6}$ alkenyl,
4) -$C_{2\text{-}6}$ alkynyl,
5) -$C_{3\text{-}7}$ cycloalkyl,
6) -$C_{3\text{-}7}$ cycloalkenyl,
7) -$C_{1\text{-}5}$ perfluorinated,
8) -heterocyclyl,

9) -aryl,

10) -heteroaryl,

11) -benzyl, or

12) 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

R^2 is

1) -H,
2) $-C_{1-6}$ alkyl,
3) $-SR^1$,
4) $-C(O)R^1$,
5) $-S(O)R^1$,
6) $-S(O)_2R^1$,
7) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,
8) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heteroaryl groups,
9) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,
10) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the aryl groups,
11) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or
12) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present;

R^A is

1) -halogen,
2) $-CF_3$,
3) -OH,
4) $-OR^1$,
5) -L-OH,
6) $-L-OR^1$,
7) $-OCF_3$,
8) -SH,
9) -SR1,

10) -CN,

11) $-NO_2$,

12) $-NH_2$,

13) $-NHR^1$,

14) $-NR^1R^1$,

15) $-L-NH_2$,

16) $-L-NHR^1$,

17) $-L-SR^1$,

18) $-L-S(O)R^1$,

19) $-L-S(O)_2R^1$,

20) -C(O)OH,

21) $-C(O)OR^1$,

22) $-C(O)NH_2$,

23) $-C(O)NHR^1$,

24) $-C(O)N(R^1)R^1$,

25) $-NHC(O)R^1$,

26) $-NR^1C(O)R^1$,

27) $-NHC(O)OR^1$,

28) $-NR^1C(O)OR^1$,

29) $-OC(O)NH_2$,

30) $-OC(O)NHR^1$,

31) $-OC(O)N(R^1)R^1$,

32) $-OC(O)R^1$,

33) $-C(O)R^1$,

34) $-NHC(O)NH_2$,

35) $-NHC(O)NHR^1$,

36) $-NHC(O)N(R^1)R^1$,

37) $-NR^1C(O)NH_2$,

38) $-NR^1C(O)NHR^1$,

39) $-NR^1C(O)N(R^1)R^1$,

40) $-NHS(O)_2R^1$,

41) $-NR^1S(O)_2R^1$,

42) $-S(O)_2NH_2$,

43) $-S(O)_2NHR^1$,

44) -$S(O)_2N(R^1)R^1$,

45) -$S(O)R^1$,

46) -$S(O)_2R^1$,

47) -$OS(O)_2R^1$,

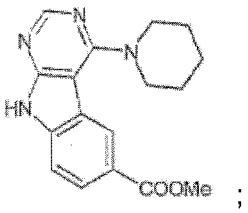
48) -$S(O)_2OR^1$,

49) -benzyl,

50) -N_3, or

51) -C(-N=N-)(CF_3),

and wherein the benzyl group is optionally substituted with 1, 2 or 3 R^A or R^1 substituents provided that the compound of Formula (I) is other than



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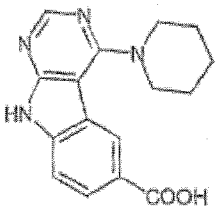

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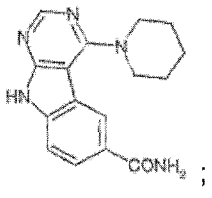

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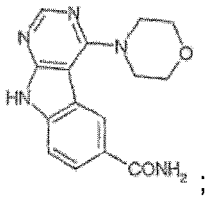

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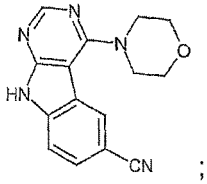

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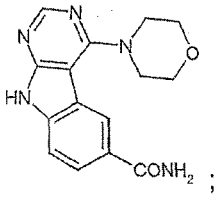

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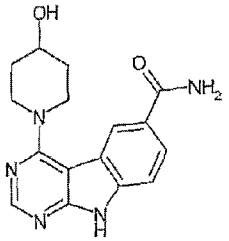

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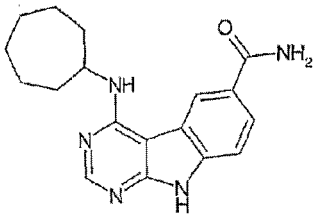

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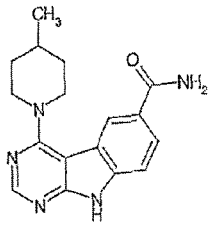

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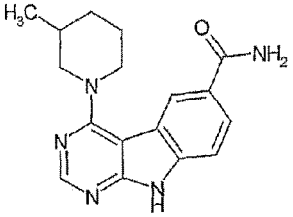

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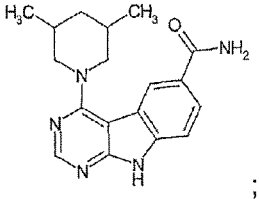

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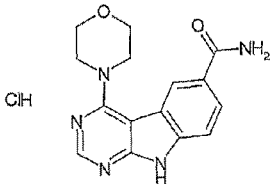

