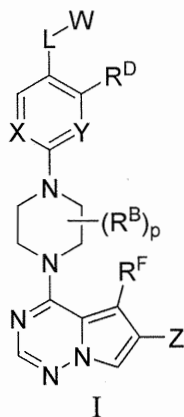
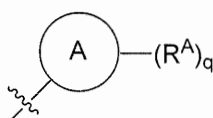


Summary of the Invention

The present ~~invention~~ disclosure features compounds and compositions for treating or preventing conditions such as mastocytosis and mast cell diseases by modulating the activity of KIT. ~~Such compounds have, in an aspect, having~~ the structural Formula I:



or a pharmaceutically acceptable salt thereof, wherein:



W is selected from hydrogen or wherein Ring A is selected from

monocyclic or bicyclic aryl, monocyclic or bicyclic heteroaryl, cycloalkyl or heterocyclyl;

each X and Y is independently selected from CR¹ or N;

Z is C₁-C₆ alkyl, cycloalkyl, monocyclic or bicyclic aryl, monocyclic or bicyclic aralkyl, monocyclic or bicyclic heteroaryl, monocyclic or bicyclic heterocyclyl, monocyclic or bicyclic heterocyclylalkyl; wherein each of C₁-C₆ alkyl, cycloalkyl, monocyclic or bicyclic aryl, monocyclic or bicyclic aralkyl, monocyclic or bicyclic heteroaryl, monocyclic or bicyclic heterocyclyl, monocyclic and bicyclic heterocyclylalkyl is independently substituted with 0-5 occurrences of R^C;

L is selected from a bond, -(C(R²)(R²))_m-, -(C₂-C₆ alkynylene)-, -(C₂-C₆ alkenylene)-, -(C₁-C₆ haloalkylene)-, -(C₁-C₆ heteroalkylene)-, -(C₁-C₆ hydroxyalkylene)-, -C(O)-, -O-, -S-, -S(O)-, -SO₂-, -N(R²)-, -O-(C₁-C₆ alkylene)-, -(C₁-C₆ alkylene)-O-, -N(R²)-CO-, -CO-N(R²)-, -(C₁-C₆ alkylene)-N(R²)-, -N(R²)-(C₁-C₆ alkylene)-, -N(R²)-CO-(C₁-C₆ alkylene)-, -CO-N(R²)-(C₁-C₆ alkylene)-, -N(R²)-SO₂-, -SO₂-N(R²)-, -N(R²)-SO₂-(C₁-C₆ alkylene)-, or -SO₂-N(R²)-(C₁-C₆ alkylene)-;

each R^A and R^B is independently selected from C_1 - C_6 alkyl, C_1 - C_6 cycloalkyl, C_1 - C_6 heterocyclyl, halo, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 heteroalkyl, monocyclic or bicyclic aralkyl, $-N(R^2)(R^2)$, cyano, $-OR^2$;

each R^C is independently selected from C_1 - C_6 alkyl, C_1 - C_6 alkynyl, halo, C_1 - C_6 heteroalkyl, C_1 - C_6 haloalkyl, C_1 - C_6 haloalkoxy, C_1 - C_6 hydroxyalkyl, cycloalkyl, monocyclic or bicyclic aryl, monocyclic or bicyclic aryloxy, monocyclic or bicyclic aralkyl, monocyclic or bicyclic heterocyclyl, monocyclic or bicyclic heterocyclalkyl, nitro, cyano, $-C(O)R^2$, $-OC(O)R^2$, $-C(O)OR^2$, $-SR^2$, $-S(O)_2R^2$, $-S(O)_2-N(R^2)(R^2)$, $-(C_1-C_6 \text{ alkylene})-S(O)_2-N(R^2)(R^2)$, $-N(R^2)(R^2)$, $-C(O)-N(R^2)(R^2)$, $-N(R^2)(R^2)-C(O)R^2$, $-(C_1-C_6 \text{ alkylene})-N(R^2)-C(O)R^2$, $-NR^2S(O)_2R^2$, $-P(O)(R^2)(R^2)$, and $-OR^2$; wherein each of heteroalkyl, haloalkyl, haloalkoxy, alkyl, alkynyl, cycloalkyl, aryl, aryloxy, aralkyl, heterocyclyl, heterocyclalkyl is independently substituted with 0-5 occurrences of R^a ; or 2 R^C together with the carbon atom(s) to which they are attached form a cycloalkyl or heterocyclyl ring substituted with 0-5 occurrences of R^a ;

each R^D and R^F is, independently, hydrogen, C_1 - C_6 alkyl, C_1 - C_6 cycloalkyl, hydroxyl, halo, C_1 - C_6 alkoxy, C_1 - C_6 haloalkyl, $-N(R^2)(R^2)$, or cyano;

each R^1 is independently selected from hydrogen, C_1 - C_6 alkyl, monocyclic aralkyl, C_1 - C_6 hydroxyalkyl, halo, C_1 - C_6 haloalkyl, $-N(R^2)(R^2)$, $-OR^2$;

each R^2 is independently selected from hydrogen, hydroxyl, halo, thiol, C_1 - C_6 thioalkyl, $-NR''R''$, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, wherein each of C_1 - C_6 alkyl, cycloalkyl and heterocyclyl is independently substituted with 0-5 occurrences of R^b , or 2 R^2 together with the carbon or nitrogen atom to which they are attached form a cycloalkyl or heterocyclyl ring;

