

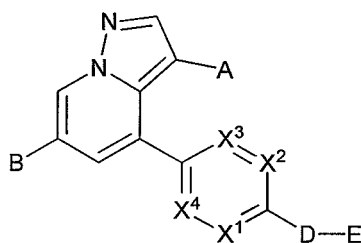
[0005] Upon binding of the ligand-co-receptor complex, RET dimerization and autophosphorylation on intracellular tyrosine residues recruits adaptor and signaling proteins to stimulate multiple downstream pathways. Adaptor protein binding to these docking sites leads to activation of Ras-MAPK and PI3K-Akt/mTOR signaling pathways or to recruitment of the CBL family of ubiquitin ligases that functions in RET downregulation of the RET-mediated functions.

[0006] Aberrant RET expression and/or activity have been demonstrated in different cancers and in gastrointestinal disorders such as irritable bowel syndrome (IBS).

SUMMARY

[0007] It has now been found that substituted pyrazolo[1,5-a]pyridine compounds are inhibitors of RET kinase, and are useful for treating diseases such as proliferative diseases including cancers.

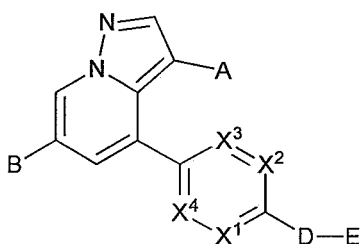
[0008] Accordingly, provided herein is a compound of the General Formula I:



I

[0009] or a pharmaceutically acceptable salt or solvate thereof, wherein A, B, D, E, X¹, X², X³ and X⁴ are as defined herein.

[0009a] In a first aspect, there is provided a compound of the General Formula I:



I

or a pharmaceutically acceptable salt or solvate thereof, wherein:

X¹ is CH, CCH₃, CF, CCl or N;

X² is CH, CF or N;

X³ is CH, CF or N;

X⁴ is CH, CF or N;

wherein zero, one or two of X¹, X², X³ and X⁴ is N;

A is H, Cl, CN, Br, CH₃, CH₂CH₃ or cyclopropyl;

B is hetAr¹;

hetAr¹ is a 5-membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, S and O, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, hydroxyC1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, cyanoC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, (C1-C4 alkoxy)CH₂C(=O)-, (C1-C4 alkoxy)C(=O)C1-C3 alkyl, C3-C6 cycloalkyl, (R^aR^bN)C1-C6 alkyl, (R^aR^bN)C(=O)C1-C6 alkyl, (C1-C6 alkylSO₂)C1-C6 alkyl, hetCyc^a, and 4-methoxybenzyl;

R^a and R^b are independently H or C1-C6 alkyl;

hetCyc^a is a 4-6 membered heterocyclic ring having a ring heteroatom selected from N and O, wherein said heterocyclic ring is optionally substituted with halogen, C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, di(C1-C3 alkyl)NCH₂C(=O), (C1-C6 alkoxy)C(=O) or (C1-C6 alkoxy)CH₂C(=O);

D is hetCyc¹, hetCyc², hetCyc³ or hetCyc⁹;

hetCyc¹ is a 4-6 membered heterocyclic ring having 1-2 ring atoms selected from N and O, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C3 alkyl, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl, trifluoroC1-C3 alkyl and OH, or said heterocyclic ring is substituted with a C3-C6 cycloalkylidene ring, or said heterocyclic ring is substituted with an oxo group;

hetCyc² is a 7-8 membered bridged heterocyclic ring having 1-3 ring heteroatoms independently selected from N and O, wherein said heterocyclic ring is optionally substituted with C1-C3 alkyl;

hetCyc³ is a 7-11 membered heterospirocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein said ring is optionally substituted with C1-C3 alkyl;

hetCyc⁹ is a fused 9-10 membered heterocyclic ring having 1-3 ring nitrogen atoms and optionally substituted with oxo;

E is

- (a) hydrogen,
- (b) OH,
- (c) R^aR^bN-, wherein R^a is H or C1-C6 alkyl and R^b is H, C1-C6 alkyl or phenyl;
- (d) C1-C6 alkyl optionally substituted with one to three fluoros,
- (e) hydroxyC1-C6 alkyl- optionally substituted with one to three fluoros,
- (f) C1-C6 alkoxy optionally substituted with one to three fluoros,
- (g) hydroxy(C1-C6 alkoxy) optionally substituted with one to three fluoros,
- (h) (C1-C6 alkoxy)hydroxy C1-C6 alkyl- optionally substituted with one to three fluoros,
- (i) (C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (j) (hydroxy C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (k) (C1-C6 alkoxy)C(=O)-,
- (l) (C1-C6 alkoxy)(C1-C6 alkyl)C(=O)-,
- (m) HC(=O)-,
- (n) Cyc¹,
- (o) Cyc¹C(=O)-,
- (p) Cyc¹(C1-C6 alkyl)C(=O)- wherein said alkyl portion is optionally substituted with one or more groups independently selected from the group consisting of OH, fluoro, C1-C3 alkoxy and R^cR^dN-, where R^c and R^d are independently H or C1-C6 alkyl,
- (q) hetCyc⁴,
- (r) hetCyc⁴C(=O)-,
- (s) hetCyc⁴(C1-C3 alkyl)C(=O)-,
- (t) (hetCyc⁴)C(=O)C1-C2 alkyl-,
- (u) hetCyc⁴C(=O)NH-,
- (v) Ar²,
- (w) Ar²C(=O)-,
- (x) Ar²C1-C6 alkyl-,
- (y) (Ar²)hydroxy C2-C6 alkyl-,

(z) $\text{Ar}^2(\text{C1-C3 alkyl})\text{C}(=\text{O})-$ wherein said alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl (optionally substituted with 1-3 fluoros), hydroxyC1-C6 alkyl, C1-C6 alkoxy and $\text{R}^e\text{R}^f\text{N}-$, where R^e and R^f are independently H or C1-C6 alkyl, or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(aa) $\text{hetAr}^2\text{C}(=\text{O})-$,

(bb) $(\text{hetAr}^2)\text{hydroxyC2-C6 alkyl}-$,

(cc) $\text{hetAr}^2(\text{C1-C3 alkyl})\text{C}(=\text{O})-$, wherein said alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy and $\text{R}^e\text{R}^f\text{N}-$, wherein R^e and R^f are independently H or C1-C6 alkyl or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(dd) $\text{R}^1\text{R}^2\text{NC}(=\text{O})-$,

(ee) $\text{R}^1\text{R}^2\text{N}(\text{C1-C3 alkyl})\text{C}(=\text{O})-$, wherein said alkyl portion is optionally substituted with phenyl,

(ff) $\text{R}^1\text{R}^2\text{NC}(=\text{O})\text{C1-C2 alkyl}-$,

(gg) $\text{R}^1\text{R}^2\text{NC}(=\text{O})\text{NH}-$,

(hh) $\text{CH}_3\text{SO}_2(\text{C1-C6 alkyl})\text{C}(=\text{O})-$,

(ii) $(\text{C1-C6 alkyl})\text{SO}_2-$,

(jj) $(\text{C3-C6 cycloalkyl})\text{CH}_2\text{SO}_2-$,

(kk) $\text{hetCyc}^5\text{-SO}_2-$,

(ll) $\text{R}^4\text{R}^5\text{NSO}_2-$,

(mm) $\text{R}^6\text{C}(=\text{O})\text{NH}-$,

(nn) hetCyc^6 ,

(oo) $\text{hetAr}^2\text{C1-C6 alkyl}-$,

(pp) $(\text{hetCyc}^4)\text{C1-C6 alkyl}-$,

(qq) $(\text{C1-C6 alkoxy})\text{C1-C6 alkyl}-$ optionally substituted with 1-3 fluoros,

(rr) $(\text{C3-C6 cycloalkoxy})\text{C1-C6 alkyl}-$,

(ss) $(\text{C3-C6 cycloalkyl})\text{C1-C6 alkyl}-$, wherein said cycloalkyl is optionally substituted with 1-2 fluoros,

- (tt) (R^gR^hN)C1-C6 alkyl-, wherein R^g and R^h are independently H or C1-C6 alkyl,
 (uu) Ar^2-O- ,
 (vv) (C1-C6 alkylSO₂)C1-C6 alkyl-,
 (ww) (C1-C6 alkoxy)C(=O)NHC1-C6 alkyl-,
 (xx) (C3-C6 cycloalkoxy)C(=O)-,
 (yy) (C3-C6 cycloalkyl)SO₂-, wherein said cycloalkyl is optionally substituted with C1-C6 alkyl,
 (zz) $Ar^4CH_2OC(=O)-$,
 (aaa) (N-(C1-C3 alkyl)pyridinonyl)C1-C3 alkyl-, and
 (bbb) (Ar^4SO_2)C1-C6 alkyl-;

Cyc¹ is a C3-C6 cycloalkyl, wherein (a) said cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of OH, halogen, C1-C6 alkoxy, CN, hydroxyC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, and C1-C6 alkyl optionally substituted with 1-3 fluoros, or (b) said cycloalkyl is substituted with phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C3 alkyl, C1-C3 alkoxy and CF, or (c) said cycloalkyl is substituted with a 5-6 membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N and O, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C3 alkyl, C1-C3 alkoxy and CF₃;

Ar^2 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, CN, a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, and R^iR^jN- wherein R^i and R^j are independently H or C1-C6 alkyl;

hetAr² is a 5-6 membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, O and S and optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, hydroxyC1-C6 alkyl, (C3-C6)cycloalkyl, (C1-C6 alkoxy)C1-C6 alkyl, CN, OH, and $R'R''N-$, wherein R' and R'' are independently H or C1-C3 alkyl;

hetCyc⁴ is (a) a 4-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N, O and S wherein said S is optionally oxidized to SO₂, (b) a 7-8 membered bridged heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, (c) a 6-12 membered fused bicyclic heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O and optionally independently substituted with 1-2 C1-C6 alkyl substituents, or (d) a 7-10 membered spirocyclic heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein each of said heterocyclic rings is optionally substituted with one or more substituents independently selected from the group consisting of halogen, OH, CN, C1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy, (C1-C6 alkoxy)C1-C6 alkyl, (C3-C6)cycloalkyl, (C1-C6 alkyl)C(=O)-, a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, and phenyl wherein said phenyl is optionally substituted with one or more substituents selected from halogen, C1-C6 alkyl and C1-C6 alkoxy;

hetCyc⁵ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N;

hetCyc⁶ is a 5 membered heterocyclic ring having one or two ring heteroatoms independently selected from N and O, wherein said ring is substituted with oxo and wherein said ring is further optionally substituted with one or more substituents independently selected from the group consisting of OH and C1-C6 alkyl;