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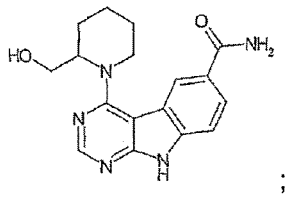
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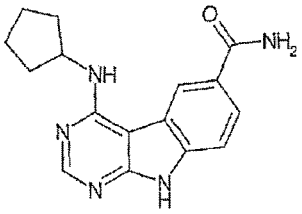
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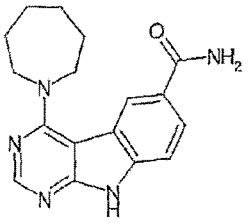
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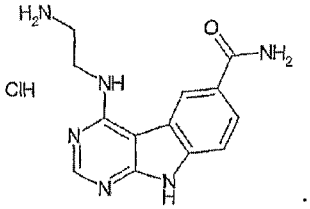
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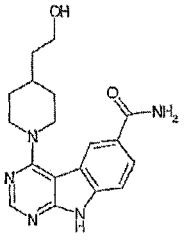
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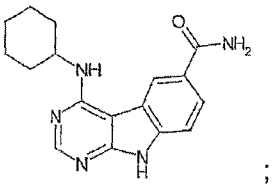
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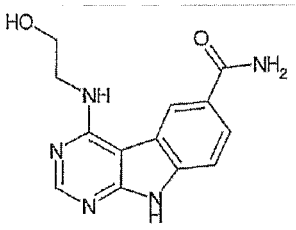
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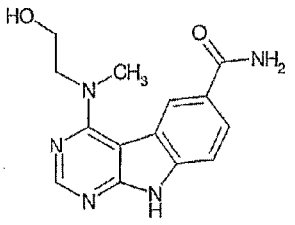
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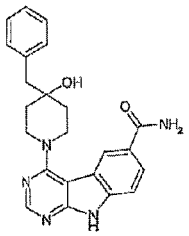
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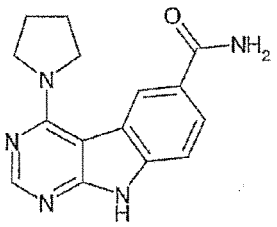
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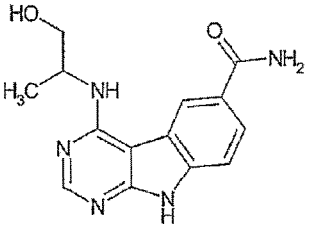
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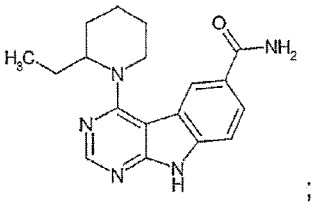
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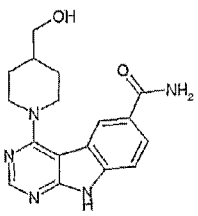
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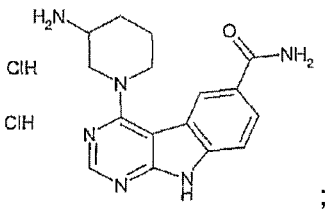
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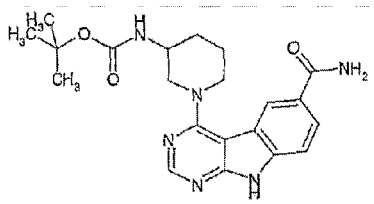
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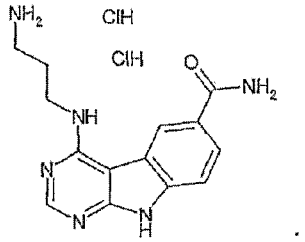
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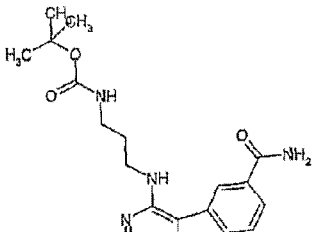
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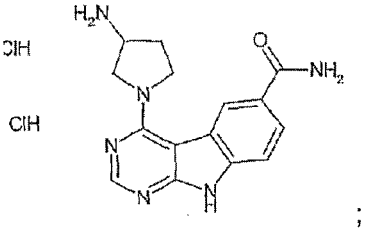
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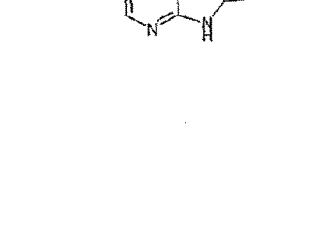
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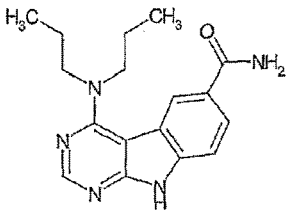
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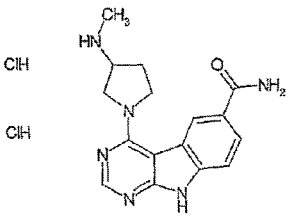
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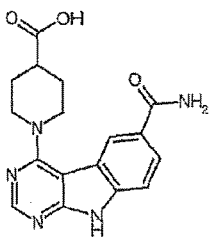
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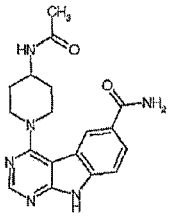
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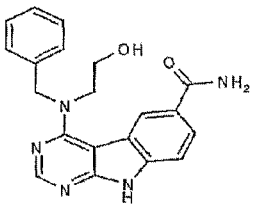
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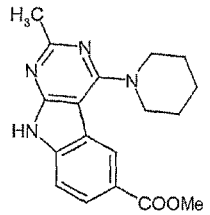
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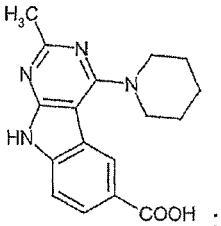
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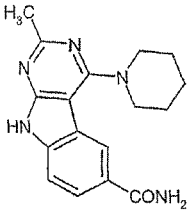
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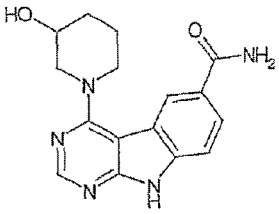
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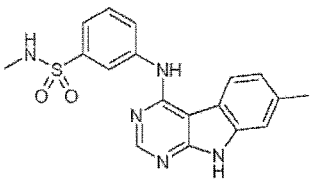
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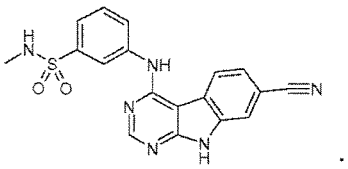
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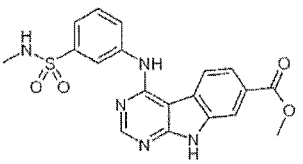
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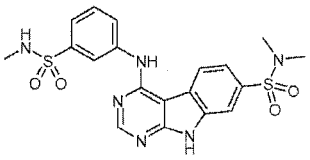
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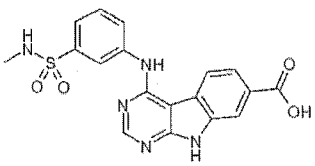
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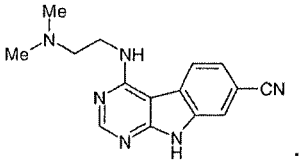
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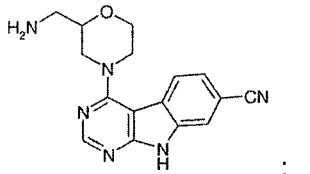
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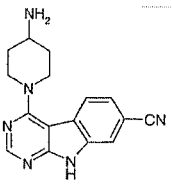
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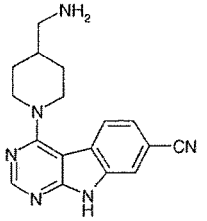
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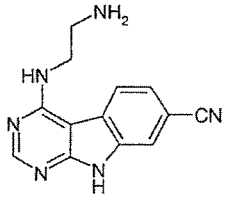
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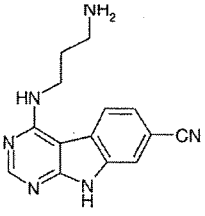
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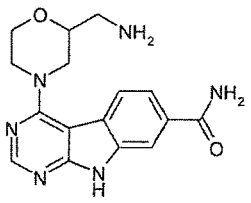
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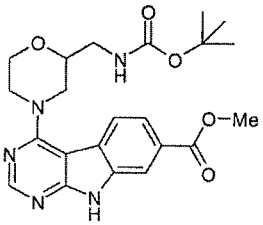
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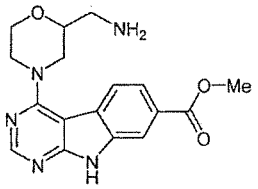
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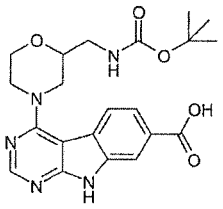
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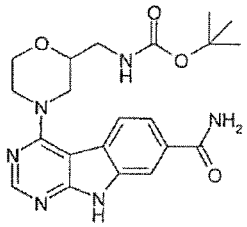
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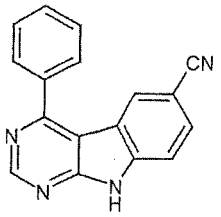
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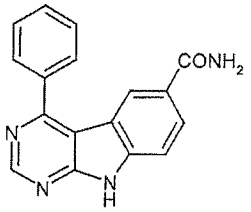
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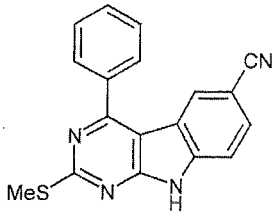
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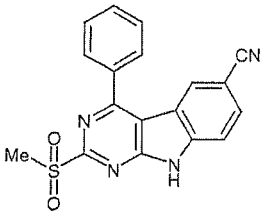
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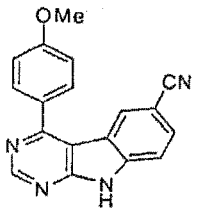
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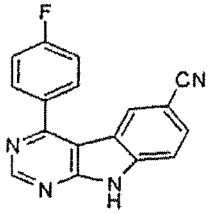
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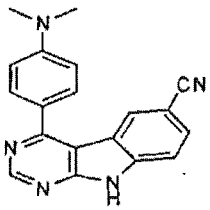
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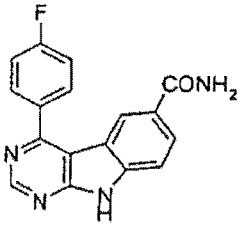
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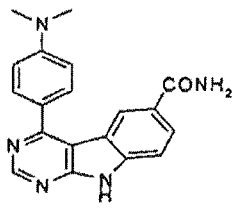
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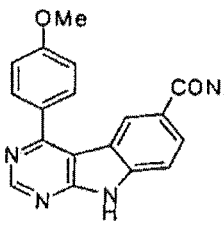
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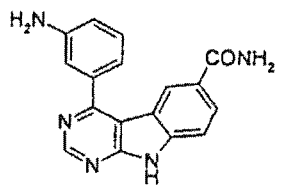

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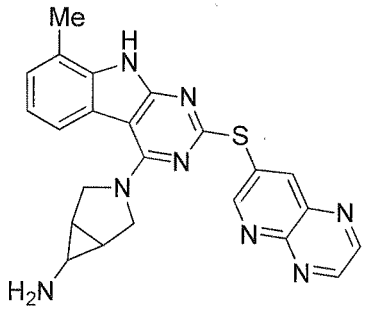
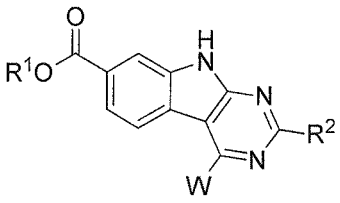
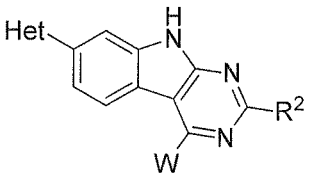


.

2. A compound according to claim 1, wherein the compound is of formula IIA, IIB or IIC

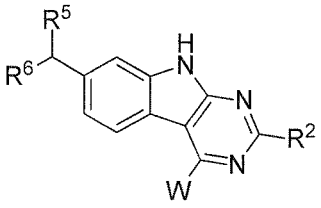


IIA



IIB

or



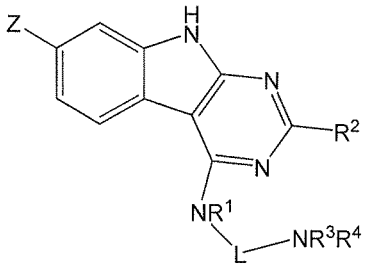
IIC

or a salt thereof

wherein Het is a 3 to 7-membered heterocycle, optionally substituted with one or more R^1 or R^A, and R^5 and R^6 are the same or different and are each independently L, or they join together with C to form a 5 to 7-membered ring which optionally includes one or more heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

3. A compound according to claim 2, wherein the ring is a 5-membered ring, and the heteroatom is N.

4. A compound according to claim 1, wherein the compound is of formula



or a salt thereof,

wherein R^3 and R^4 are the same or different and are each independently H, or R^1, or R^3 and R^4 join together with N to which they are attached to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