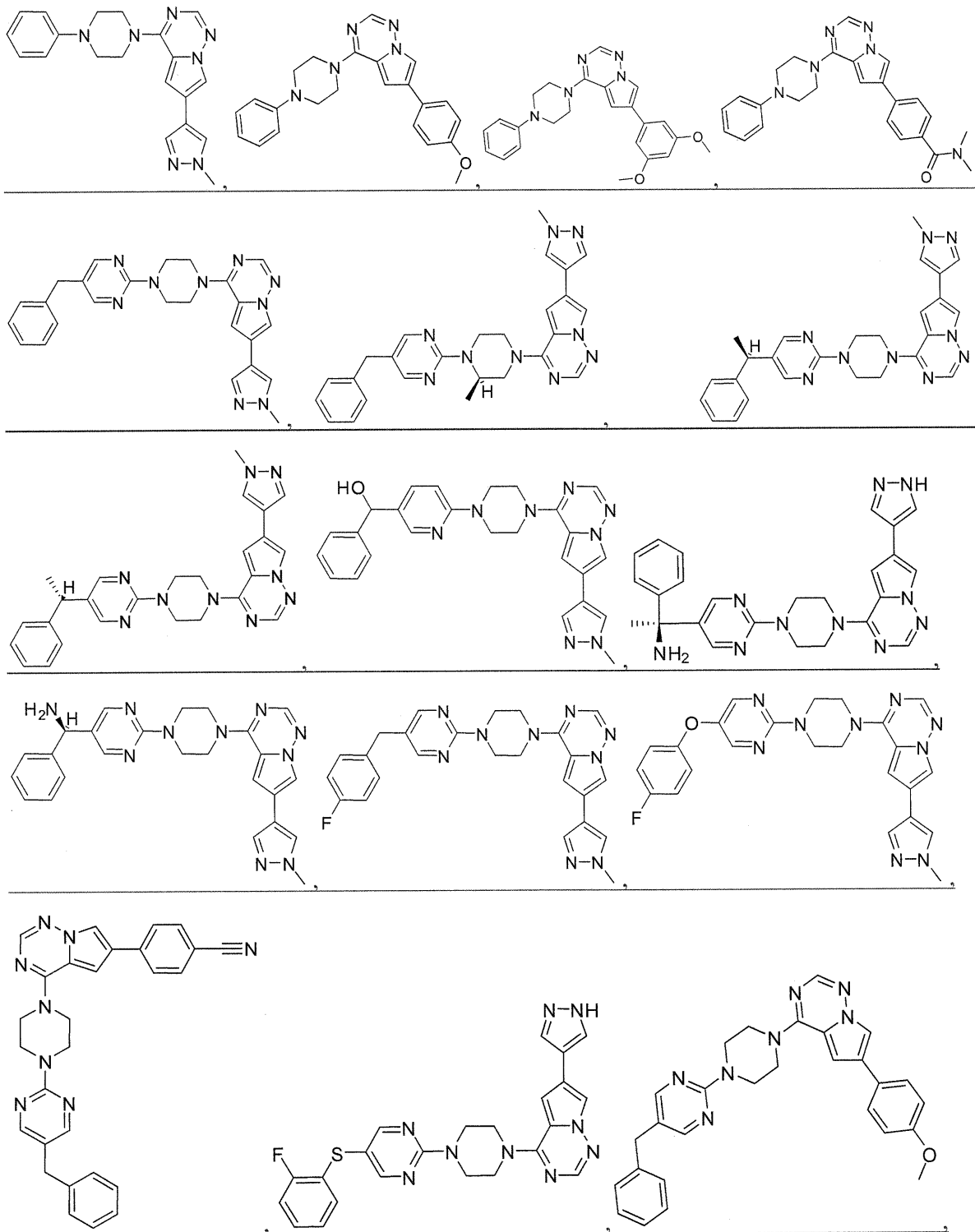
each R^a and R^b is independently hydrogen, halo, cyano, hydroxyl, C_1 - C_6 alkoxy, $-C(O)R'$, $-C(O)OR'$, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 heteroalkyl, C_1 - C_6 hydroxyalkyl, $-NR'R'$, or cycloalkyl, wherein cycloalkyl is substituted with 0-5 occurrences of R' ;

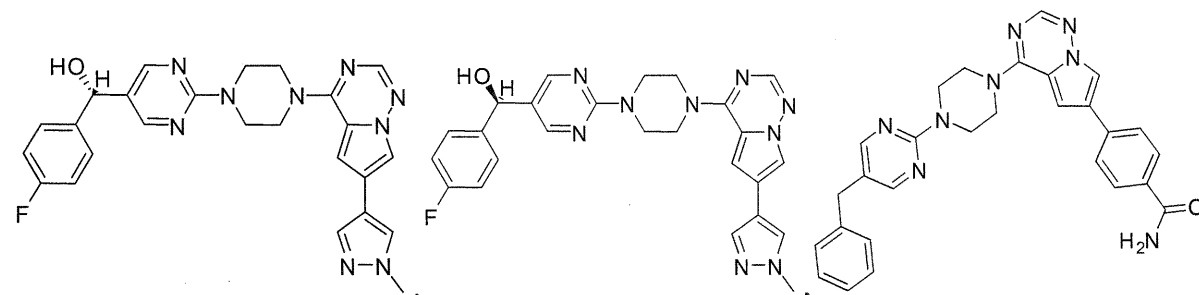
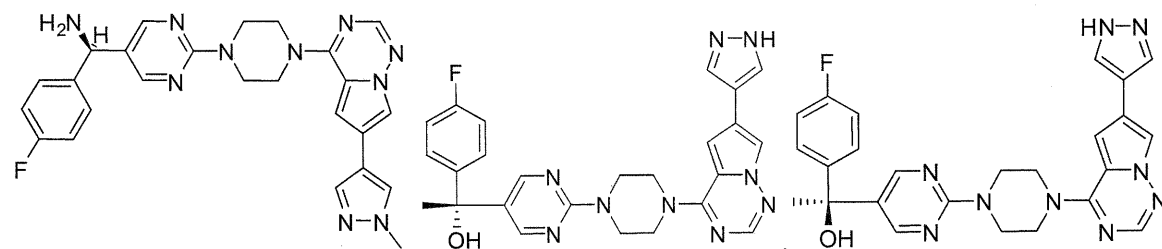
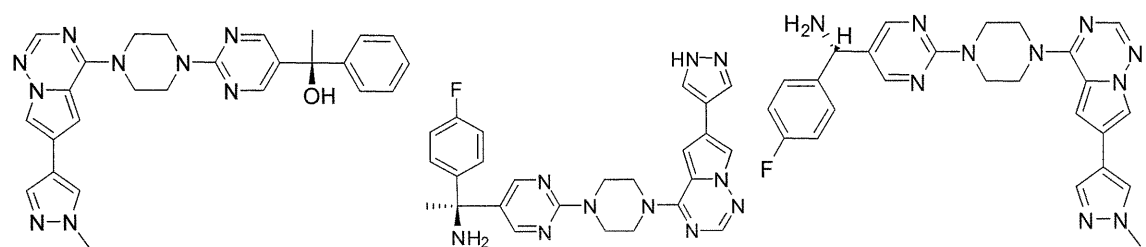
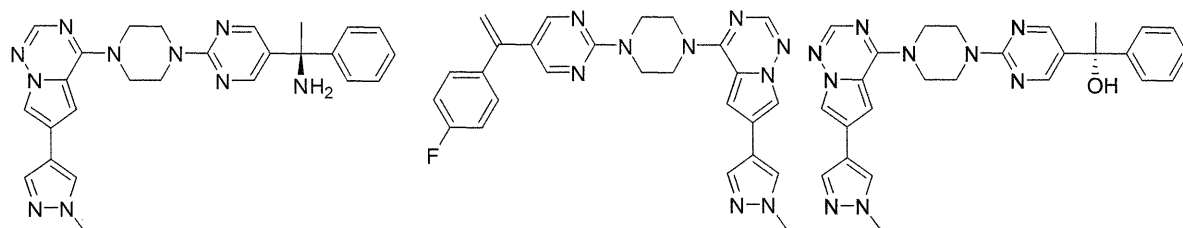
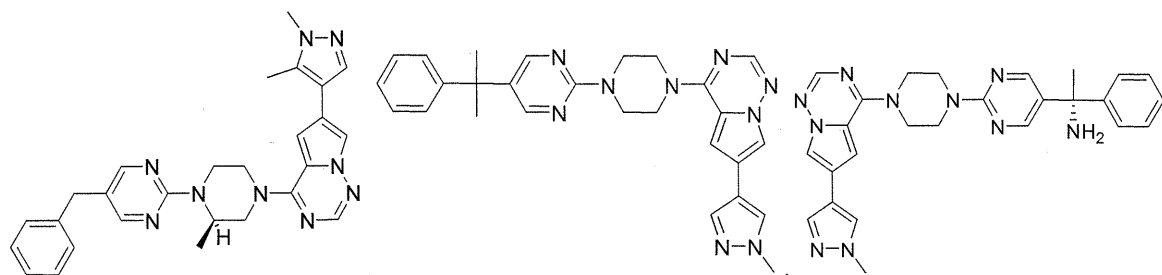
each R' is hydrogen, hydroxyl, or C_1 - C_6 alkyl;