R¹ is H, C1-C6 alkyl or (C1-C6 alkoxy)C1-C6 alkyl;

R² is H, C1-C6 alkyl (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C1-C6 alkyl (optionally substituted with 1-3 fluoros), Cyc³, hydroxyC1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C(=O), hetCyc⁷, Ar³, Ar³C1-C3 alkyl-, hydroxyC1-C6 alkoxy or (3-6C cycloalkyl)CH₂O-;

Cyc³ is a 3-6 membered carbocyclic ring optionally substituted with 1-2 groups independently selected from the group consisting of C1-C6 alkoxy, OH and halogen;

hetCyc⁷ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N wherein said ring is optionally substituted with C1-C6 alkyl;

Ar³ is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C3 alkyl, C1-C3 alkoxy, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl and trifluoroC1-C3 alkyl;

R⁴ and R⁵ are independently H or C1-C6 alkyl;

R⁶ is C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy, (C1-C6 alkoxy)C1-C6 alkyl, phenyl or hetCyc⁸;

hetCyc⁸ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N, wherein said heterocyclic ring is optionally substituted with C1-C6 alkyl; and

Ar⁴ is phenyl optionally substituted with one or more halogens.

[0010] Also provided herein is a pharmaceutical composition comprising a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, in admixture with a pharmaceutically acceptable diluent or carrier. In a second aspect, there is provided a pharmaceutical composition, comprising a compound of the first aspect, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier or excipient.

[0010a] In a third aspect, there is provided use of a compound of the first aspect or a pharmaceutical composition of the second aspect for the manufacture of a medicament for treating cancer.

[0010b] In a fourth aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a RET-associated cancer in a subject.

[0010c] In a fifth aspect, there is provided a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for use in treating a patient identified or diagnosed as having a RET-associated cancer.

[0010d] In a sixth aspect, there is provided an *in vitro* method for inhibiting RET kinase activity in a mammalian cell, the method comprising contacting the mammalian cell with a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof.

[0010e] In a seventh aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating irritable bowel syndrome in a patient in need thereof.

[0010f] In an eighth aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for reducing pain associated with irritable bowel syndrome in a patient in need thereof.

[0010g] In a ninth aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for

inhibiting metastasis of a cancer in a patient in need thereof.

[0010h] In a tenth aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a subject having a cancer,

wherein (a) prior to such treating, the subject has been administered one or more doses of a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof for a period of time and (b) a determination has been made whether a cancer cell in a sample obtained from the subject following such administration has at least one RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a);

and wherein

(c) a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof is to be administered in monotherapy or in conjunction with another anticancer agent to the subject if the subject has a cancer cell that has at least one RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a),
or

(d) additional doses of the RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a) are to be administered to the subject if the subject has a cancer cell that does not have a RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a).

[0010i] In an eleventh aspect, there is provided use of a compound of the first aspect or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a subject having a cancer, wherein

(a) after the subject has been administered one or more doses of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof for a period of time;; (b) a determination has been made whether a cancer cell in a sample obtained from the subject has one or more RET inhibitor resistance mutations that confer increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt

or solvate thereof of (a); and wherein

(c) a different RET inhibitor is to be administered as a monotherapy or in conjunction with another anticancer agent to a subject having a cancer cell that has one or more RET inhibitor resistance mutations that confer increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a); or

(d) additional doses of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a) are to be administered to a subject having a cancer cell that does not have a RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a).

[0011] Also provided herein is a method of inhibiting cell proliferation, in vitro or in vivo, the method comprising contacting a cell with an effective amount of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition thereof as defined herein.

[0012] Also provided herein is a method of treating a RET-associated disease or disorder in a patient in need of such treatment, the method comprising administering to the patient a therapeutically effective amount of a compound of General Formula I or a pharmaceutically

that include administering a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, before, during, or after administration of another anticancer drug (e.g., a RET kinase inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof).

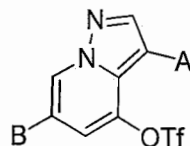
[0033] Also provided are methods of treating an individual with a RET-associated cancer that include administering a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, before, during, or after administration of another anticancer drug (e.g., a RET kinase inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof).

[0034] Also provided herein is a method for treating irritable bowel syndrome (IBS) in a patient in need thereof, the method comprising (a) determining if the IBS is associated with a dysregulation of a RET gene, a RET kinase, or expression or activity or level of any of the same; and (b) if the IBS is determined to be associated with a dysregulation of a RET gene, a RET kinase, or expression or activity or level of any of the same, administering to the patient a therapeutically effective amount of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition thereof.

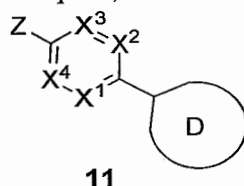
[0035] Also provided herein is a pharmaceutical combination for treating irritable bowel syndrome (IBS) in a patient in need thereof, which comprises administering (a) a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof, (b) an additional therapeutic agent, and (c) optionally at least one pharmaceutically acceptable carrier, for simultaneous, separate or sequential use for the treatment of IBS, wherein the amounts of the compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof and of the additional therapeutic agent are together effective in treating the IBS. Also provided herein is a pharmaceutical composition comprising such a combination. Also provided herein is the use of such a combination for the preparation of a medicament for the treatment of the IBS. Also provided herein is a commercial package or product comprising such a combination as a combined preparation for simultaneous, separate or sequential use; and to a method of treatment of the IBS a patient in need thereof.

[0036] Also provided herein is a process for preparing a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof. In a twelfth aspect, there is provided a process for the preparation of a compound of General Formula I of the first aspect, comprising:

(a) for a compound of the first aspect where E is H and A, B, X¹, X², X³, X⁴, and D are as defined in the first aspect, coupling a corresponding compound having the formula



where A and B are as defined in the first aspect, with a compound having the formula 11



in the presence of a palladium catalyst and optionally a ligand and in the presence of a base, where Z is -B(OR^a)(OR^b) and R^a and R^b are H or (1-6C)alkyl, or R^a and R^b together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents

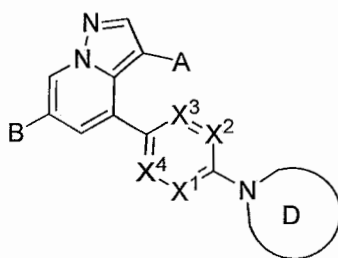
selected from (C1-C3 alkyl), the  ring is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I, and X¹, X², X³ and X⁴ are as defined for Formula B, followed by removal of a protecting group on the D ring if present; or

(b) for a compound of the first aspect where A, B, X¹, X², X³, X⁴, D and E are as defined in the first aspect with the exception that E is not hydrogen, functionalizing a corresponding compound having the formula



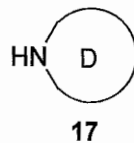
wherein the  moiety is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I, and A, B, X¹, X², X³ and X⁴ are as defined for General Formula I; or

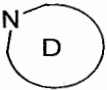
(c) for a compound of the first aspect where A is CN, D is as defined in the first aspect provided that the D ring is coupled to the ring defined by X¹, X², X³ and X⁴ through a ring nitrogen atom in the D ring, X¹, X², X³, X⁴ are as defined in the first aspect provided that at least one of X¹ and X² is nitrogen, and E is as defined in the first aspect, reacting a corresponding compound having the formula **15**



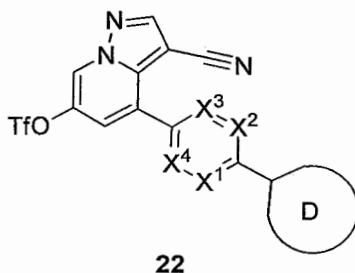
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where B, X¹, X², X³ and X⁴ are as defined in the first aspect provided that at least one of X¹ and X² is nitrogen, with a corresponding compound having the formula **17**

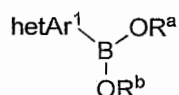


in the presence of a base, wherein the  ring is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I; or

(d) for a compound of the first aspect where A is CN, E is H, and B, X¹, X², X³, X⁴, and D are as defined in the first aspect, reacting a corresponding compound having the formula **22**



where X¹, X², X³, X⁴ and D are as defined in the first aspect, with a boronic ester having the formula



where hetAr¹ is as defined in the first aspect and R^a and R^b are H or (1-6C)alkyl, or R^a and R^b together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents selected from (C1-C3 alkyl), in the presence of a palladium catalyst and optionally a ligand and in the presence of a base; and

removing any protecting groups and optionally forming a pharmaceutically acceptable salt thereof or isolating a solvate of a free base or salt thereof.

[0037] Also provided herein is a compound of General Formula I or a pharmaceutically

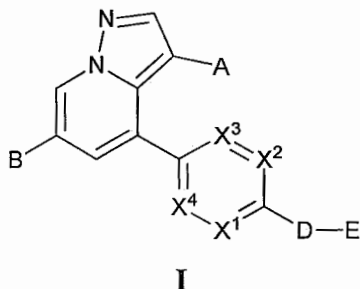
acceptable salt or solvate thereof obtained by a process of preparing the compound as defined herein.

[0038] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Methods and materials are described herein for use in the present disclosure; other, suitable methods and materials known in the art can also be used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control.

[0039] Other features and advantages of the disclosure will be apparent from the following detailed description and figures, and from the claims.