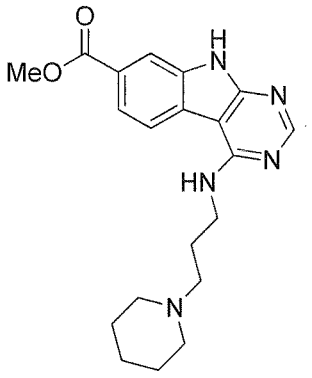
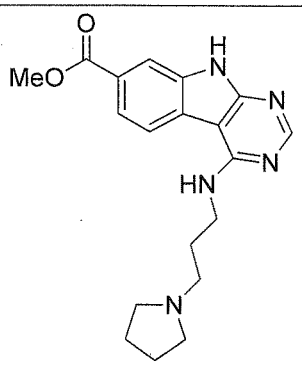
5. A compound according to claim 1, wherein:

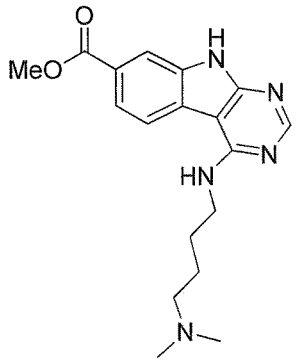
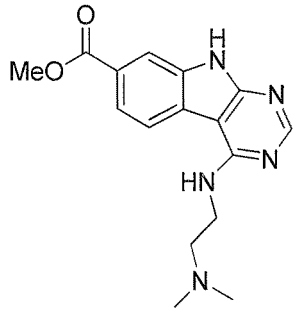
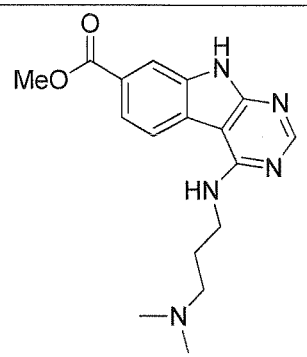
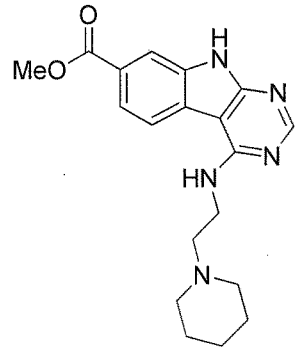
Z is CO_2Me or 2-methyl-2H-tetrazol-5-yl;

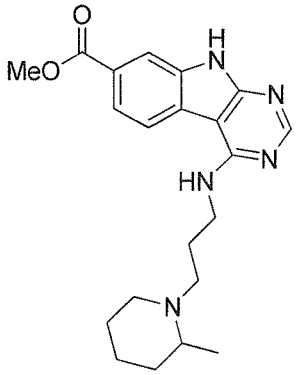
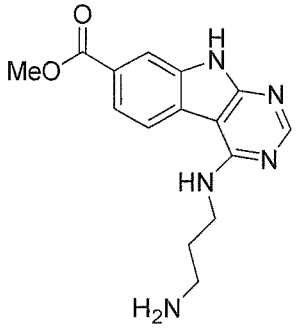
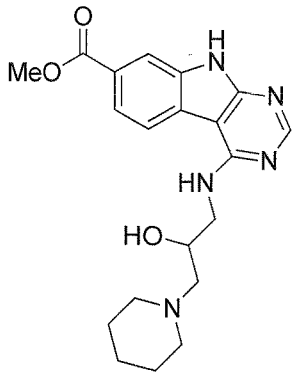
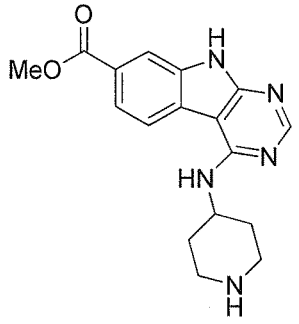
R^2 is benzyl or H; and

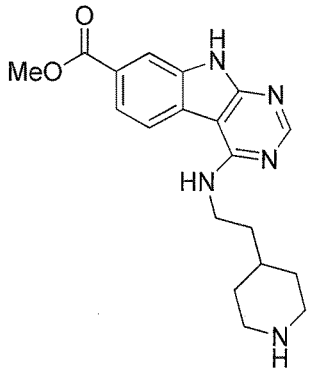
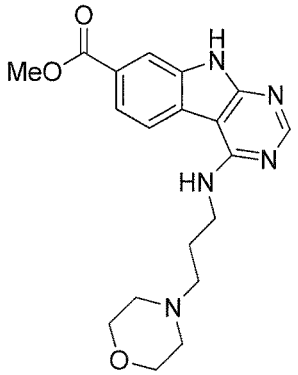
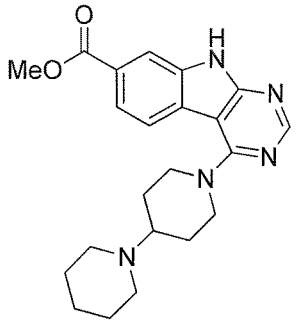
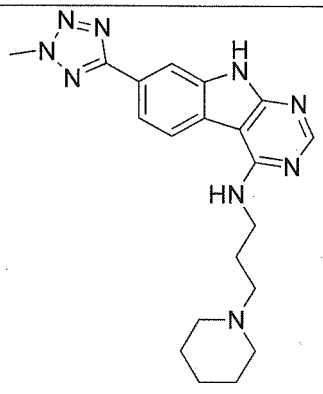
W is NH-L-N(R^1)R^1 wherein L is C_{2-4} alkyl or C_{3-7} cycloalkyl and R^1 and (R1) is C_{1-4} alkyl or H; or (R^1) and R^1 join together with the nitrogen atom to which they are attached to form a 3 to 7-membered ring, which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

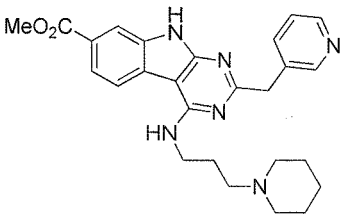
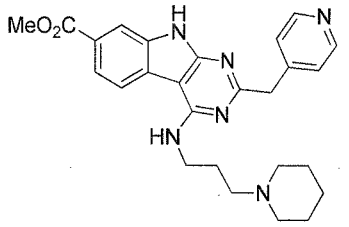
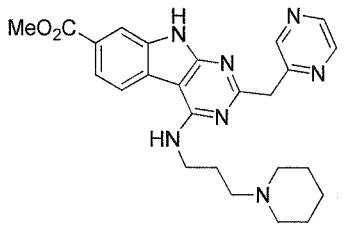
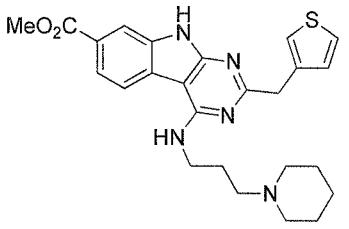
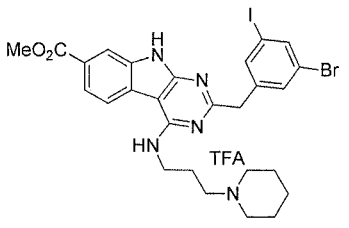
6. A compound according to claim 1 which is:

Compound number	**Structure**
1	
2	

Compound number	Structure
3	
4	
5	
6	

Compound number	Structure
7	
8	
9	
10	

Compound number	Structure
11	
12	
13	
14	

Compound number	Structure
15	
16	
17	
18	
19	

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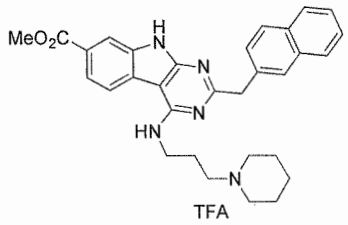
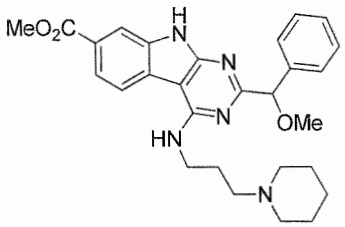
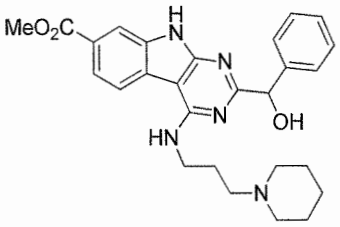
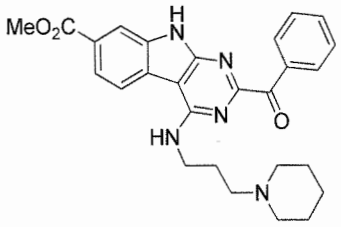
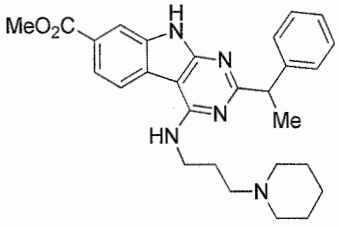
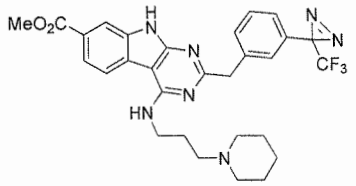
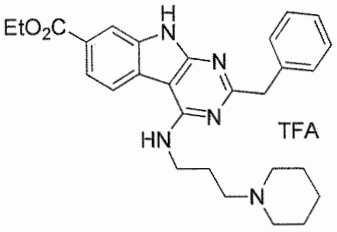
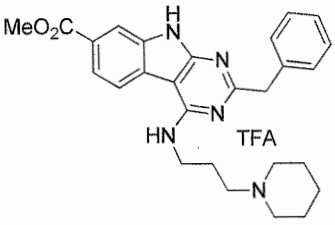
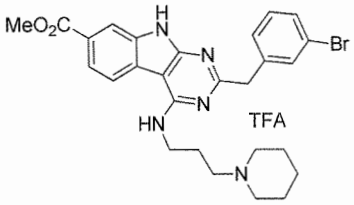
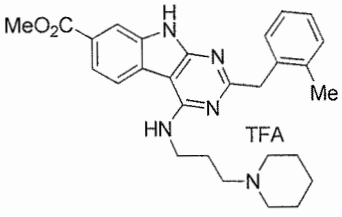
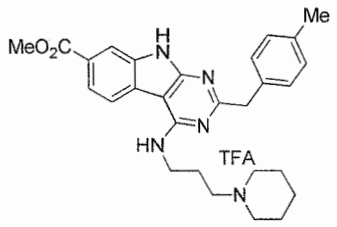
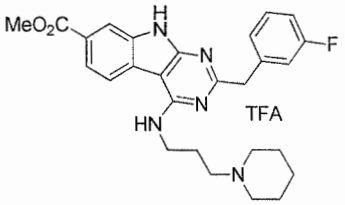
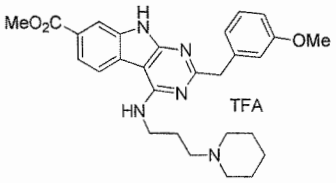
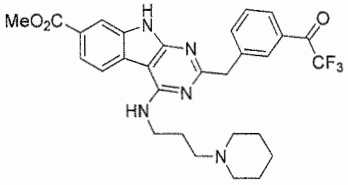
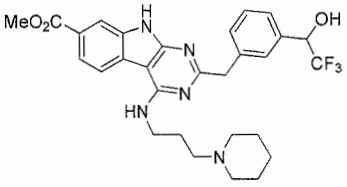
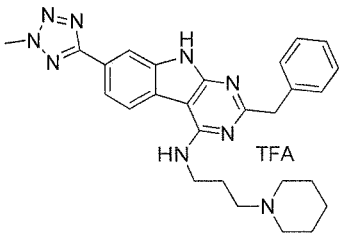
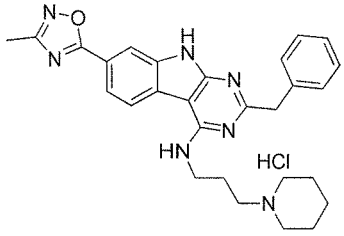
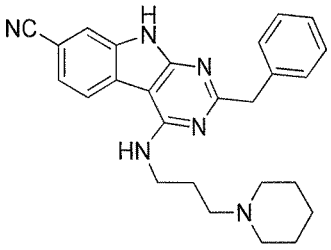
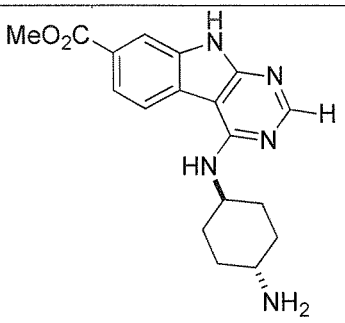
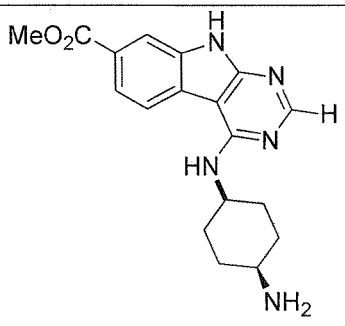
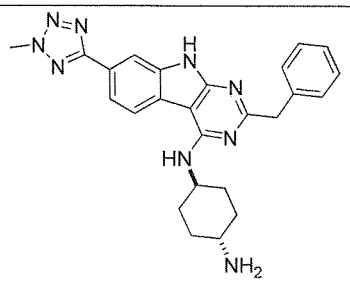
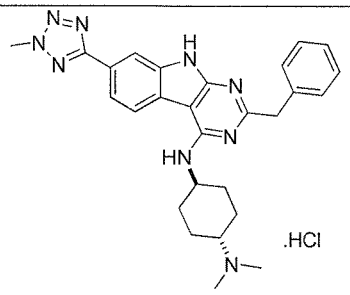
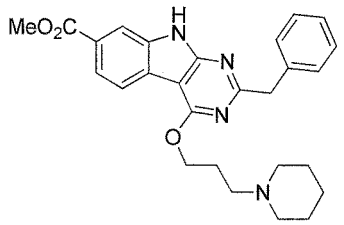
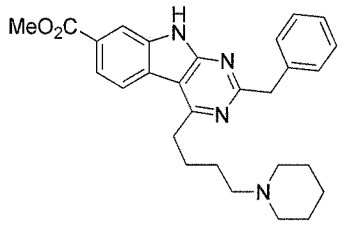
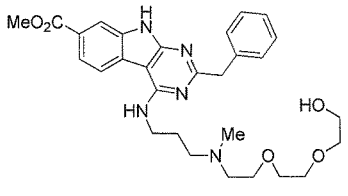
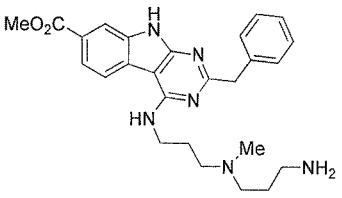
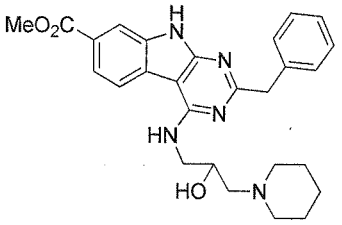
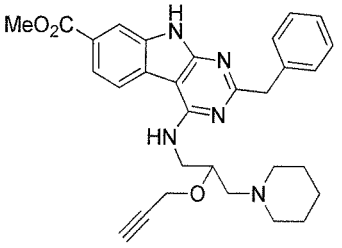
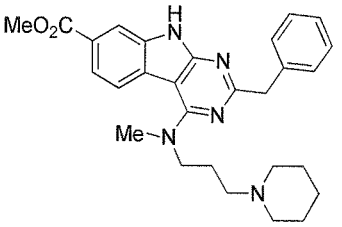
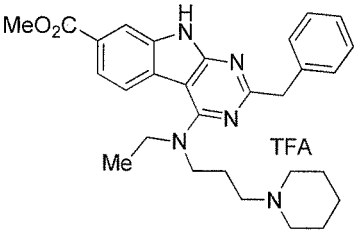
20	
21	
22	
23	
24	

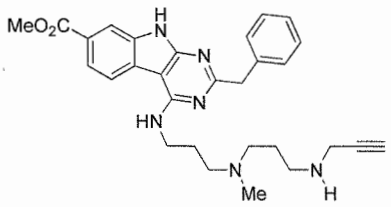
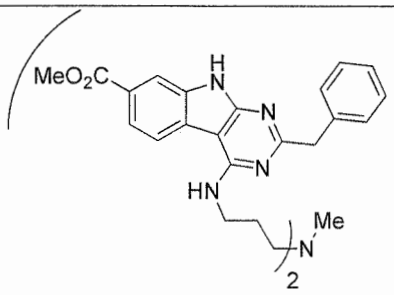
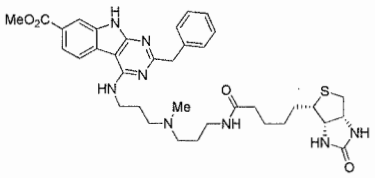
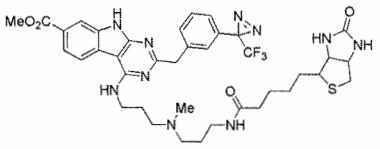
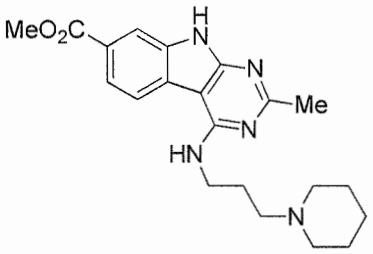
Compound number	Structure
25	
26	
27	
28	
29	

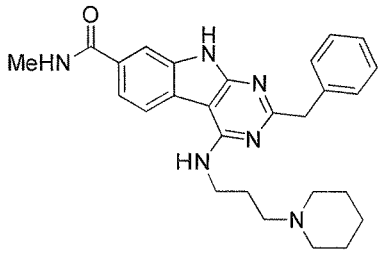
Compound number	Structure
30	
31	
32	
33	
34	

Compound number	Structure
35	
36	
37	
38	
39	

Compound number	Structure
40	
41	
42	
43	
44	

Compound number	Structure
45	
46	
47	
48	
49	

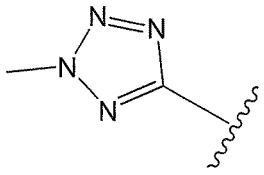
Compound number	Structure
50	
51	
52	
53	
54	

Compound number	Structure
55	

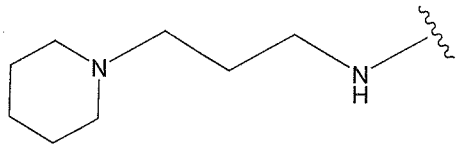
or a salt thereof.