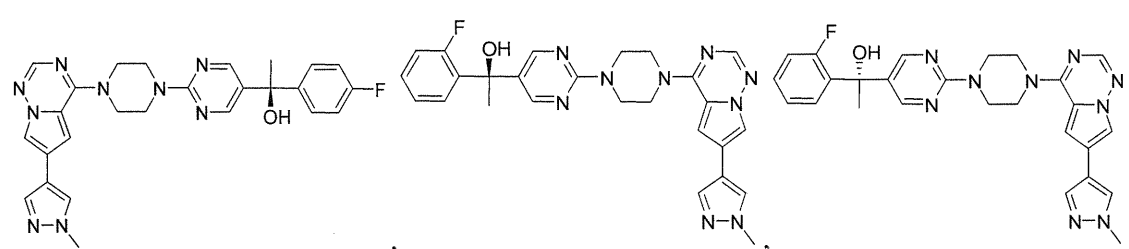
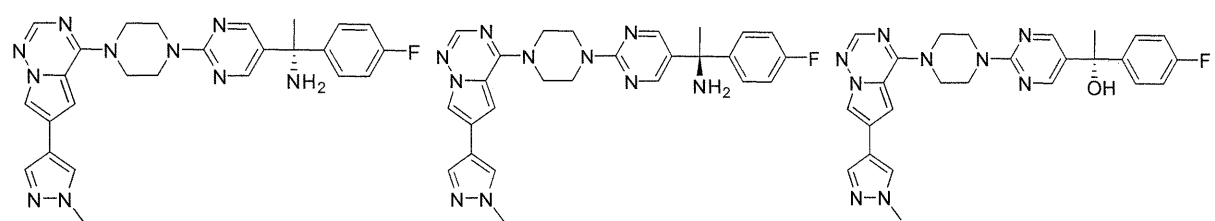
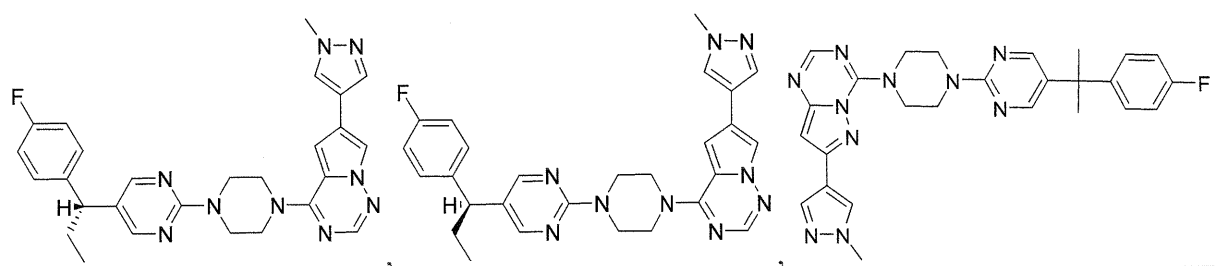
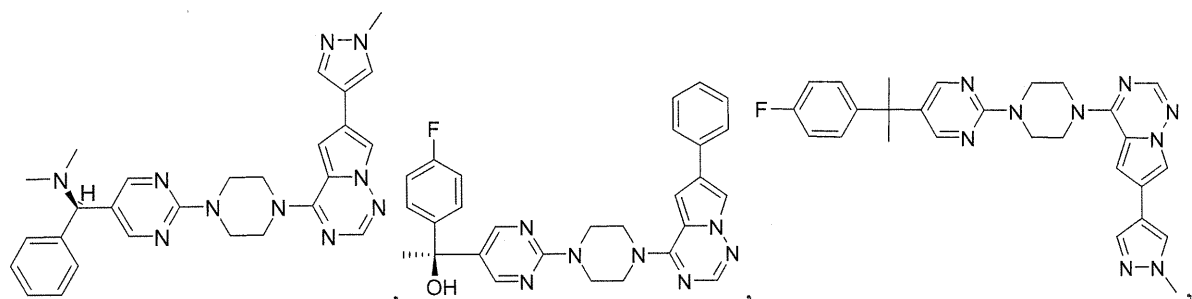
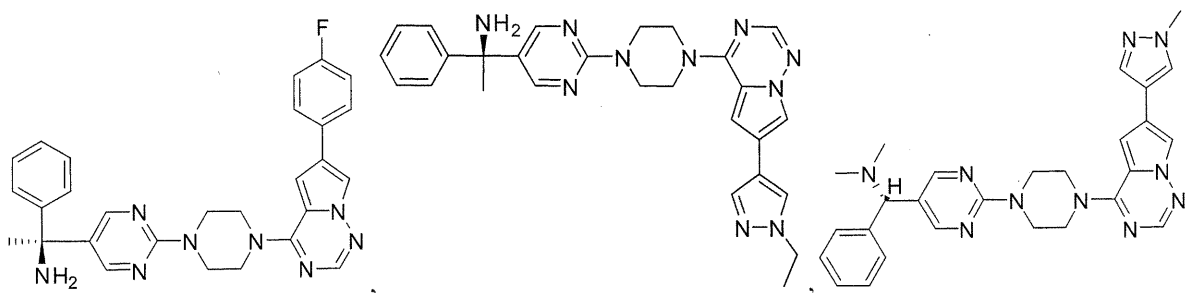
each R'' is hydrogen, C_1 - C_6 alkyl, $-C(O)-C_1-C_6$ alkyl, $-C(O)-NR'R'$; $-C(S)-NR'R'$; and