DETAILED DESCRIPTION OF THE INVENTION

[0040] Provided herein is a compound of the General Formula I:



[0041] or a pharmaceutically acceptable salt or solvate thereof, wherein:

[0042] X^1 is CH, CCH₃, CF, CCl or N;

[0043] X^2 is CH, CF or N;

[0044] X^3 is CH, CF or N;

[0045] X^4 is CH, CF or N;

[0046] wherein zero, one or two of X^1 , X^2 , X^3 and X^4 is N;

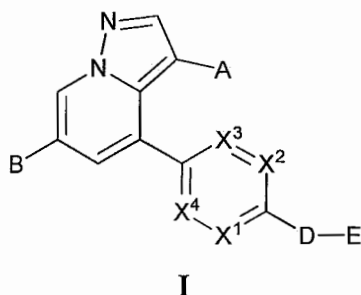
[0047] A is H, Cl, CN, Br, CH₃, CH₂CH₃ or cyclopropyl;

[0048] B is hetAr¹;

[0049] hetAr¹ is a 5-membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, S and O, wherein the heteroaryl ring is optionally substituted with one or more

What is claimed is:

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



or a pharmaceutically acceptable salt or solvate thereof, wherein:

X¹ is CH, CCH₃, CF, CCl or N;

X² is CH, CF or N;

X³ is CH, CF or N;

X⁴ is CH, CF or N;

wherein zero, one or two of X¹, X², X³ and X⁴ is N;

A is H, Cl, CN, Br, CH₃, CH₂CH₃ or cyclopropyl;

B is hetAr¹;

hetAr¹ is a 5-membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, S and O, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, hydroxyC1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, cyanoC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, (C1-C4 alkoxy)CH₂C(=O)-, (C1-C4 alkoxy)C(=O)C1-C3 alkyl, C3-C6 cycloalkyl, (R^aR^bN)C1-C6 alkyl, (R^aR^bN)C(=O)C1-C6 alkyl, (C1-C6 alkylSO₂)C1-C6 alkyl, hetCyc^a, and 4-methoxybenzyl;

R^a and R^b are independently H or C1-C6 alkyl;

hetCyc^a is a 4-6 membered heterocyclic ring having a ring heteroatom selected from N and O, wherein said heterocyclic ring is optionally substituted with halogen, C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, di(C1-C3 alkyl)NCH₂C(=O), (C1-C6 alkoxy)C(=O) or (C1-C6 alkoxy)CH₂C(=O);

D is hetCyc¹, hetCyc², hetCyc³ or hetCyc⁹;

hetCyc¹ is a 4-6 membered heterocyclic ring having 1-2 ring atoms selected from N and

O, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C3 alkyl, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl, trifluoroC1-C3 alkyl and OH, or said heterocyclic ring is substituted with a C3-C6 cycloalkylidene ring, or said heterocyclic ring is substituted with an oxo group;

hetCyc² is a 7-8 membered bridged heterocyclic ring having 1-3 ring heteroatoms independently selected from N and O, wherein said heterocyclic ring is optionally substituted with C1-C3 alkyl;

hetCyc³ is a 7-11 membered heterospirocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein said ring is optionally substituted with C1-C3 alkyl;

hetCyc⁹ is a fused 9-10 membered heterocyclic ring having 1-3 ring nitrogen atoms and optionally substituted with oxo;

E is

- (a) hydrogen,
- (b) OH,
- (c) R^aR^bN-, wherein R^a is H or C1-C6 alkyl and R^b is H, C1-C6 alkyl or phenyl;
- (d) C1-C6 alkyl optionally substituted with one to three fluoros,
- (e) hydroxyC1-C6 alkyl- optionally substituted with one to three fluoros,
- (f) C1-C6 alkoxy optionally substituted with one to three fluoros,
- (g) hydroxy(C1-C6 alkoxy) optionally substituted with one to three fluoros,
- (h) (C1-C6 alkoxy)hydroxy C1-C6 alkyl- optionally substituted with one to three fluoros,
- (i) (C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (j) (hydroxy C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (k) (C1-C6 alkoxy)C(=O)-,
- (l) (C1-C6 alkoxy)(C1-C6 alkyl)C(=O)-,
- (m) HC(=O)-,
- (n) Cyc¹,
- (o) Cyc¹C(=O)-,
- (p) Cyc¹(C1-C6 alkyl)C(=O)- wherein said alkyl portion is optionally substituted with one or more groups independently selected from the group consisting of OH, fluoro, C1-C3

alkoxy and R^eR^fN- , where R^e and R^f are independently H or C1-C6 alkyl,

(q) hetCyc^4 ,

(r) $\text{hetCyc}^4C(=O)-$,

(s) $\text{hetCyc}^4(C1-C3 \text{ alkyl})C(=O)-$,

(t) $(\text{hetCyc}^4)C(=O)C1-C2 \text{ alkyl}-$,

(u) $\text{hetCyc}^4C(=O)NH-$,

(v) Ar^2 ,

(w) $Ar^2C(=O)-$,

(x) $Ar^2C1-C6 \text{ alkyl}-$,

(y) $(Ar^2)\text{hydroxy } C2-C6 \text{ alkyl}-$,

(z) $Ar^2(C1-C3 \text{ alkyl})C(=O)-$ wherein said alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl (optionally substituted with 1-3 fluoros), hydroxyC1-C6 alkyl, C1-C6 alkoxy and R^eR^fN- , where R^e and R^f are independently H or C1-C6 alkyl, or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(aa) $\text{hetAr}^2C(=O)-$,

(bb) $(\text{hetAr}^2)\text{hydroxy}C2-C6 \text{ alkyl}-$,

(cc) $\text{hetAr}^2(C1-C3 \text{ alkyl})C(=O)-$, wherein said alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy and R^eR^fN- , wherein R^e and R^f are independently H or C1-C6 alkyl or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(dd) $R^1R^2NC(=O)-$,

(ee) $R^1R^2N(C1-C3 \text{ alkyl})C(=O)-$, wherein said alkyl portion is optionally substituted with phenyl,

(ff) $R^1R^2NC(=O)C1-C2 \text{ alkyl}-$,

(gg) $R^1R^2NC(=O)NH-$,

(hh) $CH_3SO_2(C1-C6 \text{ alkyl})C(=O)-$,

(ii) $(C1-C6 \text{ alkyl})SO_2-$,

(jj) $(C3-C6 \text{ cycloalkyl})CH_2SO_2-$,

- (kk) $\text{hetCyc}^5\text{-SO}_2\text{-}$,
- (ll) $\text{R}^4\text{R}^5\text{NSO}_2\text{-}$,
- (mm) $\text{R}^6\text{C(=O)NH-}$,
- (nn) $\text{hetCyc}^6\text{-}$,
- (oo) $\text{hetAr}^2\text{C1-C6 alkyl-}$,
- (pp) $(\text{hetCyc}^4)\text{C1-C6 alkyl-}$,
- (qq) $(\text{C1-C6 alkoxy})\text{C1-C6 alkyl-}$ optionally substituted with 1-3 fluoros,
- (rr) $(\text{C3-C6 cycloalkoxy})\text{C1-C6 alkyl-}$,
- (ss) $(\text{C3-C6 cycloalkyl})\text{C1-C6 alkyl-}$, wherein said cycloalkyl is optionally substituted with 1-2 fluoros,
- (tt) $(\text{R}^g\text{R}^h\text{N})\text{C1-C6 alkyl-}$, wherein R^g and R^h are independently H or C1-C6 alkyl,
- (uu) $\text{Ar}^2\text{-O-}$,
- (vv) $(\text{C1-C6 alkylSO}_2)\text{C1-C6 alkyl-}$,
- (ww) $(\text{C1-C6 alkoxy})\text{C(=O)NHC1-C6 alkyl-}$,
- (xx) $(\text{C3-C6 cycloalkoxy})\text{C(=O)-}$,
- (yy) $(\text{C3-C6 cycloalkyl})\text{SO}_2\text{-}$, wherein said cycloalkyl is optionally substituted with C1-C6 alkyl,
- (zz) $\text{Ar}^4\text{CH}_2\text{OC(=O)-}$,
- (aaa) $(\text{N-(C1-C3 alkyl)pyridinonyl})\text{C1-C3 alkyl-}$, and
- (bbb) $(\text{Ar}^4\text{SO}_2)\text{C1-C6 alkyl-}$;

Cyc^1 is a C3-C6 cycloalkyl, wherein (a) said cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of OH, halogen, C1-C6 alkoxy, CN, hydroxyC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, and C1-C6 alkyl optionally substituted with 1-3 fluoros, or (b) said cycloalkyl is substituted with phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C3 alkyl, C1-C3 alkoxy and CF, or (c) said cycloalkyl is substituted with a 5-6 membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N and O, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C3 alkyl, C1-C3 alkoxy and CF_3 ;

Ar^2 is phenyl optionally substituted with one or more substituents independently selected

from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, CN, a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, and R^iR^jN - wherein R^i and R^j are independently H or C1-C6 alkyl;

hetAr² is a 5-6 membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, O and S and optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, hydroxyC1-C6 alkyl, (C3-C6)cycloalkyl, (C1-C6 alkoxy)C1-C6 alkyl, CN, OH, and $R'R''N$ -, wherein R' and R'' are independently H or C1-C3 alkyl;

hetCyc⁴ is (a) a 4-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N, O and S wherein said S is optionally oxidized to SO₂, (b) a 7-8 membered bridged heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, (c) a 6-12 membered fused bicyclic heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O and optionally independently substituted with 1-2 C1-C6 alkyl substituents, or (d) a 7-10 membered spirocyclic heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein each of said heterocyclic rings is optionally substituted with one or more substituents independently selected from the group consisting of halogen, OH, CN, C1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy, (C1-C6 alkoxy)C1-C6 alkyl, (C3-C6)cycloalkyl, (C1-C6 alkyl)C(=O)-, a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, and phenyl wherein said phenyl is optionally substituted with one or more substituents selected from halogen, C1-C6 alkyl and C1-C6 alkoxy;

hetCyc⁵ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N;

hetCyc⁶ is a 5 membered heterocyclic ring having one or two ring heteroatoms independently selected from N and O, wherein said ring is substituted with oxo and wherein said ring is further optionally substituted with one or more substituents independently selected from the group consisting of OH and C1-C6 alkyl;

R^1 is H, C1-C6 alkyl or (C1-C6 alkoxy)C1-C6 alkyl;

R^2 is H, C1-C6 alkyl (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C1-C6

alkyl (optionally substituted with 1-3 fluoros), Cyc³, hydroxyC1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C(=O), hetCyc⁷, Ar³, Ar³C1-C3 alkyl-, hydroxyC1-C6 alkoxy or (3-6C cycloalkyl)CH₂O-;

Cyc³ is a 3-6 membered carbocyclic ring optionally substituted with 1-2 groups independently selected from the group consisting of C1-C6 alkoxy, OH and halogen;

hetCyc⁷ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N wherein said ring is optionally substituted with C1-C6 alkyl;

Ar³ is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C3 alkyl, C1-C3 alkoxy, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl and trifluoroC1-C3 alkyl;

R⁴ and R⁵ are independently H or C1-C6 alkyl;

R⁶ is C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy, (C1-C6 alkoxy)C1-C6 alkyl, phenyl or hetCyc⁸;

hetCyc⁸ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N, wherein said heterocyclic ring is optionally substituted with C1-C6 alkyl; and

Ar⁴ is phenyl optionally substituted with one or more halogens.