7. A compound according to claim 2, wherein R^2 is benzyl or H.

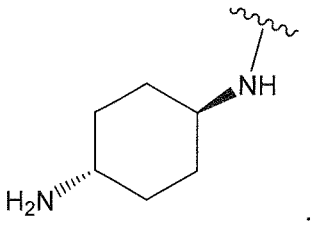
8. A compound according to claim 2, wherein R^5 and R^6 join together with C to form:



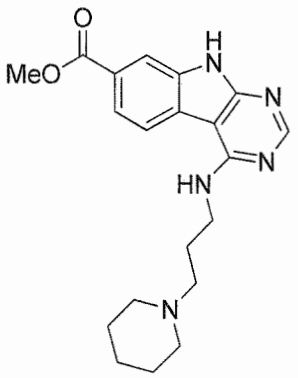
9. A compound according to claim 2, wherein W is

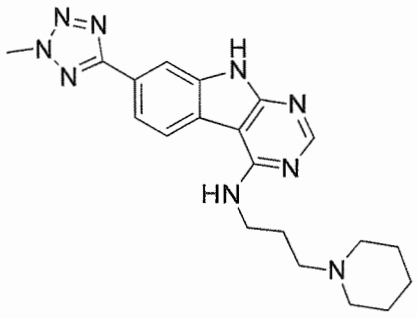


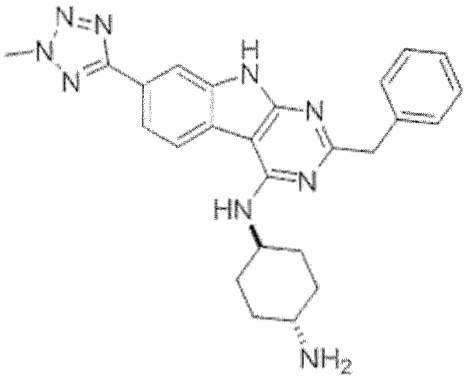
or



10. The compound according to claim 1, wherein the compound is

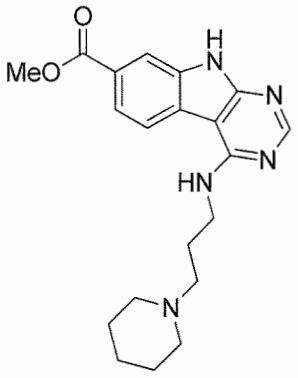




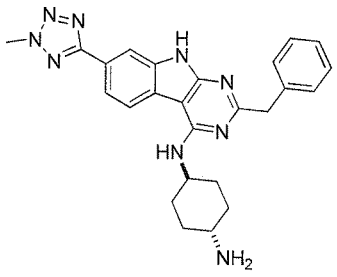


or a pharmaceutically acceptable salt thereof.

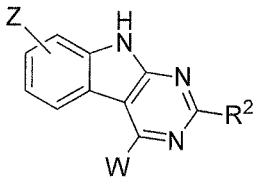
11. The compound of claim 1 which is a hydrochloride salt of



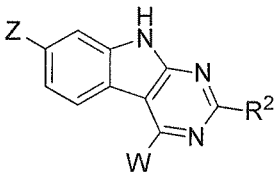
12. The compound of claim 1 which is a hydrobromide salt of



13. A method of increasing stem and progenitor cells, the method comprising; contacting a starting population in the presence of at least one compound, optionally together with at least one cell expanding factor which is a biologic or another small molecule, wherein said compound is of general formula I or II



I



II

or a salt thereof,

wherein:

Z is

1) -P(O) (OR^1) (OR^1),
2) -C(O)OR^1,
3) -C(O)NHR^1,
4) -C(O)N(R^1)R^1,
5) -C(O)R^1,
6) -CN,
7) -SR^1,
8) -S(O)$_2$NH_2,
9) -S(O)$_2$NHR^1,
10) -S(O)$_2$N(R^1)R^1,
11) -S(O)R^1,

12) -$S(O)_2R^1$,

13) -L,

14) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

15) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

16) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,

17) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

18) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

19) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present, and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the is substituted with one or more R^1 or R^A;

W is

1) -H,

2) -halogen,

3) -OR^1,

4) -L-OH,

5) -L-OR^1,

6) -SR^1,

7) -CN,

8) -$P(O)(OR^1)(OR^1)$,

9) -NHR^1,

10) –$N(R^1)R^1$,

11) -L-NH_2,

12) -L-NHR^1,

13) -L-$N(R^1)R^1$,

14) -L-SR^1,

15) -L-$S(O)R^1$,

16) -L-$S(O)_2R^1$,

17) -L-P(O)(OR^1)(OR^1),

18) -C(O)OR^1,

19) -C(O)NH_2,

20) -C(O)NHR^1,

21) -C(O)$N(R^1)R^1$,

22) -NHC(O)R^1,

23) -NR^1C(O)R^1,

24) -NHC(O)OR^1,

25) -NR^1C(O)OR^1,

26) -OC(O)NH_2,

27) -OC(O)NHR^1,

28) -OC(O)$N(R^1)R^1$,

29) -OC(O)R^1,

30) -C(O)R^1,

31) -NHC(O)NH_2,

32) -NHC(O)NHR^1,

33) -NHC(O)$N(R^1)R^1$,

34) -NR^1C(O)NH_2,

35) -NR^1C(O)NHR^1,

36) -NR^1C(O)$N(R^1)R^1$,

37) -NHS$(O)_2R^1$,

38) -NR^1S$(O)_2R^1$,

39) -S$(O)_2NH_2$,

40) -S$(O)_2NHR^1$,

41) -S$(O)_2N(R^1)R^1$,

42) -S(O)R^1,

43) -S$(O)_2R^1$,

44) -OS$(O)_2R^1$,

45) -S$(O)_2OR^1$,

46) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,

47) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heteroaryl groups,

48) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and the heterocyclyl groups,

49) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

50) -L-$NR^1(R^1)$,

51) –$(L-)_2$ NR^1,

52) -L-$(N(R^1)-L)_n$ – $N(R^1)R^1$,

53) -L-$(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

54) -L-$(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

55) -L-$(N(R^1)-L)_n$ – aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

56) -O-L-$N(R^1)R^1$,

57) -O-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

58) -O-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

59) -O-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

60) –$(O-L)_2$-NR^1,

61) -O-L-$(N(R^1)-L)_n$ – $N(R^1)R^1$,

62) -O-L-$(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heteroaryl groups,

63) -O-L-$(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and heterocyclyl groups,

64) -O-L-$(N(R^1)-L)_n$- aryl optionally substituted with one or more R^A or R^1 substituents,

65) -S-L- heteroaryl optionally substituted with one or more R^A or R^1 substituents,

66) -S-L- heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

67) -S-L- aryl optionally substituted with one or more R^A or R^1 substituents attached on either or both the L and aryl groups,

68) –$(S-L)_2$ NR^1,

69) -S-L-$(N(R^1)-L)_n$ – $N(R^1)R^1$,

70) -S-L-$(N(R^1)-L)_n$ – heteroaryl optionally substituted with one or more R^A substituents,

71) -S-L-$(N(R^1)-L)_n$ – heterocyclyl optionally substituted with one or more R^A substituents,

72) -S-L-(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A substituents,

73) -NR^1(R^1),

74) -(N(R^1)-L)$_n$ – N(R^1)R^1,

75) –(N(R^1)L)$_2$ –NR^1,

76) -(N(R^1)-L)$_n$ – N(R^1)R^A,

77) -(N(R^1)-L)$_n$ – heteroaryl optionally substituted with one or more R^A or R^1 substituents,

78) -(N(R^1)-L)$_n$ – heterocyclyl optionally substituted with one or more R^A or R^1 substituents,

79) -(N(R^1)-L)$_n$ – aryl optionally substituted with one or more R^A or R^1 substituents,

80) -heteroaryl optionally substituted with one or more R^A substituents, or

81) -aryl optionally substituted with one or more R^A substituents,

and wherein each substituent is optionally attached to the L group if it is not already present,

and wherein when two R^1 substituents are present on the same nitrogen atom, then each R^1 substituent is independently selected from the list of R^1 values described thereafter,

and wherein n is an integer equal to either 0, 1, 2, 3, 4, or 5,

and wherein, when (R^1) and R^1 are attached to a nitrogen atom, optionally they join together with the nitrogen atom to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A;

L is

1) -C_{1-6} alkyl,
2) -C_{2-6} alkenyl,
3) -C_{2-6} alkynyl,
4) -C_{3-7} cycloalkyl,
5) -C_{3-7} cycloalkenyl,
6) heterocyclyl,
7) -C_{1-6} alkyl-C_{3-7} cycloalkyl,
8) -C_{1-6} alkyl-heterocyclyl,
9) aryl, or
10) heteroaryl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkyl, the cycloalkenyl, the heterocyclyl, the aryl and the heteroaryl groups are each independently optionally substituted with one or two R^A substituent;

R^1 is

1) –H,
2) -C_{1-6} alkyl,
3) -C_{2-6} alkenyl,
4) -C_{2-6} alkynyl,
5) -C_{3-7} cycloalkyl,
6) -C_{3-7} cycloalkenyl,
7) -C_{1-5} perfluorinated,
8) -heterocyclyl,
9) -aryl,
10) -heteroaryl,
11) -benzyl, or
12) 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoyl,

and wherein the alkyl, the alkenyl, the alkynyl, the cycloalkenyl, the perfluorinated alkyl, the heterocyclyl, the aryl, the heteroaryl and the benzyl groups are each independently optionally substituted with 1, 2 or 3 R^A or R^1 substituents;