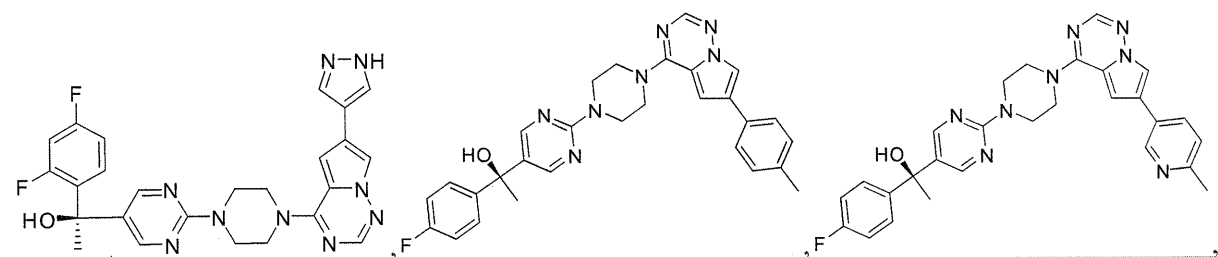
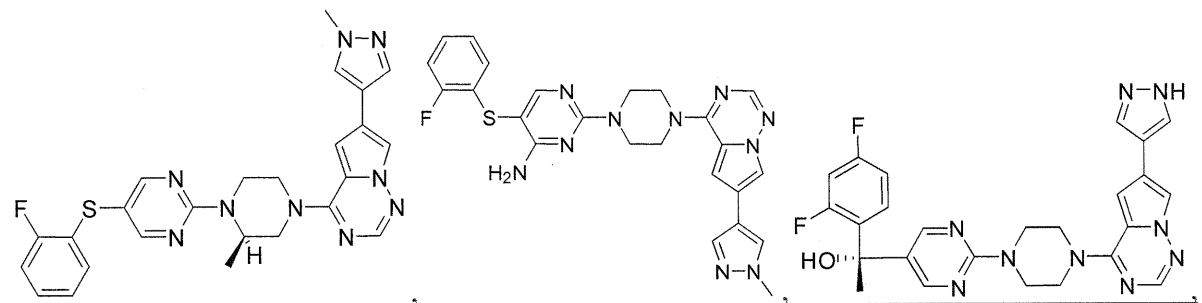
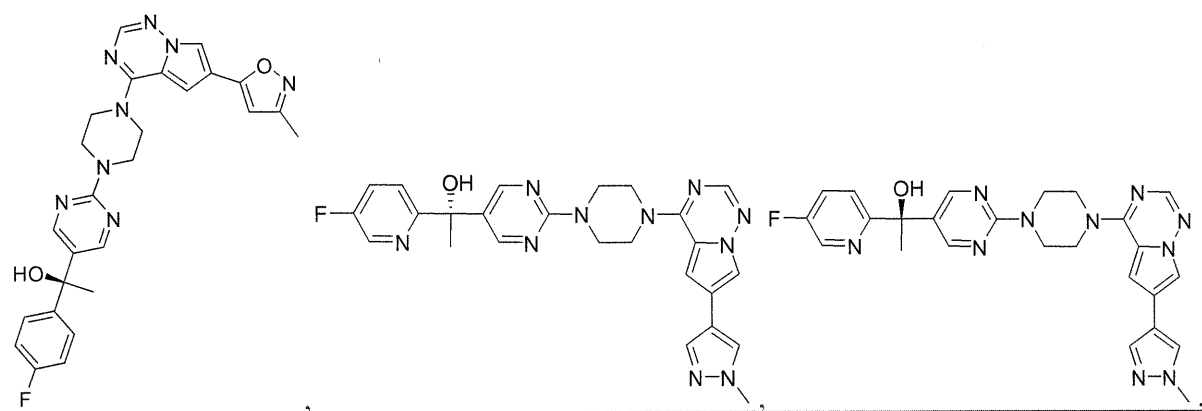
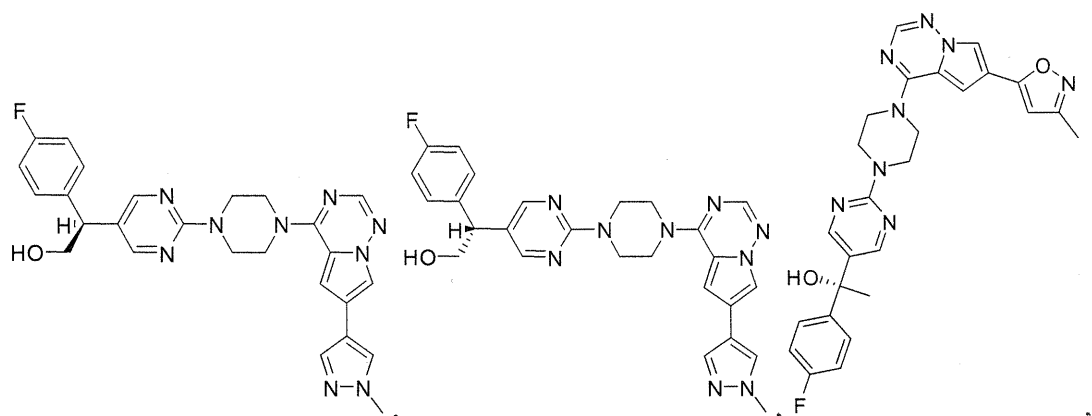
m , p , and q are each independently 0, 1, 2, 3, or 4.