2. The compound according to claim 1, wherein D is hetCyc¹.
3. The compound according to claim 2, wherein hetCyc¹ is a pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl or azetidinyl ring optionally substituted with one or more substituents independently selected from the group consisting of C1-C3 alkyl, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl, trifluoroC1-C3 alkyl and OH, or hetCyc¹ is a piperazinyl ring substituted with a C3-C6 cycloalkylidene ring, or hetCyc¹ is a piperazinyl ring substituted with an oxo group.
4. The compound according to claim 3, wherein hetCyc¹ is piperazinyl.
5. The compound according to anyone of claims 1-4, wherein E is
 - (a) hydrogen,
 - (d) C1-C6 alkyl optionally substituted with one to three fluoros,

- (e) hydroxyC1-C6 alkyl optionally substituted with one to three fluoros,
- (i) (C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (j) (hydroxy C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,
- (k) (C1-C6 alkoxy)C(=O)-,
- (l) (C1-C6 alkoxy)(C1-C6 alkyl)C(=O)-,
- (n) Cyc¹,
- (o) Cyc¹C(=O)-,
- (p) Cyc¹(C1-C6 alkyl)C(=O)- wherein the alkyl portion is optionally substituted with one or more groups independently selected from the group consisting of OH, fluoro, C1-C3 alkoxy and R^eR^dN-, where R^e and R^d are independently H or C1-C6 alkyl,
- (q) hetCyc⁴,
- (r) hetCyc⁴C(=O)-,
- (s) hetCyc⁴(C1-C3 alkyl)C(=O)-,
- (t) (hetCyc⁴)C(=O)C1-C2 alkyl,
- (w) Ar²C(=O)-,
- (x) Ar²C1-C6 alkyl,
- (y) (Ar²)hydroxy C2-C6 alkyl,
- (z) Ar²(C1-C3 alkyl)C(=O)- wherein the alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy and R^eR^fN-, wherein R^e and R^f are independently H or C1-C6 alkyl,
- (aa) hetAr²C(=O)-,
- (bb) (hetAr²)hydroxyC2-C6 alkyl,
- (cc) hetAr²(C1-C3 alkyl)C(=O)- wherein the alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy and R^eR^fN-, wherein R^e and R^f are independently H or C1-C6 alkyl,
- (dd) R¹R²NC(=O)-,
- (ee) R¹R²N(C1-C3 alkyl)C(=O)- wherein the alkyl portion is optionally substituted with phenyl,
- (ff) R¹R²NC(=O)C1-C2 alkyl,

- (hh) $\text{CH}_3\text{SO}_2(\text{C1-C6 alkyl})\text{C}(=\text{O})-$,
- (ii) $(\text{C1-C6 alkyl})\text{SO}_2-$,
- (jj) $(\text{C3-C6 cycloalkyl})\text{CH}_2\text{SO}_2-$,
- (kk) $\text{hetCyc}^5\text{-SO}_2-$,
- (ll) $\text{R}^4\text{R}^5\text{NSO}_2-$,
- (mm) $\text{R}^6\text{C}(=\text{O})\text{NH}-$,
- (oo) $\text{hetAr}^2\text{C1-C6 alkyl}$,
- (pp) $(\text{hetCyc}^4)\text{C1-C6 alkyl}$,
- (qq) $(\text{C1-C6 alkoxy})\text{C1-C6 alkyl}$ wherein said alkoxy portion is optionally substituted

with 1-3 fluoros,

- (rr) $(\text{C3-C6 cycloalkoxy})\text{C1-C6 alkyl}$,
- (ss) $(\text{C3-C6 cycloalkyl})\text{C1-C6 alkyl}$ wherein said cycloalkyl is optionally substituted

with 1-2 fluoros,

- (tt) $(\text{R}^g\text{R}^h\text{N})\text{C1-C6 alkyl}$ wherein R^g and R^h are independently H or C1-C6 alkyl,
- (vv) $(\text{C1-C6 alkylSO}_2)\text{C1-C6 alkyl}$,
- (ww) $(\text{C1-C6 alkoxy})\text{C}(=\text{O})\text{NHC1-C6 alkyl}$, $(\text{C3-C6 cycloalkyl})\text{SO}_2-$ wherein said

cycloalkyl is optionally substituted with C1-C6 alkyl,

- (aaa) $(\text{N}-(\text{C1-C3 alkyl})\text{pyridinonyl})\text{C1-C3 alkyl}$, or
- (bbb) $(\text{Ar}^4\text{SO}_2)\text{C1-C6 alkyl}$.

6. The compound according to claim 5, wherein E is

- (d) C1-C6 alkyl optionally substituted with one to three fluoros,
- (e) hydroxyC1-C6 alkyl optionally substituted with one to three fluoros,
- (i) $(\text{C1-C6 alkyl})\text{C}(=\text{O})-$ optionally substituted with one to three fluoros,
- (j) $(\text{hydroxy C1-C6 alkyl})\text{C}(=\text{O})-$ optionally substituted with one to three fluoros,
- (o) $\text{Cyc}^1\text{C}(=\text{O})-$,
- (r) $\text{hetCyc}^4\text{C}(=\text{O})-$,
- (x) $\text{Ar}^2\text{C1-C6 alkyl}$,
- (y) $(\text{Ar}^2)\text{hydroxy C2-C6 alkyl}$, or
- (oo) $\text{hetAr}^2\text{C1-C6 alkyl}$.

7. The compound according to claim 6, wherein E is
 - (x) $\text{Ar}^2\text{C1-C6 alkyl}$, or (oo) $\text{hetAr}^2\text{C1-C6 alkyl}$.
8. The compound according to claim 7, wherein E is $\text{hetAr}^2\text{C1-C6 alkyl}$.
9. The compound according to claim 8, wherein hetAr^2 is pyridyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, trifluoroC1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), hydroxyC1-C6 alkyl, CN and $(\text{R}^a\text{R}^b\text{N})\text{C1-C6 alkyl}$.
10. A compound according to claim 6, wherein E is $\text{hetCyc}^4\text{C(=O)-}$ and hetCyc^4 is a 5-membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from halogen, OH, CN, C1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy and $(\text{C1-C6 alkoxy})\text{C1-C6 alkyl}$.
11. A compound according to claim 10, wherein hetCyc^4 is a 5-membered heterocyclic ring having a ring nitrogen atom, wherein said heterocyclic ring is optionally substituted with C1-C6 alkoxy.
12. A compound according to claim 3, wherein hetCyc^1 is piperidinyl, pyrrolidinyl or azetidiny.
13. A compound according to claim 12, wherein E is:
 - (a) hydrogen,
 - (b) OH,
 - (c) $\text{R}^a\text{R}^b\text{N-}$,
 - (f) C1-C6 alkoxy optionally substituted with one to three fluoros,
 - (g) hydroxy(C1-C6 alkoxy) optionally substituted with one to three fluoros,
 - (k) $(\text{C1-C6 alkoxy})\text{C(=O)-}$,
 - (m) HC(=O)- ,

- (r) $\text{hetCyc}^4\text{C}(=\text{O})-$,
- (u) $\text{hetCyc}^4\text{C}(=\text{O})\text{NH}-$,
- (v) Ar^2 ,
- (dd) $\text{R}^1\text{R}^2\text{NC}(=\text{O})-$,
- (ff) $\text{R}^1\text{R}^2\text{NC}(=\text{O})\text{C1-C2 alkyl}$,
- (gg) $\text{R}^1\text{R}^2\text{NC}(=\text{O})\text{NH}-$,
- (mm) $\text{R}^6\text{C}(=\text{O})\text{NH}-$,
- (nn) hetCyc^6 ,
- (oo) $\text{hetAr}^2\text{C1-C6 alkyl}$, or
- (uu) $\text{Ar}^2-\text{O}-$.

14. A compound according to claim 1, wherein D is hetCyc^2 .

15. A compound according to claim 14, wherein E is

- (a) hydrogen,
- (b) OH ,
- (c) $\text{R}^a\text{R}^b\text{N}-$, wherein R^a is H or C1-C6 alkyl and R^b is H, C1-C6 alkyl or phenyl,
- (d) C1-C6 alkyl optionally substituted with one to three fluoros,
- (e) hydroxyC1-C6 alkyl optionally substituted with one to three fluoros,
- (f) C1-C6 alkoxy optionally substituted with one to three fluoros,
- (i) $(\text{C1-C6 alkyl})\text{C}(=\text{O})-$ optionally substituted with one to three fluoros,
- (k) $(\text{C1-C6 alkoxy})\text{C}(=\text{O})-$,
- (o) $\text{Cyc}^1\text{C}(=\text{O})-$,
- (w) $\text{Ar}^2\text{C}(=\text{O})-$,
- (x) $\text{Ar}^2\text{C1-C6 alkyl}$,
- (y) $(\text{Ar}^2)\text{hydroxy C2-C6 alkyl}$,
- (aa) $\text{hetAr}^2\text{C}(=\text{O})-$,
- (cc) $\text{hetAr}^2(\text{C1-C3 alkyl})\text{C}(=\text{O})-$ wherein the alkyl portion is optionally substituted with

one or two groups independently selected from the group consisting of OH , C1-C6 alkyl, hydroxyC1-C6 alkyl, C1-C6 alkoxy and $\text{R}^e\text{R}^f\text{N}-$, where R^e and R^f are independently H or C1-C6 alkyl, or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered

azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(ee) $R^1R^2N(C1-C3 \text{ alkyl})C(=O)-$ wherein said alkyl portion is optionally substituted with phenyl; or

(oo) $hetAr^2C1-C6 \text{ alkyl}$, or

(qq) $(C1-C6 \text{ alkoxy})C1-C6 \text{ alkyl}$ wherein said alkoxy portion is optionally substituted with 1-3 fluoros.