R^2 is

1) -H,
2) -C_{1-6} alkyl,
3) -SR^1,
4) -$C(O)R^1$,
5) -$S(O)R^1$,
6) -$S(O)_2R^1$,
7) -benzyl optionally substituted with 1, 2 or 3 R^A or R^1 substituents,
8) -L-heteroaryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heteroaryl groups,
9) -L-heterocyclyl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the heterocyclyl groups,
10) -L-aryl optionally substituted with one or more R^A or R^1 substituents attached on either one or both the L and the aryl groups,

11) -heteroaryl optionally substituted with one or more R^A or R^1 substituents, or

12) -aryl optionally substituted with one or more R^A or R^1 substituents,

and wherein each substituent is optionally attached to the L group if it is not already present;

R^A is

1) -halogen,
2) $-CF_3$,
3) -OH,
4) $-OR^1$,
5) -L-OH,
6) $-L-OR^1$,
7) $-OCF_3$,
8) -SH,
9) -SR1,
10) -CN,
11) $-NO_2$,
12) $-NH_2$,
13) $-NHR^1$,
14) $-NR^1R^1$,
15) $-L-NH_2$,
16) $-L-NHR^1$,
17) $-L-SR^1$,
18) $-L-S(O)R^1$,
19) $-L-S(O)_2R^1$,
20) -C(O)OH,
21) $-C(O)OR^1$,
22) $-C(O)NH_2$,
23) $-C(O)NHR^1$,
24) $-C(O)N(R^1)R^1$,
25) $-NHC(O)R^1$,
26) $-NR^1C(O)R^1$,
27) $-NHC(O)OR^1$,
28) $-NR^1C(O)OR^1$,
29) $-OC(O)NH_2$,

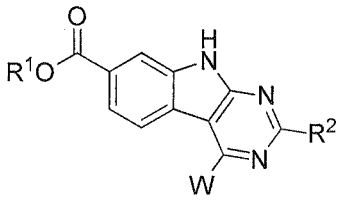
30) -OC(O)NHR^1,
31) -OC(O)N(R^1)R^1,
32) -OC(O)R^1,
33) -C(O)R^1,
34) -NHC(O)NH$_2$,
35) -NHC(O)NHR^1,
36) -NHC(O)N(R^1)R^1,
37) -NR^{1}C(O)NH$_2$,
38) -NR^{1}C(O)NHR^1,
39) -NR^{1}C(O)N(R^1)R^1,
40) -NHS(O)$_2$R^1,
41) -NR^{1}S(O)$_2$R^1,
42) -S(O)$_2$NH$_2$,
43) -S(O)$_2$NHR^1,
44) -S(O)$_2$N(R^1)R^1,
45) -S(O)R^1,
46) -S(O)$_2$R^1,
47) -OS(O)$_2$R^1,
48) -S(O)$_2$OR^1,
49) -benzyl,
50) -N$_3$, or
51) -C(-N=N-)(CF$_3$),

and wherein the benzyl group is optionally substituted with 1, 2 or 3 R^A or R^1 substituents.

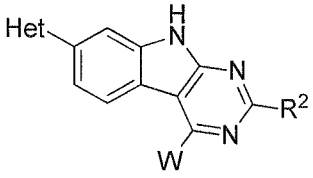
14. The method of claim 13, which is ex vivo.

15. The method of claim 14, comprising contacting the starting population with at least one cell expanding factor which is a biologic.

16. The method of claim 13, wherein the compound is of formula IIA, IIB or IIC

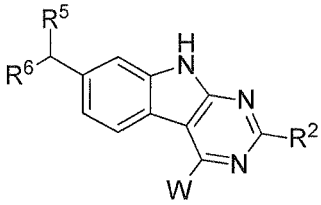


IIA



IIB

or



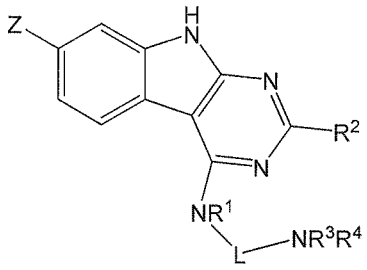
IIC

or a salt thereof

wherein Het is a 3 to 7-membered heterocycle, optionally substituted with one or more R^1 or R^A and R^5 and R^6 join together with C to form a 5 to 7-membered ring which optionally includes one or more heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

17. The method of claim 16, wherein the ring is a 5-membered ring, and the heteroatom is N.

18. The method of claim 13, wherein the compound is of formula



or a salt thereof,

wherein R^3 and R^4 are the same or different and are each independently H or R^1, or R^3 and R^4 join together with N to which they are attached to form a 3 to 7-membered ring which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

19. The method of claim 13, wherein:

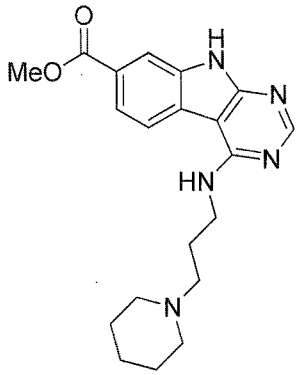
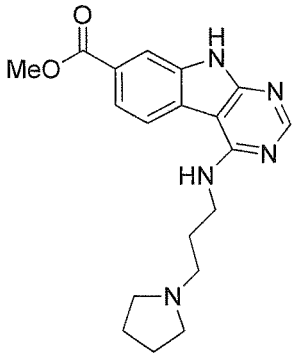
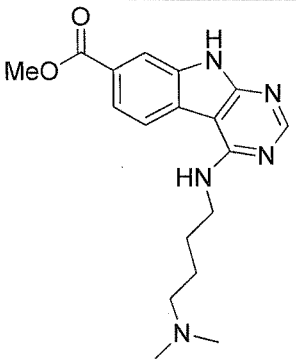
Z is CO_2Me or 2-methyl-2H-tetrazol-5-yl;

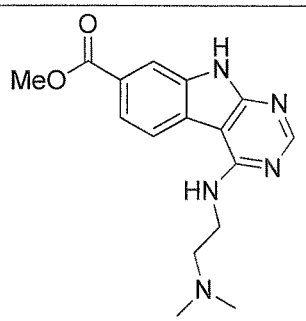
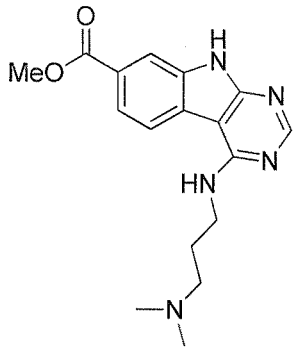
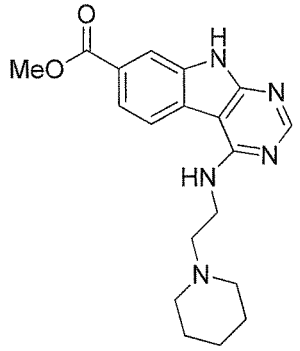
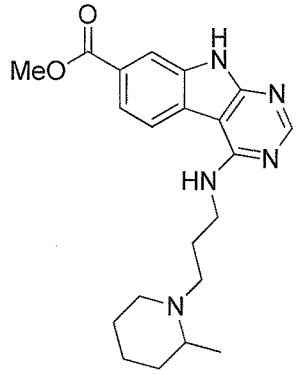
R^2 is benzyl, or H; and

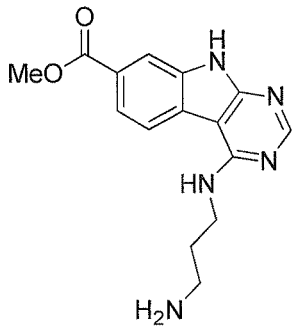
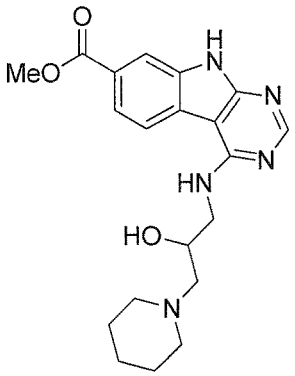
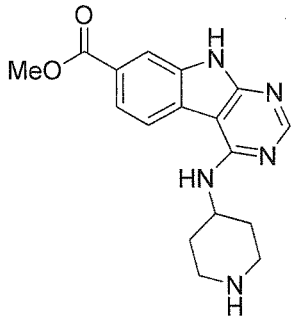
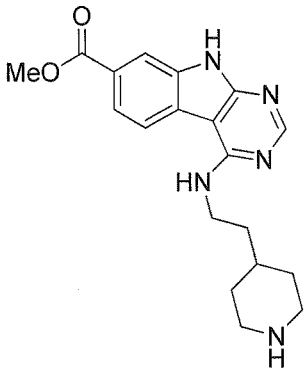
W is NH-L-N(R^1)R^1 wherein L is C_{2-4} alkyl or C_{3-7} cycloalkyl and R^1 and (R1) is C_{1-4} alkyl or H; or (R^1) and R^1 join together with the nitrogen atom to which they are attached to form a 3 to 7-

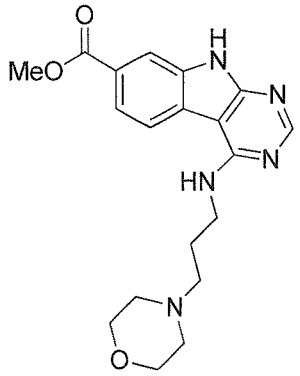
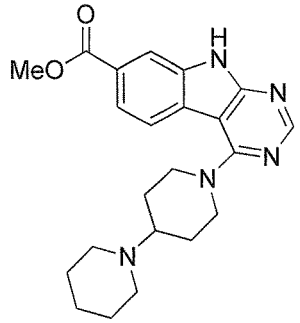
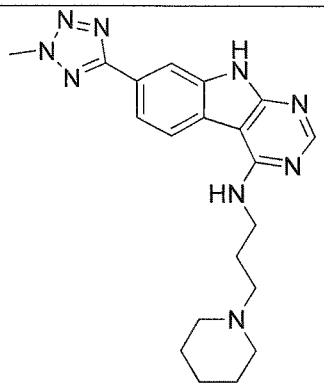
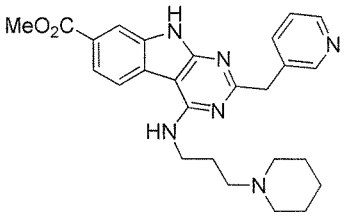
membered ring, which optionally includes one or more other heteroatom selected from N, O and S, optionally the ring is substituted with one or more R^1 or R^A.