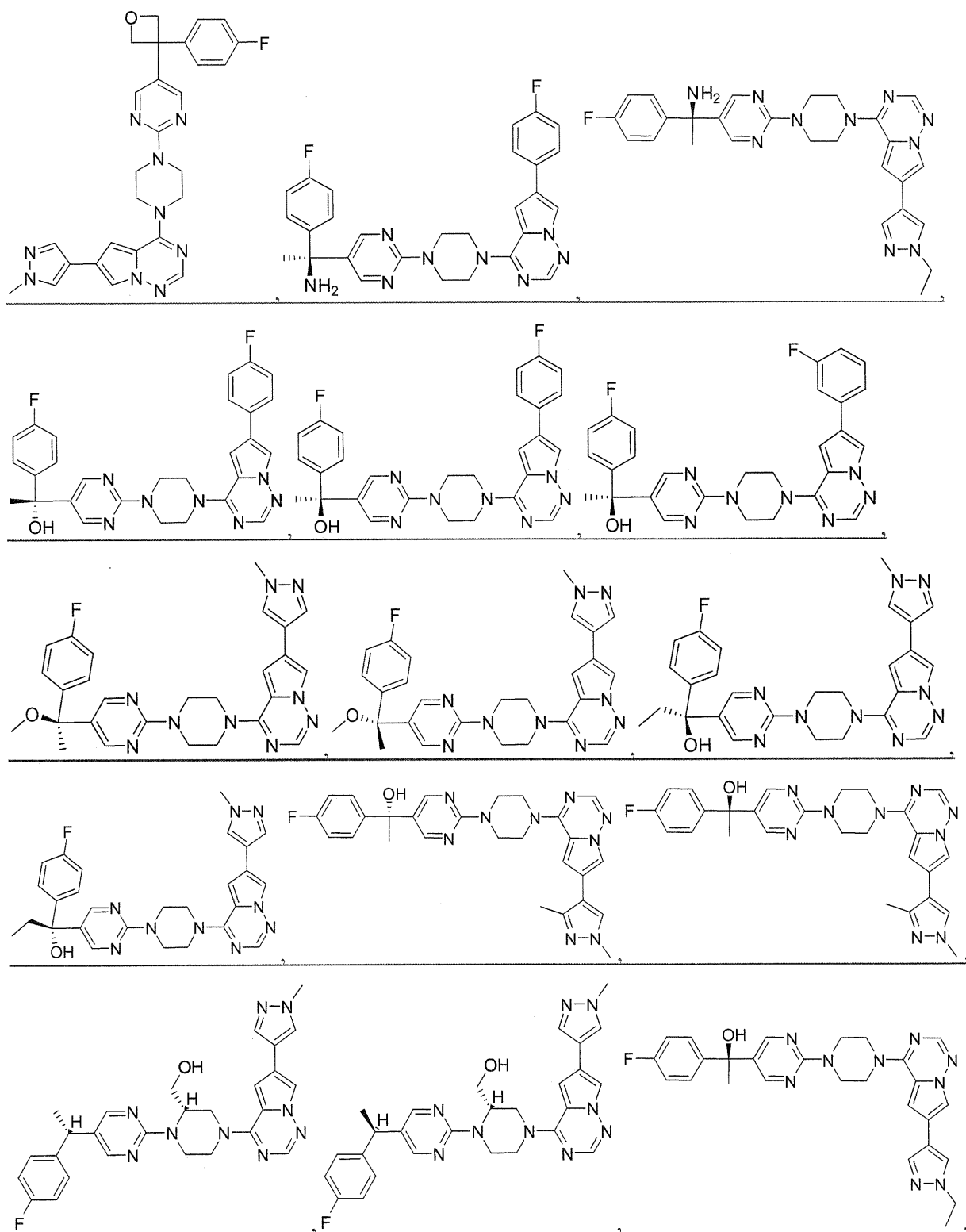
In another aspect, there is provided a compound selected from the group consisting of the compounds below, or a pharmaceutically acceptable salt thereof:

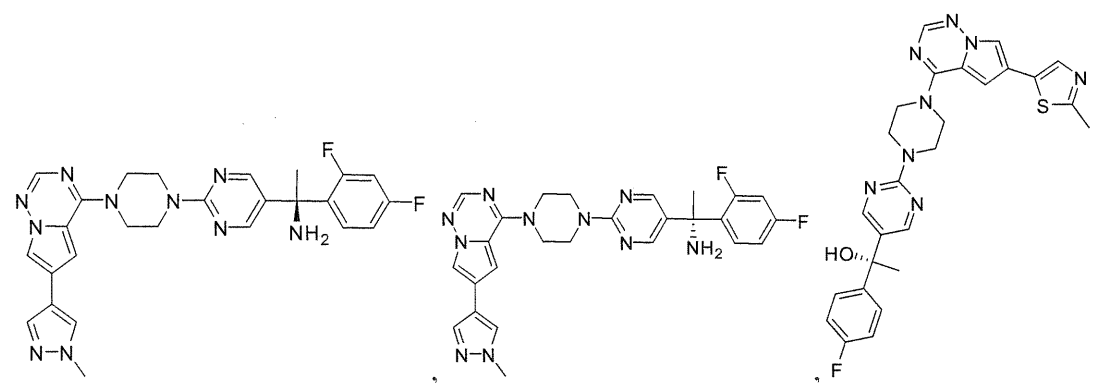
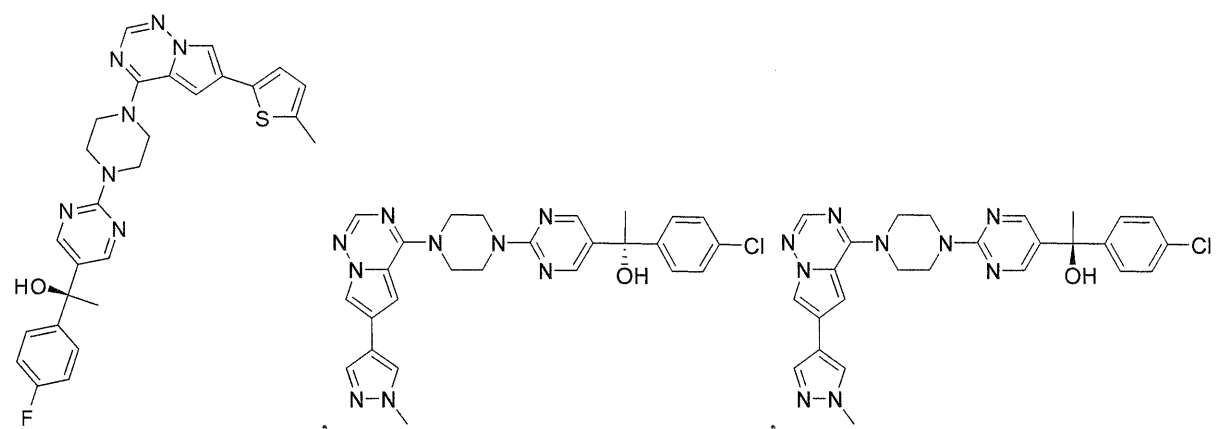
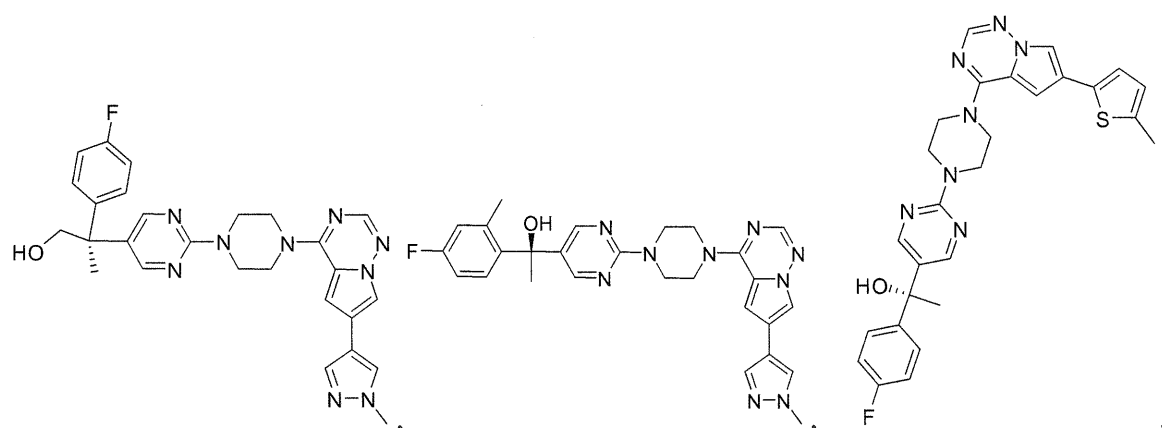
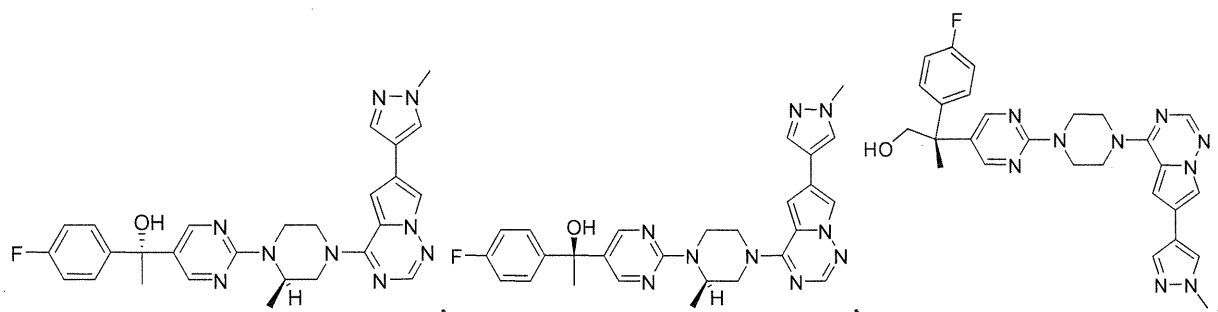