16. A compound according to claim 1, wherein D is $hetCyc^3$.

17. A compound according to claim 16, wherein E is

(a) hydrogen,

(c) R^aR^bN- , wherein R^a is H or C1-C6 alkyl and R^b is H, C1-C6 alkyl or phenyl;

(d) C1-C6 alkyl optionally substituted with one to three fluoros,

(e) hydroxyC1-C6 alkyl optionally substituted with one to three fluoros,

(i) $(C1-C6 \text{ alkyl})C(=O)-$ optionally substituted with one to three fluoros,

(j) $(\text{hydroxy } C1-C6 \text{ alkyl})C(=O)-$ optionally substituted with one to three fluoros,

(k) $(C1-C6 \text{ alkoxy})C(=O)-$,

(o) $Cyc^1C(=O)-$,

(p) $Cyc^1(C1-C6 \text{ alkyl})C(=O)$,

(r) $hetCyc^4C(=O)-$,

(w) $Ar^2C(=O)-$,

(x) $Ar^2C1-C6 \text{ alkyl}$,

(y) $(Ar^2)\text{hydroxy } C2-C6 \text{ alkyl}$,

(z) $Ar^2(C1-C3 \text{ alkyl})C(=O)-$ wherein said alkyl portion is optionally substituted with one or two groups independently selected from the group consisting of OH, C1-C6 alkyl (optionally substituted with 1-3 fluoros), hydroxyC1-C6 alkyl, C1-C6 alkoxy and R^eR^fN- , wherein R^e and R^f are independently H or C1-C6 alkyl, or R^e and R^f together with the nitrogen to which they are attached form a 5-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O,

(dd) $R^1R^2NC(=O)-$,

(ee) $R^1R^2N(C1-C3 \text{ alkyl})C(=O)-$,

- (mm) $R^6C(=O)NH-$,
- (xx) (C3-C6 cycloalkoxy) $C(=O)-$,
- (zz) $Ar^4CH_2OC(=O)-$, or
- (oo) $hetAr^2C1-C6$ alkyl.

18. A compound according to any one of claims 1-17, wherein $hetAr^1$ is a 5-membered heteroaryl ring having 1-2 ring nitrogen atoms, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, and hydroxyC1-C6 alkyl.

19. A compound according to claim 18, wherein $hetAr^1$ is pyrazolyl or imidazolyl optionally substituted with C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl or hydroxyC1-C6 alkyl.

20. A compound according to claim 19, wherein $hetAr^1$ is pyrazolyl optionally substituted with C1-C6 alkyl.

21. A compound according to any one of claims 1-20, wherein X^1 is N, CH or CH_3 , X^2 is CH or N, X^3 is CH or N, and X^4 is CH or N, wherein one of X^1 , X^2 , X^3 and X^4 is N.

22. A compound according to claim 21, wherein

X^1 is N, and

X^2 , X^3 and X^4 are CH.

23. A compound according to any one of claims 1-20, wherein

X^1 is CCH_3 ,

X^2 is CH, CF or N;

X^3 is CH, CF or N; and

X^4 is CH, CF or N;

wherein one of X^2 , X^3 and X^4 is N.

24. A compound according to any one of claims 1-20, wherein
X¹ is CH, CCH₃, CF, CCl or N;
X² is CH, CF or N;
X³ is CH, CF or N; and
X⁴ is CH, CF or N,
wherein two of X¹, X², X³ and X⁴ are N.
25. A compound according to claim 24, wherein X¹ and X² are N, and X³ and X⁴ are CH or CF.
26. A compound according to claim 24, wherein X¹ and X³ are N, and X² and X⁴ are CH or CF.
27. A compound according to any one of claims 1-20, wherein X¹ is CH or CH₃, and X², X³ and X⁴ are CH.
28. A compound according to any one of claims 1-27, where A is H, Cl, CN, Br, CH₃, or CH₂CH₃.
29. A compound according to claim 28, wherein A is H.
30. A compound according to claim 28, wherein A is Cl.
31. A compound according to claim 28, wherein A is CN.
32. A compound according to claim 1, wherein:
X¹ is N and each of X², X³ and X⁴ is CH;
A is CN or Cl;
B is hetAr¹;

hetAr¹ is a 5-membered heteroaryl ring having 1-2 ring nitrogen atoms, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl and hydroxyC1-C6 alkyl;

D is hetCyc¹; and

hetCyc¹ is piperazinyl.

33. A compound according to claim 1, wherein:

X¹ is N and each of X², X³ and X⁴ is CH;

A is CN;

B is hetAr¹;

hetAr¹ is a 5-membered heteroaryl ring having 2 ring nitrogen atoms, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl and hydroxyC1-C6 alkyl;

D is hetCyc¹;

hetCyc¹ is piperazinyl;

E is (i) (C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros, (j) (hydroxy C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros, or (r) hetCyc⁴C(=O)-; and

hetCyc⁴ is a 5-membered heterocyclic ring having a ring nitrogen atom, wherein said heterocyclic ring is optionally substituted with C1-C6 alkoxy.

34. A compound according to claim 1, wherein:

X¹, X², X³ and X⁴ are CH;

A is H, Cl or CN;

B is hetAr¹;

hetAr¹ is a 5-membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, S and O, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, hydroxyC1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, cyanoC1-C6

alkyl, (C1-C6 alkoxy)C1-C6 alkyl, (C1-C4 alkoxy)CH₂C(=O)-, (C1-C4 alkoxy)C(=O)C1-C3 alkyl, C3-C6 cycloalkyl, (R^aR^bN)C1-C6 alkyl and hetCyc^a;

D is hetCyc¹;

hetCyc¹ is a 5-6 membered heterocyclic ring having 1-2 ring nitrogen atoms, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C3 alkyl;

E is

(a) hydrogen,

(i) (C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,

(j) (hydroxy C1-C6 alkyl)C(=O)- optionally substituted with one to three fluoros,

(k) (C1-C6 alkoxy)C(=O)-,

(ee) R¹R²N(C1-C3 alkyl)C(=O)- wherein said alkyl portion is optionally substituted with phenyl, or

(ii) (C1-C6 alkyl)SO₂-;

R¹ is H or C1-C6 alkyl;

R² is H, C1-C6 alkyl (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C1-C6 alkyl (optionally substituted with 1-3 fluoros), Cyc³, hydroxyC1-C6 alkyl (optionally substituted with 1-3 fluoros), C1-C6 alkoxy (optionally substituted with 1-3 fluoros), (C1-C6 alkoxy)C(=O), hetCyc⁷, Ar³ or Ar³C1-C3 alkyl-;

Cyc³ is a 3-6 membered carbocyclic ring optionally substituted with 1-2 groups independently selected from the group consisting of C1-C6 alkoxy, OH and halogen;

Ar³ is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C3 alkyl, C1-C3 alkoxy, fluoroC1-C3 alkyl, difluoroC1-C3 alkyl and trifluoroC1-C3 alkyl; and

hetCyc⁷ is a 5-6 membered heterocyclic ring having a ring heteroatom selected from O and N wherein said ring is optionally substituted with C1-C6 alkyl.

35. A compound according to claim 1, wherein:

X¹ is N and each of X², X³ and X⁴ is CH;

A is CN;

hetAr¹ is a 5-membered heteroaryl ring having 1-3 ring heteroatoms independently selected

from N, S and O, wherein the heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, hydroxyC1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, cyanoC1-C6 alkyl, (C1-C6 alkoxy)C1-C6 alkyl, (C1-C4 alkoxy)CH₂C(=O)-, (C1-C4 alkoxy)C(=O)C1-C3 alkyl, C3-C6 cycloalkyl, (R^aR^bN)C1-C6 alkyl, and hetCyc^a;

D is hetCyc¹;

hetCyc¹ is piperazinyl;

E is (x) Ar²C1-C6 alkyl or (oo) hetAr²C1-C6 alkyl;

Ar² is phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, CN, a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, and RⁱR^jN- where Rⁱ and R^j are independently H and C1-C6 alkyl; and

hetAr² is a 5-6 membered heteroaryl ring having 1-3 ring heteroatoms independently selected from N, O and S and optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6 alkyl, C1-C6 alkoxy, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl, (C3-C6)cycloalkyl, (C1-C6 alkoxy)C1-C6 alkyl, CN and R'R"N-, wherein R' and R" are independently H or C1-C3 alkyl.

36. The compound of claim 35, wherein hetAr¹ is a 5-membered heteroaryl ring having 1-2 ring nitrogen atoms, wherein the heteroaryl ring is optionally substituted with one or more substituents independently selected from the group consisting of C1-C6 alkyl, fluoroC1-C6 alkyl, difluoroC1-C6 alkyl, trifluoroC1-C6 alkyl and hydroxyC1-C6 alkyl.

37. The compound of claim 36, wherein hetAr¹ is pyrazolyl optionally substituted with C1-C6 alkyl.

38. The compound according to any one of claims 35-37, wherein E is hetAr²C1-C6 alkyl.

39. The compound according to claim 38, wherein hetAr² is pyridyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, C1-C6

alkyl, trifluoroC1-C6 alkyl, C1-C6 alkoxy (optionally substituted with 1-3 fluoros), hydroxyC1-C6 alkyl, CN and (R^aR^bN)C1-C6 alkyl.

40. The compound according to claim 39, wherein hetAr² is pyridyl optionally substituted with C1-C6 alkoxy (optionally substituted with 1-3 fluoros).