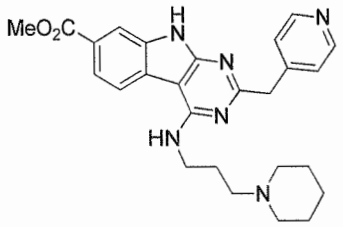
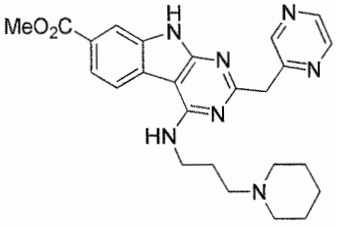
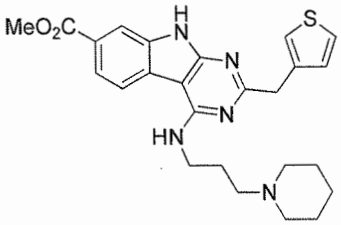
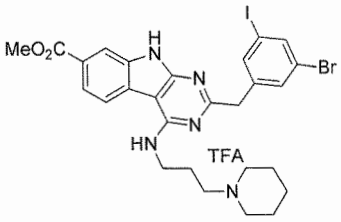
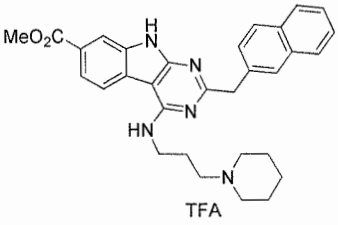
20. The method of claim 13, wherein the compound is:

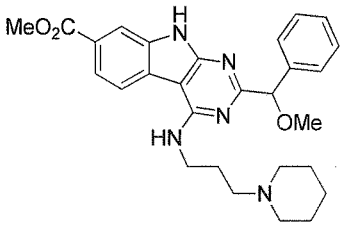
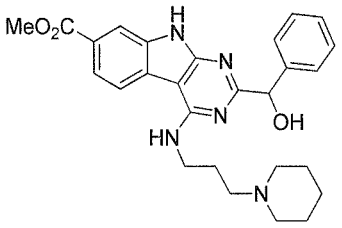
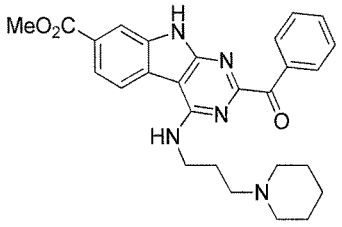
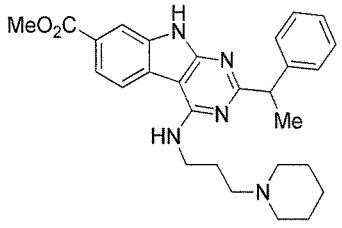
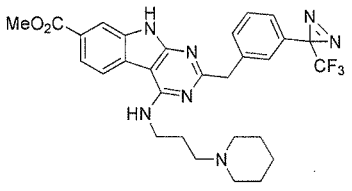
Compound number	Structure
1	
2	
3	

Compound number	Structure
4	
5	
6	
7	

Compound number	Structure
8	
9	
10	
11	

Compound number	Structure
12	
13	
14	
15	

Compound number	Structure
16	
17	
18	
19	
20	

Compound number	Structure
21	
22	
23	
24	
25	

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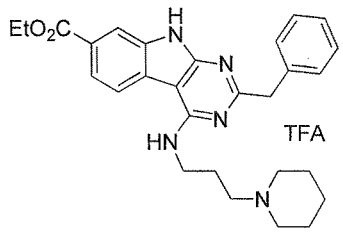
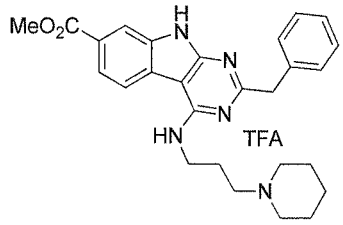
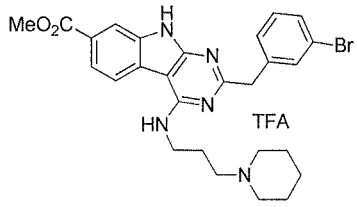
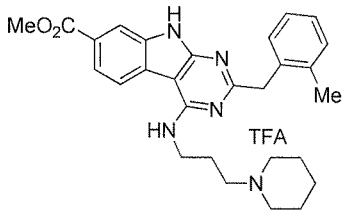
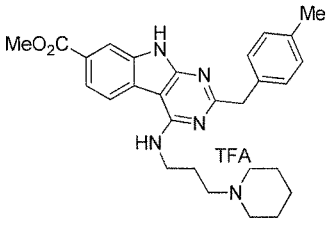
26	
27	
28	
29	
30	

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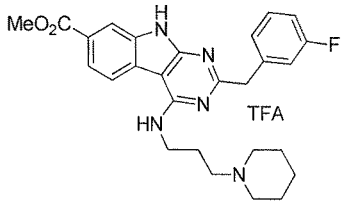
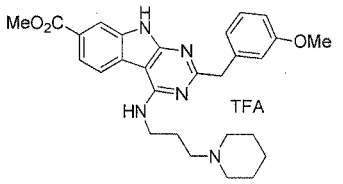
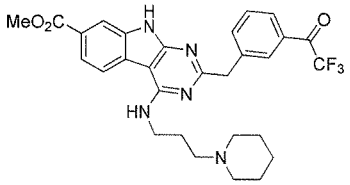
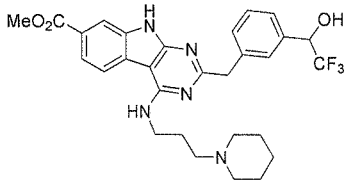
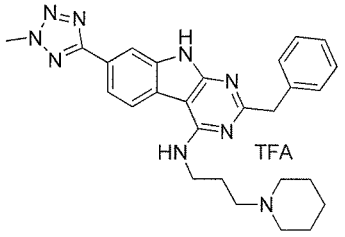
31	
32	
33	
34	
35	

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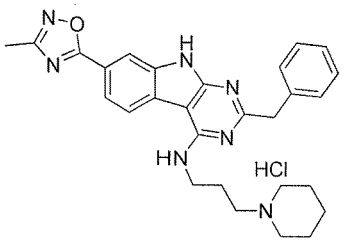
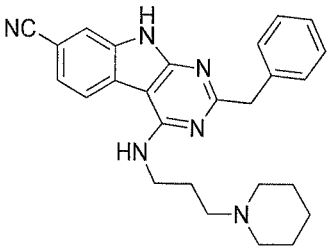
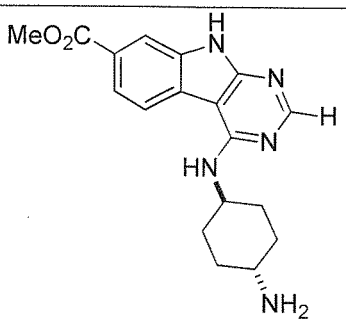
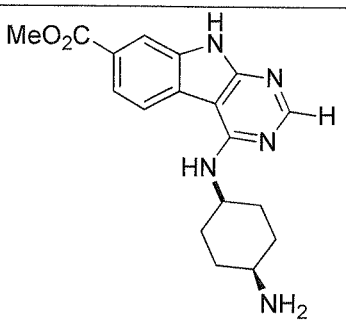
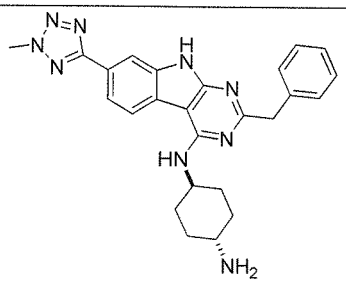
36	
37	
38	
39	
40	