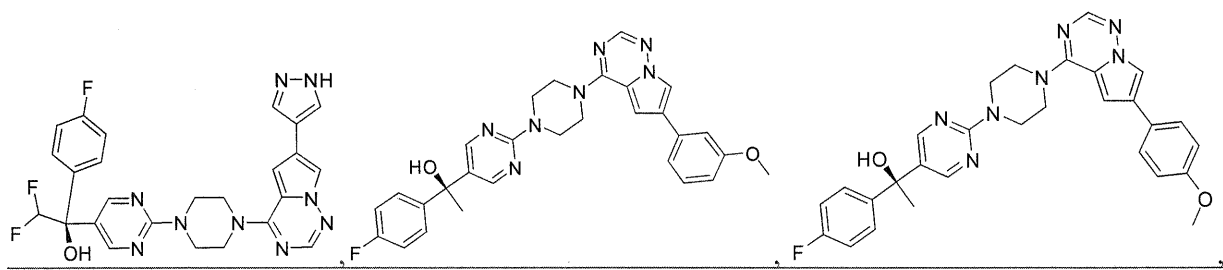
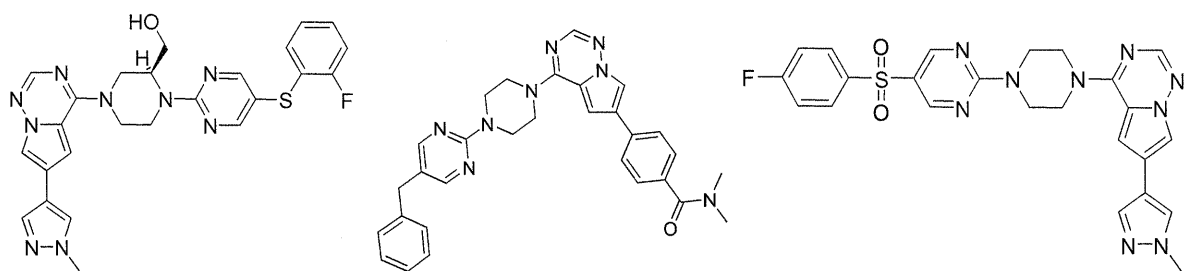
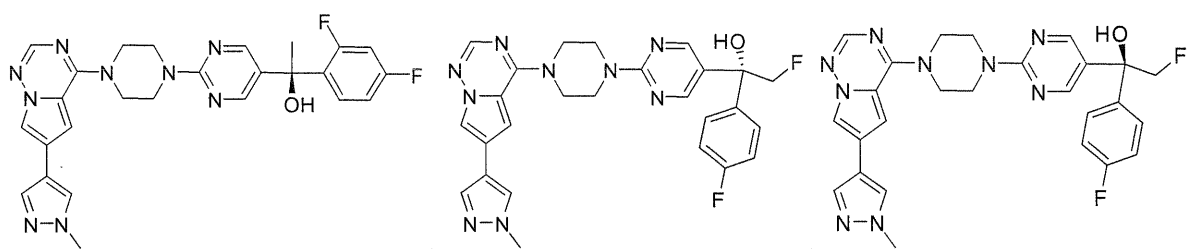
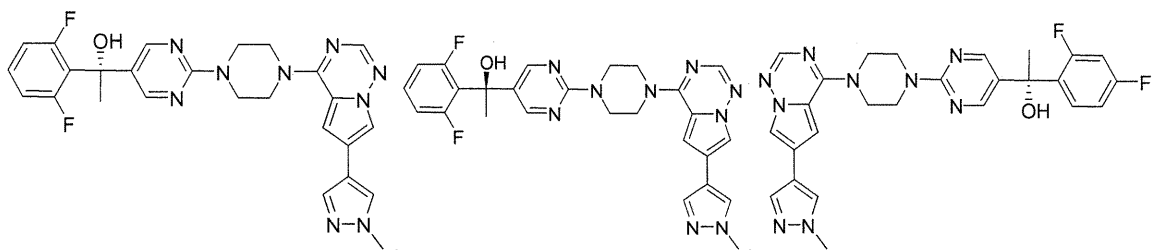
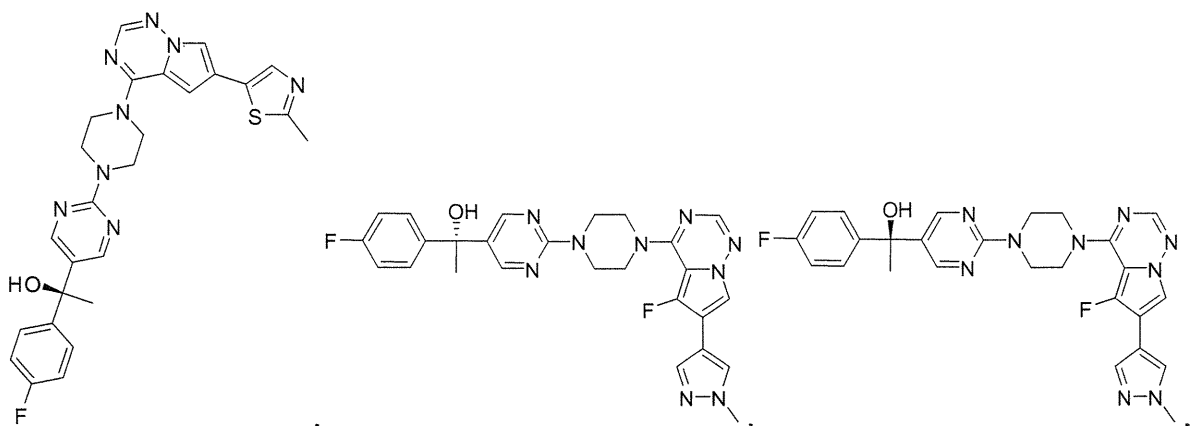