41. The compound of claim 1, selected from the following compounds:

tert-butyl 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-(methylsulfonyl)propanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

((S)-4-(6-(4-(2-hydroxy-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(pyridin-2-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(3-hydroxy-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(3-hydroxy-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(2-hydroxy-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-(2-fluorophenyl)-2-hydroxyacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((1S,3S)-3-hydroxycyclopentane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((1S,3R)-3-hydroxycyclopentane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(3,3-difluorocyclopentane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-hydroxy-2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-tert-butyl (3-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-3-oxo-1-phenylpropyl)carbamate;

tert-butyl tert-butyl(2-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-oxoethyl)carbamate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(6-methylpyridin-3-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(1-methyl-1H-pyrazol-5-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(cyclopentanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-(tert-butylamino)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(S)-4-(6-(4-(3-amino-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-phenylcyclopentanecarbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-phenylcyclopropane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-methyl-2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-phenylcyclobutane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-phenylcyclohexane-1-carbonyl)piperazin-1-yl)pyridin-

3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-methyl-2-phenylbutanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(2-hydroxypropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-hydroxy-2-methylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-hydroxypropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-(dimethylamino)propanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-pivaloylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-methyl-1H-pyrazole-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(1-methyl-1H-imidazole-4-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(5-methylisoxazole-3-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrazine-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(2-(2,6-difluorophenyl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(2-methoxyacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(1,3-dimethyl-1H-pyrazole-4-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(2-(1-methyl-1H-pyrazol-3-yl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-(pyridin-3-yl)propanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-prolylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-prolylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(piperidine-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(piperidine-3-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(R)-4-(6-(4-(2-amino-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(5-methylpyrazine-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(S)-4-(6-(4-(2-amino-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(2,6-difluorobenzoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

4-(6-(4-(4-(dimethylamino)butanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(R)-4-(6-(4-(2-hydroxy-4-methylpentanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(3-hydroxybutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-hydroxy-4-methylpentanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(3-hydroxybutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(tetrahydrofuran-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2,2-difluoropropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(tetrahydrofuran-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3,3,3-trifluoro-2-hydroxypropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(tetrahydrofuran-3-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-hydroxy-3-methylpentanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(pyrrolidin-1-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-isobutyrylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-propionylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-benzoylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-butyrylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(pyridin-3-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-picolinoylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-nicotinoylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(tetrahydro-2H-pyran-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(tetrahydro-2H-pyran-4-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-cyclopropylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((1*r*,4*r*)-4-hydroxycyclohexanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(1-hydroxycyclopropane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(*R*)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(*R*)-4-(6-(4-(2-methoxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(*S*)-4-(6-(4-(2-methoxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(*R*)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(*R*)-4-(6-(4-(2-methoxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((cyclopropylmethyl)sulfonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(neopentylsulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(isobutylsulfonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((tetrahydro-2H-pyran-4-yl)sulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(4-hydroxypiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(piperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3,3-difluoropiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(7-azabicyclo[2.2.1]heptane-7-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1-hydroxybutan-2-yl)piperazine-1-carboxamide;
 (S)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N,N-diethylpiperazine-1-carboxamide;
 (R)-4-(6-(4-(3-hydroxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(3-hydroxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3,3-difluoropyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(3-fluoropyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(3-fluoropyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(tetrahydrofuran-3-yl)piperazine-1-carboxamide;

(R)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(tetrahydrofuran-3-yl)piperazine-1-carboxamide;

(R)-4-(6-(4-(3-isopropoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(3-isopropoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-methyl-N-phenylpiperazine-1-carboxamide;

(R)-4-(6-(4-(2-(methoxymethyl)pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-(methoxymethyl)pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-cyanopyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(trifluoromethyl)pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(4-fluoropiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(4,4-difluoropiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-fluoropiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(5-azaspiro[2.4]heptane-5-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3,3-dimethylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(morpholine-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(4-methylpiperazine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-

(tetrahydro-2H-pyran-4-yl)piperazine-1-carboxamide;

(S)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1-hydroxybutan-2-yl)piperazine-1-carboxamide;

4-(6-(4-(hexahydro-1H-furo[3,4-c]pyrrole-5-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2,2-dimethylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpiperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-phenylpiperazine-1-carboxamide;

N-(tert-butyl)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxamide;

N-benzyl-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-methoxyethyl)-N-methylpiperazine-1-carboxamide 2,2,2-trifluoroacetate;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-cyclopropylpiperazine-1-carboxamide 2,2,2-trifluoroacetate;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N,N-dimethylpiperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isobutylpiperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-ethylpiperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-methoxyethyl)piperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-ethyl-N-methylpiperazine-1-carboxamide;

N-(tert-butyl)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-sulfonamide;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrrolidin-1-ylsulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(4-chlorophenethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-formylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-methyl-2-oxopyrrolidin-3-yl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 2-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-N,N-dimethylacetamide 2,2,2-trifluoroacetate;
 2-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-N-isopropylacetamide 2,2,2-trifluoroacetate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-oxo-2-(pyrrolidin-1-yl)ethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 3-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-N,N-dimethylpropanamide 2,2,2-trifluoroacetate;
 4-(6-(4-((1R,2R)-1-hydroxy-1-phenylpropan-2-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-hydroxy-3,3-dimethylbutyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1S,2S)-1-hydroxy-1-phenylpropan-2-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(2-hydroxybutyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-hydroxy-3-methoxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-(4-chlorophenyl)-2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-

pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-(3-chlorophenyl)-2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-(2,6-difluorophenyl)-2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1*r*,2*r*)-2-hydroxycyclohexyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-hydroxy-2-methylpropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((3*r*,4*s*)-4-hydroxytetrahydrofuran-3-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-hydroxy-3-methylbutyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-hydroxy-2-phenylethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(2-hydroxy-2-phenylethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1*r*,2*r*)-2-hydroxycyclopentyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-(4-fluorophenyl)-2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 rac-4-(6-(4-((2*R**,3*S**)-3-hydroxybutan-2-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4,7-diazaspiro[2.5]octane-4-carboxylate;
 4-(6-(4,7-diazaspiro[2.5]octan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(4-(3-hydroxy-3-methylbutanoyl)-4,7-diazaspiro[2.5]octan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3,3-dimethylbutanoyl)-4,7-diazaspiro[2.5]octan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(1S,4S)-tert-butyl 5-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate;

4-(6-((1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-((1S,4S)-5-(3,3-dimethylbutanoyl)-2,5-diazabicyclo[2.2.1]heptan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl 3-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate;

4-(6-(3,8-diazabicyclo[3.2.1]octan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(8-(3,3-dimethylbutanoyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl (1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)carbamate;

4-(6-(4-aminopiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(R)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)tetrahydrofuran-2-carboxamide;

N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-2-hydroxy-2-methylpropanamide;

(S)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-2-hydroxypropanamide;

(R)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-2-hydroxypropanamide;

(S)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)tetrahydrofuran-2-carboxamide;

N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-

yl)piperidin-4-yl)-2-methoxyacetamide;
 N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)benzamide;
 N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)isobutyramide;
 3-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-1,1-dimethylurea;
 1-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-3-isopropylurea;
 Isopropyl (1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)carbamate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-oxopyrrolidin-1-yl)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(3-hydroxy-2-oxopyrrolidin-1-yl)piperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-oxooxazolidin-3-yl)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-butyl ((1R,3s,5S)-8-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl)carbamate;
 4-(6-((1R,3s,5S)-3-amino-8-azabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 tert-butyl ((1R,3r,5S)-8-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl)carbamate;
 4-(6-((1R,3r,5S)-3-amino-8-azabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 4-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-isobutoxypiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-((1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-((1R,3r,5S)-3-methoxy-8-azabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl (1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-methylpiperidin-4-yl)carbamate;

4-(6-(4-amino-4-methylpiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-methylpiperidin-4-yl)isobutyramide;

tert-butyl 8-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,8-diazaspiro[4.5]decane-2-carboxylate;

4-(6-(2,8-diazaspiro[4.5]decan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(R)-4-(6-(2-(2-hydroxy-3-methylbutanoyl)-2,8-diazaspiro[4.5]decan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(2-isobutyryl-2,8-diazaspiro[4.5]decan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,7-diazaspiro[4.5]decane-2-carboxylate;

4-(6-(2,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2-((R)-2-hydroxy-3-methylbutanoyl)-2,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-((S)-2-((R)-2-hydroxy-3-methylbutanoyl)-2,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-((R)-2-((R)-2-hydroxy-3-methylbutanoyl)-2,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(2-isobutyryl-2,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-

2,7-diazaspiro[3.5]nonane-2-carboxylate;
 4-(6-(2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 (R)-4-(6-(2-(2-hydroxy-3-methylbutanoyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-benzoyl-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(2-(2-phenylacetyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(cyclopentanecarbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-acetyl-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-isobutyryl-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 isopropyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;
 tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-morpholinopyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-3-yl)isobutyramide;
 (R)-N-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-3-yl)isobutyramide;
 (R)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylmorpholine-2-carboxamide;
 (S)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylmorpholine-2-carboxamide;
 (R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpiperidine-3-carboxamide;

(S)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpiperidine-3-carboxamide;

(S)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1,1,1-trifluoropropan-2-yl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1-methoxypropan-2-yl)piperidine-4-carboxamide;

(R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1,1,1-trifluoropropan-2-yl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-isopropoxyethyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(3,3,3-trifluoro-2-methoxypropyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-methoxy-3-methylbutyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-ethoxypiperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(3,3-difluorocyclobutyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-methoxypropyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-((1r,3r)-3-methoxycyclobutyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-((1s,3s)-3-methoxycyclobutyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(3,3,3-trifluoropropyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2,2,2-trifluoroethyl)piperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isobutyl-N-methylpiperidine-4-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-

hydroxypropyl)-N-methylpiperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpiperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropyl-N-methylpiperidine-4-carboxamide;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrrolidine-1-carbonyl)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 2-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidin-4-yl)-N-isopropylacetamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-methyl-N-(3,3,3-trifluoropropyl)piperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropyl-4-methylpiperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1-methoxypropan-2-yl)-4-methylpiperidine-4-carboxamid;
 (R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-methyl-N-(1,1,1-trifluoropropan-2-yl)piperidine-4-carboxamide;
 Methyl 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-methylpiperidine-4-carboxylate;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-(3,3,3-trifluoropropyl)piperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-isopropylpiperidine-4-carboxamide;
 (R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-(1,1,1-trifluoropropan-2-yl)piperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-(2-hydroxy-2-methylpropyl)piperidine-4-carboxamide;
 (R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(3,3,3-trifluoropropyl)pyrrolidine-3-carboxamide;
 (R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(3-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpyrrolidine-3-carboxamide;