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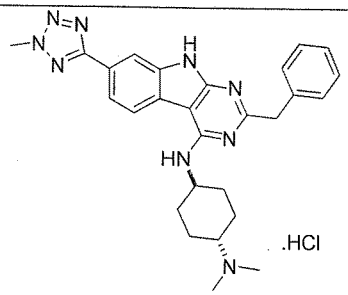
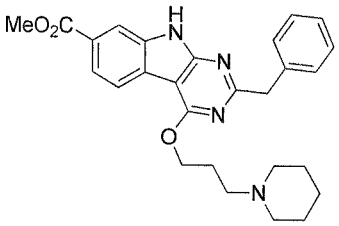
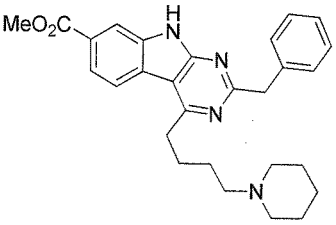
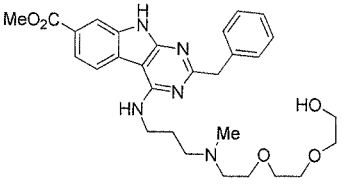
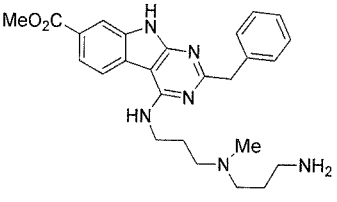
41	
42	
43	
44	
45	

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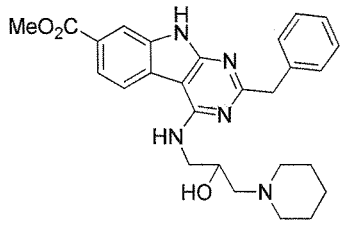
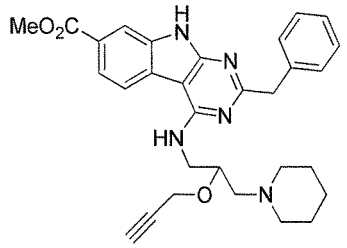
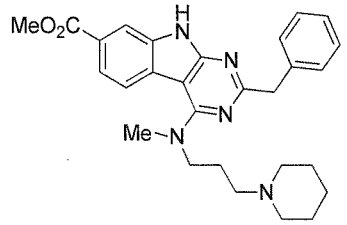
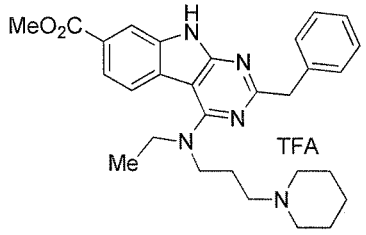
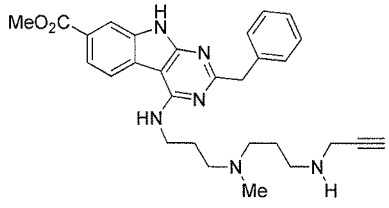
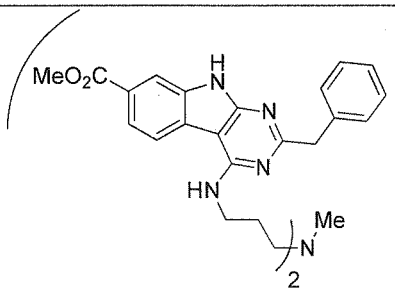
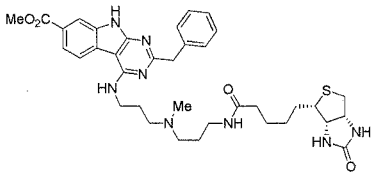
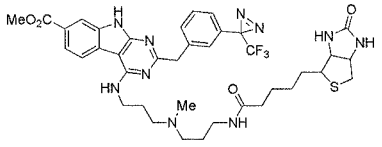
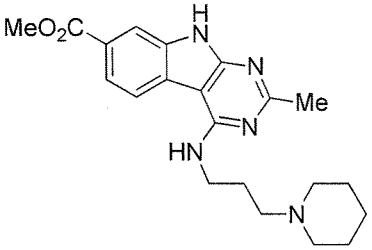
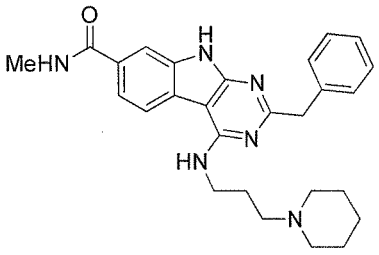
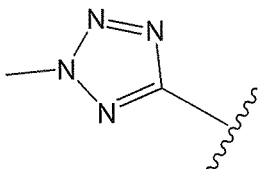
46	
47	
48	
49	
50	

Compound number	Structure
51	
52	
53	
54	
55	

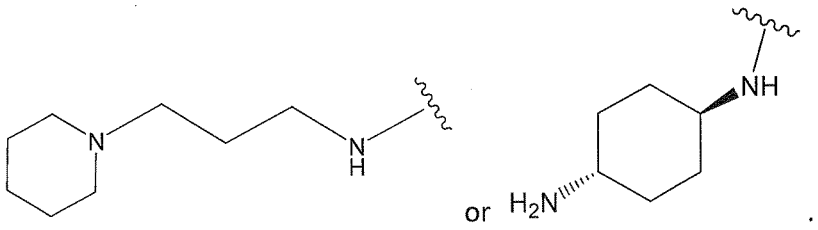
or a salt thereof.

21. The method of claim 16, wherein R^2 is benzyl or H.

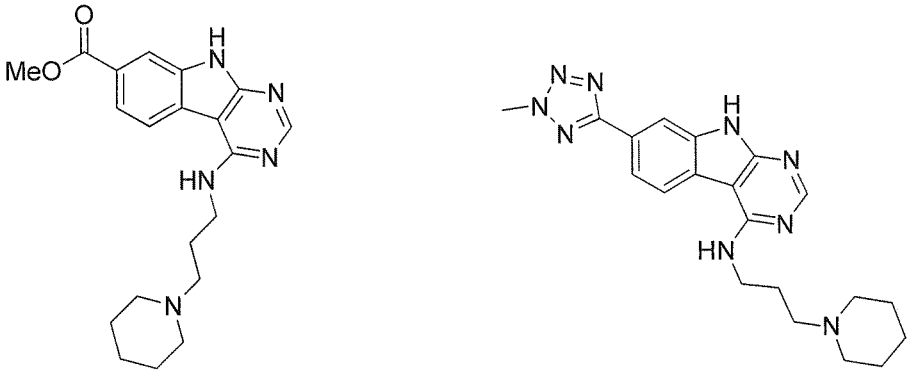
22 The method of claim 16, wherein R^5 and R^6 join together with C to form:

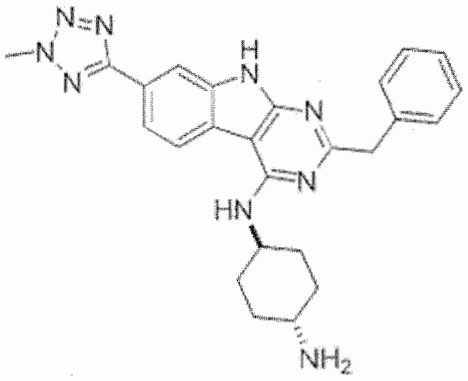


23. The method of claim 16, wherein W is



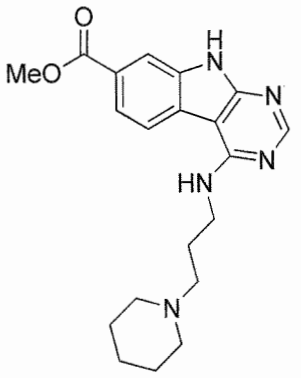
24. The method of claim 13, wherein the compound is



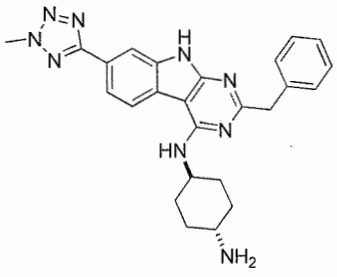


or a pharmaceutically acceptable salt thereof.

25. The method of claim 13, wherein the compound is a hydrochloride salt of



26. The method of claim 13, wherein the compound is a hydrobromide salt of



27. The method according to claim 13, wherein the stem and progenitor cells are human hematopoietic stem and progenitor cells.

28. The method according to claim 13, wherein the starting cell population includes CD34+ cells harvested from mobilized peripheral blood (mPB), bone marrow (BM) or umbilical cord blood (UCB).

29. The method according to claim 28, wherein the starting cell population includes CD34+ cells harvested from umbilical cord blood (UCB).

30. The method according to claim 13, wherein the starting cell population essentially consists of CD34+ cells purified from one or two umbilical cord blood units.

31. The method according to claim 30, comprising culturing the starting cell population in presence of said compound from about 2 days to about 21 days.

32. The method according to claim 30, comprising administering said compound to the starting cell population at a concentration between 1 nM and 3000 nM.

33. The method of claim 15, wherein the biologic comprises Interleukin-3 (IL-3), Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF), Thrombopoietin (TPO), FMS-Like Tyrosine Kinase 3 Ligand (FLT3-L), Stem Cell Factor (SCF), Interleukin-6 (IL-6) or a combination thereof.

34. The method of claim 33, wherein the biologic comprises SCF, FLT3-L, TPO, IL-6 or a combination thereof.

35. The method of claim 13, wherein the other small molecule is StemRegenin 1 (SR1).

36. A cell population as expanded according to a method as defined in claim 13.