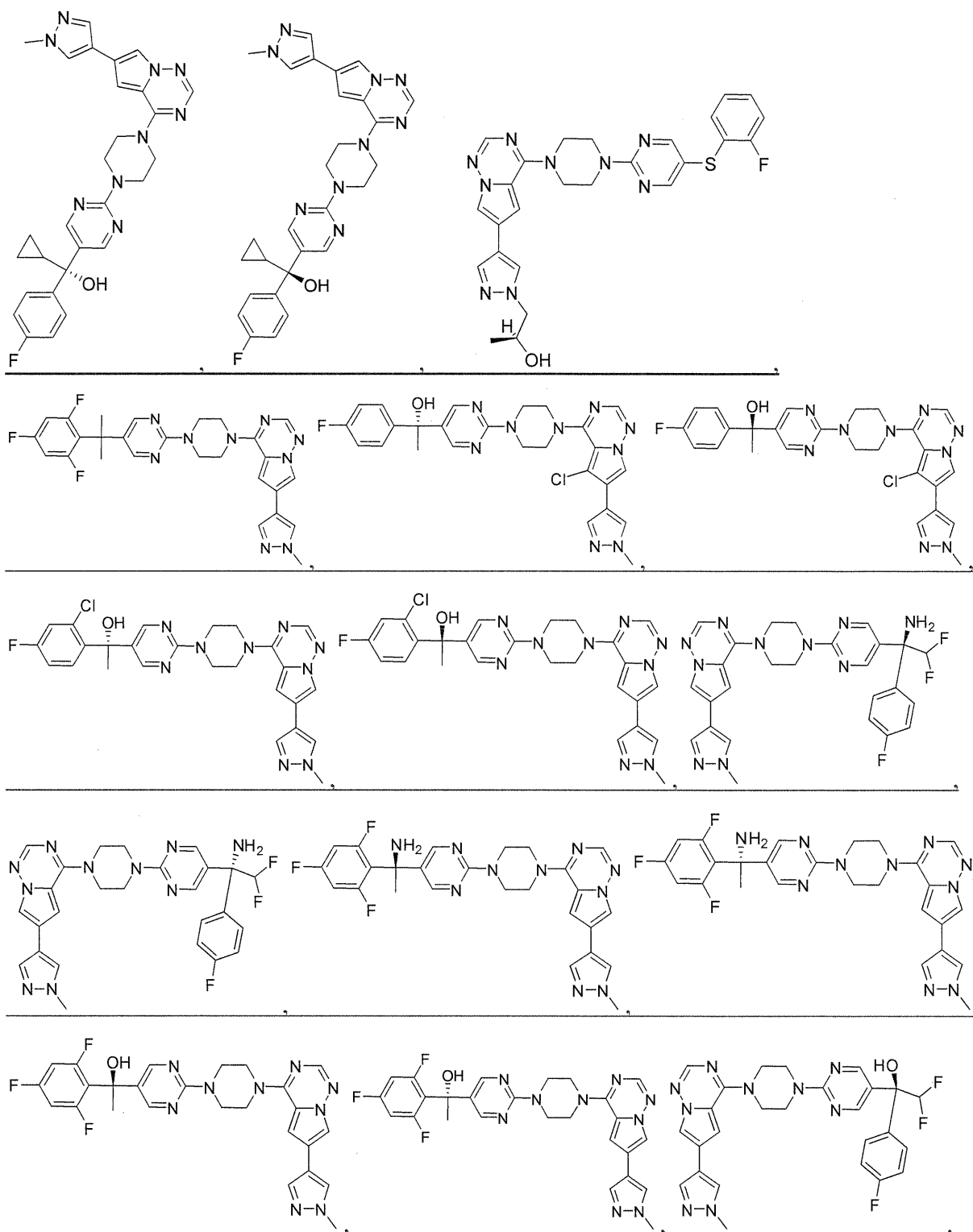


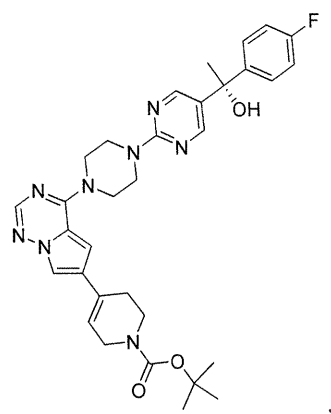
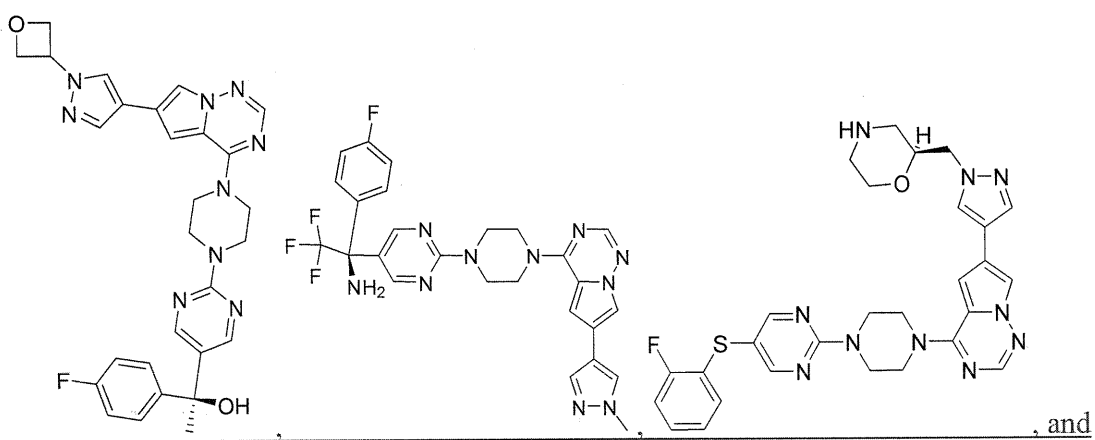
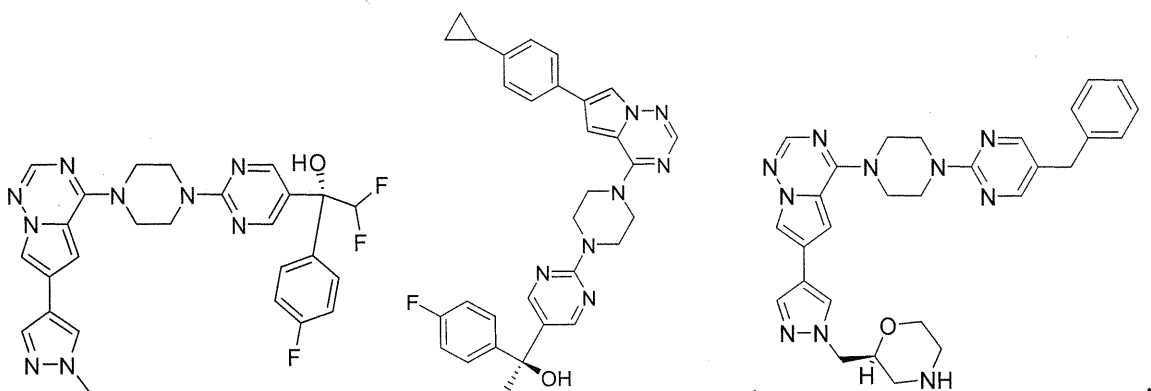












In yet another aspect, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound as disclosed herein.

Any of the compounds disclosed herein may be used to treat any of the diseases disclosed herein.

In an aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating mastocytosis.

5 In another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating gastrointestinal stromal tumor.

10 In a further aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating acute myeloid leukemia.

In yet another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 9.

15 In still another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 11.

In yet a further aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 17.

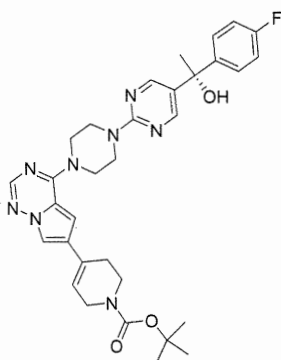
20 In still a further aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT is mutated at residue 816.

25 In another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by mutant PDGFR α , wherein said PDGFR α has a mutation in Exon 18.

In yet another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above in the manufacture of a medicament for treating a condition mediated by KIT.

30 In still another aspect, there is provided the use of a compound as disclosed herein or a pharmaceutical composition as disclosed above, in combination with a second agent, wherein the second agent is active against a mutant KIT having a mutation in Exon 9 or Exon 11, in the manufacture of a medicament for treating a condition mediated by KIT.

In a further aspect, there is provided the use of (a) a compound as disclosed herein or a pharmaceutical composition as disclosed above; (b) an agent active against mutant KIT A, wherein such mutant KIT A has a mutation in Exon 9 or Exon 11; and (c) an agent active against a mutant KIT B, wherein such mutant KIT B has a mutation that is not in Exon 9 or 11, in the manufacture of a medicament for treating a condition mediated by KIT.



16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of any of claims 1 to 15.

17. ~~A method of treating mastocytosis comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating mastocytosis.

18. ~~A method of treating gastrointestinal stromal tumor, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating gastrointestinal stromal tumor.

19. ~~A method of treating acute myeloid leukemia, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating acute myeloid leukemia.