(S)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(3,3,3-trifluoropropyl)pyrrolidine-3-carboxamide;

(S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(3-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpyrrolidine-3-carboxamide;

tert-Butyl 4-(5-(3-cyano-6-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-(3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-Butyl 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

6-(1-methyl-1H-pyrazol-3-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(R)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-3-yl)-4-(6-(4-(3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-Butyl 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)-3-methylpyridin-2-yl)piperazine-1-carboxylate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(5-methyl-6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-

a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(4-(3-hydroxy-3-methylbutanoyl)piperazin-1-yl)-5-methylpyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)-5-methylpyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)-5-methylpyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(5-methyl-6-(4-(pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(2-(piperazin-1-yl)pyrimidin-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(R)-4-(2-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyrimidin-5-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(2-(4-(3-methylbutanoyl)piperazin-1-yl)pyrimidin-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(2-(4-(2-methoxy-2-phenylacetyl)piperazin-1-yl)pyrimidin-5-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(2-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyrimidin-5-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(2-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyrimidin-5-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(5-(piperazin-1-yl)pyrazin-2-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(5-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyrazin-2-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(5-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyrazin-2-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-Butyl 4-(4-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)phenyl)piperazine-1-carboxylate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(4-(piperazin-1-yl)phenyl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(4-(4-(2-methoxyacetyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(4-(4-(2-hydroxyacetyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile hydrochloride;

4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(4-(4-acetyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

Methyl 4-(4-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)phenyl)piperazine-1-carboxylate;

4-(4-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)phenyl)-N-methylpiperazine-1-sulfonamide;

tert-butyl 4-(4-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)phenyl)piperidine-1-carboxylate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(4-(piperidin-4-yl)phenyl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(4-(1-(3,3-dimethylbutanoyl)piperidin-4-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(4-(1-(2-(dimethylamino)acetyl)piperidin-4-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-(2-hydroxypropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-(2-hydroxypropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-(3-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-(3-hydroxy-2-methylpropyl)-1H-

pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-imidazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(4-(4-(3,3-dimethylbutanoyl)piperazin-1-yl)phenyl)-6-(5-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-Butyl 4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine dihydrochloride;
 (R)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-phenylethanone;
 2-(2,6-difluorophenyl)-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 (2,6-difluorophenyl)(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)methanone;
 (R)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-(p-tolyl)ethanone;
 2-(2,4-difluorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 2-(2,6-difluorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 2-(3,5-difluorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 (R)-2-(2-chlorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 (R)-2-(2-fluorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 (R)-2-(3-chlorophenyl)-2-hydroxy-1-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;

N-methyl-4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-phenylpiperazine-1-carboxamide;
 (R)-2-(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-1-phenylethanol;
 tert-butyl 4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;
 3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine dihydrochloride;
 (R)-1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxy-2-phenylethanone;
 1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-(dimethylamino)ethanone;
 1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-methoxyethanone;
 1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
 1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-3,3-dimethylbutan-1-one;
 3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;
 3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;
 tert-butyl 8-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,8-diazabicyclo[3.2.1]octane-3-carboxylate;
 4-(6-(3,8-diazabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine dihydrochloride;
 1-(8-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-2-(dimethylamino)ethanone;
 tert-butyl 3-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate;
 3-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,6-

diazabicyclo[3.1.1]heptane dihydrochloride;
 3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(pyrrolidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;
 4-(6-(7-azabicyclo[2.2.1]heptan-7-yl)pyridin-3-yl)-3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine;
 4-(6-(4-(1-(4-chlorophenyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(4-phenyltetrahydro-2H-pyran-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(2,4-dichlorophenyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(4-methoxyphenyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(4-fluorophenyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-(trifluoromethyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(hydroxymethyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-cyanocyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(3-fluorophenyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-(pyrazin-2-yl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-(dimethylamino)-2-(4-fluorophenyl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-methoxy-2,2-dimethylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1-(methoxymethyl)cyclopropanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(1-(methoxymethyl)cyclobutanecarbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(piperidine-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(1-(3-chlorophenyl)cyclopropane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(4-(trifluoromethoxy)phenyl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-morpholinobenzoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-(pyridine-2-yl)cyclopropane-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(2-(5-fluoropyridin-2-yl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(4-methylpiperazin-1-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile tris(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-morpholinoacetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-morpholino-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(2-(diethylamino)-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(2-(4-cyanophenyl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

4-(6-(4-(1-(2-methoxyethyl)-1H-pyrazole-3-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-methyl-5-propylisoxazole-4-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-phenyl-2-(piperidin-1-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(1-(pyridine-3-yl)cyclopropane-1-carbonyl)piperazin-1-

yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 4-(6-(4-(5-cyclopropyl-1H-pyrazole-3-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 (S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(3-hydroxy-2-phenylpropanol)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((1-methylcyclopropyl)sulfonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-phenylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(4-methoxypiperidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 N-butyl-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)-N-phenylpiperazine-1-carboxamide;
 (R)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-phenylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-morpholinopyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-azabicyclo[3.1.0]hexane-3-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(octahydropyrrolo[1,2-a]pyrazine-2-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)-N-(2-methoxyphenyl)-N-methylpiperazine-1-carboxamide;
 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-4-yl)pyridin-2-yl)-N-(4-methoxyphenyl)-N-methylpiperazine-1-carboxamide;
 4-(6-(4-(6,6-dimethyl-3-azabicyclo[3.1.0]hexane-3-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)-N,N-bis(2-methoxyethyl)piperazine-1-carboxamide;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-4-yl)pyridin-2-yl)-N-cyclopropyl-N-methylpiperazine-1-carboxamide 2,2,2-trifluoroacetate;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-methylpiperazine-1-carboxamide;

4-(6-(4-(3-cyclopropylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-ethylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-isopropylpyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(3-(trifluoromethyl)pyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(cyclopropylmethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(pyridine-2-yl)ethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-ethoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(trifluoromethoxy)ethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((2-methoxypyridin-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((4,6-dimethylpyrimidin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-(isopropylsulfonyl)ethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((tetrahydro-2H-pyran-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-methoxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((tetrahydrofuran-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-cyclopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-propylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-ethylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-isopropylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-phenethylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-methoxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-methoxy-3-methylbutyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-methoxy-2-methylpropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-(2-methoxypropyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((3*r*,4*s*)-4-methoxytetrahydrofuran-3-yl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2-methoxy-3,3-dimethylbutyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2,2-difluoroethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

6-(1-methyl-1*H*-pyrazol-4-yl)-4-(6-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2-(*tert*-butoxy)ethyl)piperazin-1-yl)pyridine-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

(*R*)-6-(1-methyl-1*H*-pyrazol-4-yl)-4-(6-(4-(1-phenylethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile dihydrochloride;

(*S*)-6-(1-methyl-1*H*-pyrazol-4-yl)-4-(6-(4-(1-phenylethyl)piperazin-1-yl)pyridine-3-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile dihydrochloride;

4-(6-(4-((5-fluoropyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(4-fluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(4-chlorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2,4-difluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2-fluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(3-fluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-(2,5-difluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

4-(6-(4-((5-chloropyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1*H*-pyrazol-4-yl)pyrazolo[1,5-*a*]pyridine-3-carbonitrile;

6-(1-methyl-1*H*-pyrazol-4-yl)-4-(6-(4-((6-methylpyrazin-2-yl)methyl)piperazin-1-yl)pyridin-3-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(4-methoxybenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((6-methylpyridin-2-yl)methyl)piperazin-1-yl)pyridine-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((3-fluoropyridin-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1,5-dimethyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((5-methylisoxazol-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1-methyl-1H-imidazol-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((3-methylpyridin-2-yl)methyl)piperazin-1-yl)pyridine-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1-methyl-1H-pyrazol-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1,3-dimethyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2,6-difluorobenzyl)piperazin-1-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((5-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((4-methylpyridin-2-yl)methyl)piperazin-1-yl)pyridine-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((5-methylpyrazin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1-isopropyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((1-ethyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3,5-difluorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((1-methyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((1-methyl-1H-imidazol-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-methoxybenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-methoxybenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((2-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrazin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-chlorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(3-chlorobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((1-acetypiperidin-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((5-fluoro-2-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((5-methoxypyridin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((3,3-difluorocyclobutyl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-(dimethylamino)benzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(4-(dimethylamino)benzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((5-fluoropyridin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((3-methoxypyridin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile formate;
 4-(6-(4-(2-cyanobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((2-methylpyrimidin-5-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((tetrahydro-2H-pyran-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((2-methylpyrimidin-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(3-cyanobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(4-cyanobenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2,6-dimethylbenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridin-3-ylmethyl)piperazin-1-yl)pyridine-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridine-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(tetrahydro-2H-pyran-4-yl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-cyclobutylpiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(oxetan-3-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-morpholinoethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(oxetan-3-yl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(methylamino)ethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-(dimethylamino)ethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzyl-3-oxopiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-((1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(8-benzyl-3,8-diazabicyclo[3.2.1]octan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(7-benzyl-2,7-diazaspiro[3.5]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(3,6-Diazabicyclo[3.1.1]heptan-6-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(3,8-Diazabicyclo[3.2.1]octan-8-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-benzyl-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(3-benzyl-3,6-diazabicyclo[3.1.1]heptan-6-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(3-benzyl-3,8-diazabicyclo[3.2.1]octan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(2-(cyclopropanecarbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(2-(cyclobutanecarbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-

pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(2-(dimethylamino)acetyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(cyclohexanecarbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(2-ethylbutanoyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(2-cyclopentylacetyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-(2-cyclohexylacetyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 Cyclopentyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(2-(pyrrolidine-1-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N,N-dimethyl-2,7-diazaspiro[3.5]nonane-2-carboxamide;
 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N,N-diethyl-2,7-diazaspiro[3.5]nonane-2-carboxamide;
 4-(6-(2-benzyl-2,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-Butyl 9-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)-2,9-diazaspiro[5.5]undecane-2-carboxylate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 tert-butyl (2-(4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)ethyl)carbamate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(phenylamino)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-phenoxy piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(4-chlorophenoxy)piperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