20. ~~A method of treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 9, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 9.

21. ~~A method of treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 11, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 11.

22. ~~A method of treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 17, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT has a mutation in Exon 17.
23. ~~A method of treating a condition mediated by mutant KIT, wherein said KIT is mutated at residue 816, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by mutant KIT, wherein said KIT is mutated at residue 816.
24. ~~A method of treating a condition mediated by mutant PDGFR α , wherein said PDGFR α has a mutation in Exon 18, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by mutant PDGFR α , wherein said PDGFR α has a mutation in Exon 18.
25. ~~A method of treating a condition mediated by KIT, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a condition mediated by KIT.
26. ~~A method of treating a condition mediated by KIT, the method comprising administering to a patient a therapeutically effective amount~~ Use of a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16, in combination with a therapeutically effective amount of a second agent, wherein the second agent is active against a mutant KIT having a mutation in Exon 9 or Exon 11, in the manufacture of a medicament for treating a condition mediated by KIT.
27. ~~The method~~ use of claim 26, wherein the compound and the agent are to be administered during the same time period.
28. ~~The method~~ use of claim 26, wherein the compound and the agent are not to be administered during the same time period.
29. ~~A method of treating a condition mediated by KIT, the method comprising administering to a patient:~~

~~(a) a therapeutically effective amount~~ Use of (a) a compound of any of claims 1 to 15 or a pharmaceutical composition of claim 16;

~~(b) a therapeutically effective amount of an agent active against mutant KIT A, wherein~~
such mutant KIT A has a mutation in Exon 9 or Exon 11; and

~~(c) a therapeutically effective amount of an agent active against a mutant KIT B, wherein~~
such mutant KIT B has a mutation that is not in Exon 9 or 11,

in the manufacture of a medicament for treating a condition mediated by KIT.

30. The ~~method~~ use of claim 29, wherein the compound and the agents are to be administered during the same time period.

31. The ~~method~~ use of claim 29, wherein the compound and the agents are not to be administered during the same time period.