tert-butyl 9-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-3,9-diazaspiro[5.5]undecane-3-carboxylate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,9-diazaspiro[5.5]undecane-9-carboxylate;

tert-butyl 8-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-1,8-diazaspiro[4.5]decane-1-carboxylate;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-1,7-diazaspiro[4.5]decane-1-carboxylate;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-1,7-diazaspiro[3.5]nonane-1-carboxylate;

tert-butyl (7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-7-azaspiro[3.5]nonan-2-yl)carbamate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,8-diazaspiro[4.5]decane-8-carboxylate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,7-diazaspiro[4.5]decane-7-carboxylate;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,7-diazaspiro[4.4]nonane-2-carboxylate;

tert-butyl 7-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-1,7-diazaspiro[4.4]nonane-1-carboxylate;

tert-butyl 6-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,6-diazaspiro[3.4]octane-2-carboxylate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,6-diazaspiro[3.5]nonane-6-carboxylate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-2,5-diazaspiro[3.5]nonane-5-carboxylate;

tert-butyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-

2,5-diazaspiro[3.4]octane-5-carboxylate;
 benzyl 2-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-
 2,5-diazaspiro[3.4]octane-5-carboxylate 2,2,2-trifluoroacetat;
 tert-butyl 6-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-
 2,6-diazaspiro[3.3]heptane-2-carboxylate;
 4-(6-(7-oxa-2-azaspiro[3.5]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(6-oxa-2-azaspiro[3.4]octan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(7-oxa-2-azaspiro[4.5]decan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile;
 4-(6-(2-oxa-7-azaspiro[4.4]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(3-hydroxy-3-(trifluoromethyl)pyrrolidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-
 yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(2-(4-fluorophenyl)pyrrolidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(3-phenylpyrrolidin-1-yl)pyridin-3-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-(4-chlorophenyl)piperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;
 4-(6-(4-benzylpiperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile;
 4-(6-(4-(4-chlorobenzyl)piperidin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile;
 4-(6-(2,9-diazaspiro[5.5]undecan-9-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile dihydrochloride;
 4-(6-(4-(2-aminoethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile dihydrochloride;
 4-(6-(3,9-diazaspiro[5.5]undecan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-
 a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,9-diazaspiro[5.5]undecan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(1,8-diazaspiro[4.5]decan-8-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(1,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(1,7-diazaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2-amino-7-azaspiro[3.5]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,8-diazaspiro[4.5]decan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,7-diazaspiro[4.5]decan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,7-diazaspiro[4.4]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(1,7-diazaspiro[4.4]nonan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,6-diazaspiro[3.4]octan-6-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,7-diazaspiro[3.5]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,6-diazaspiro[3.5]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,5-diazaspiro[3.5]nonan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

4-(6-(2,5-diazaspiro[3.4]octan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(7-methyl-2,7-diazaspiro[3.5]nonan-2-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(9-methyl-2,9-diazaspiro[5.5]undecan-2-yl)pyridin-3-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(2-methyl-2,9-diazaspiro[5.5]undecan-9-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(1-methyl-1,7-diazaspiro[4.5]decan-7-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2-benzyl-2,6-diazaspiro[3.4]octan-6-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(2,6-diazaspiro[3.3]heptan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(6-benzyl-2,6-diazaspiro[3.3]heptan-2-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-hydroxyethyl)-N-isopropylpiperidine-4-carboxamide 2,2,2-trifluoroacetate;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-4-yl)pyridine-2-yl)-N,N-dimethylpiperidine-4-carboxamide 2,2,2-trifluoroacetate;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(cyclopropylmethoxy)piperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-methoxypiperidine-4-carboxamide;
 N-(tert-butoxy)-1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperidine-4-carboxamide;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-hydroxyethoxy)piperidine-4-carboxamide;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(methylsulfonyl)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylpiperidine-4-sulfonamide;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridin-2-ylmethyl)piperidin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isopropylazetidine-3-carboxamide;

2-(1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)azetidin-3-yl)-N-isopropylacetamide;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperidin-4-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(1-benzylpiperidin-4-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(azetidin-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(pyrrolidin-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperidin-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(1-benzylazetidin-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(1-benzylpiperidin-3-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(1-benzylpyrrolidin-3-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(1-((tetrahydro-2H-pyran-4-yl)methyl)pyrrolidin-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-(pyridine-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-3-yl)-4-(6-(4-(pyridine-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-Butyl 4-(5-(3-cyano-6-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-

yl)pyridine-2-yl)piperazine-1-carboxylate;
 6-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-(3-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (S)-4-(6-(4-benzylpiperazin-1-yl)pyridine-3-yl)-6-(1-(3-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-butyl 3-(4-(4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-3-cyanopyrazolo[1,5-a]pyridine-6-yl)-1H-pyrazol-1-yl)azetidine-1-carboxylate;
 6-(1-(azetidin-3-yl)-1H-pyrazol-4-yl)-4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-(1-isopropylazetidin-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 1-(5-(3-cyano-6-(1,5-dimethyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-isopropylpiperidine-4-carboxamide;
 (S)-6-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 1-(5-(3-cyano-6-(1,3-dimethyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-4-ethyl-N-isopropylpiperidine-4-carboxamide;
 (S)-6-(1,3-dimethyl-1H-pyrazol-4-yl)-4-(6-(4-(3-methoxypyrrolidine-1-carbonyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(3-ethyl-1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-isopropyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-isobutyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(piperazin-1-yl)pyridin-3-yl)-6-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(tert-butyl)-3-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1,3-diethyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-ethyl-3-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(3-ethyl-1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-isopropyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-isobutyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1,3-diethyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(1-(tert-butyl)-3-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl 4-(5-(3-cyano-6-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

6-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridin-2-ylmethyl)piperazin-1-yl)pyridin-

3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 tert-butyl 4-(5-(3-cyano-6-(3-methylisoxazol-5-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;
 tert-butyl 4-(5-(3-cyano-6-(3-methyl-1H-pyrazol-5-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;
 tert-butyl 4-(5-(3-cyano-6-(1,5-dimethyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;
 6-(2-methyloxazol-5-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 6-(3-methylisoxazol-5-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile hydrochloride;
 6-(3-methyl-1H-pyrazol-5-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 6-(1,5-dimethyl-1H-pyrazol-3-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-benzylpiperazin-1-yl)pyridine-3-yl)-6-(3-methylisoxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(3-methyl-1H-pyrazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(3-methylisoxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-ethylpiperazin-1-yl)pyridine-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-ethoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-(2-isopropoxyethyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(3-methylisoxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(3-methyl-1H-pyrazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1,5-dimethyl-1H-pyrazol-3-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1,5-dimethyl-1H-pyrazol-3-yl)-4-(6-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(2-(4-benzylpiperazin-1-yl)pyrimidin-5-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

tert-butyl 4-(6-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-4-yl)pyridin-3-yl)piperazine-1-carboxylate;

6-(1-methyl-1H-pyrazol-4-yl)-4-(5-(piperazin-1-yl)pyridin-2-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(5-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-2-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-(3-methoxypyrrolidin-1-yl)(4-(5-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)methanone;

3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;

(S)-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)(3-methoxypyrrolidin-1-yl)methanone;

1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-3-methylbutan-1-one;

4-(6-(4-benzylpiperazin-1-yl)pyridine-3-yl)-3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine;

1-(4-(5-(3-chloro-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridine-2-yl)piperazin-1-yl)-3-methylbutan-2-ol;

4-(5-(3-bromo-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

tert-butyl 4-(5-(3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

3-methyl-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-

a]pyridine;

(R)-2-hydroxy-1-(4-(5-(3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-phenylethan-1-one;

4-(6-(4-benzylpiperazin-1-yl)pyridin-3-yl)-3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine;

3-methyl-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridine-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;

tert-butyl 4-(5-(3-ethyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

3-ethyl-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;

(R)-1-(4-(5-(3-ethyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxy-2-phenylethanone;

(S)-(4-(5-(3-ethyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazin-1-yl)(3-methoxypyrrolidin-1-yl)methanone;

3-cyclopropyl-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;

(S)-4-(6-(4-(2-(dimethylamino)-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

Isobutyl 4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

(R)-4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(1-(4-fluorophenyl)ethyl)piperazine-1-carboxamide;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(phenylsulfonyl)ethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-(dimethylamino)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((5-fluoro-6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((5-chloro-6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-ethoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-isopropoxy-pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((5,6-dimethoxy-pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((2,6-dimethoxy-pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-methoxy-4-methylpyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-ethoxy-5-fluoropyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-(difluoromethoxy)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-methoxy-5-methylpyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((6-(trifluoromethyl)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-methoxy-2-methylpyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-(tert-butyl)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-(2-hydroxypropan-2-yl)pyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(6-(4-((6-cyanopyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((1-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile dihydrochloride;

(S)-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-((tetrahydro-2H-pyran-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)-2-oxopiperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(2-benzyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(6-methoxynicotinoyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(5-fluoro-6-methoxynicotinoyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(3-fluoro-4-methoxybenzoyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(3-chloro-4-methoxybenzoyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(2-(5-fluoropyridin-2-yl)acetyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-((6-methoxypyridin-3-yl)methyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(6-(pyridin-2-ylmethyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(6-(2-ethoxyethyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(6-propyl-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-isopropyl-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-2-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1H-pyrazol-4-

yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-6-(1-(2-hydroxypropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

S)-6-(1-(2-hydroxypropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(2-(isopropylsulfonyl)ethyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(2-isopropoxyethyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

3-(4-(3-cyano-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridin-6-yl)-1H-pyrazol-1-yl)-N,N-dimethylpropanamide;

(R)-6-(1-(3-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-6-(1-(3-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-(2-methoxypropyl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

2-(4-(3-cyano-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridin-6-yl)-1H-pyrazol-1-yl)-N,N-dimethylacetamide;

6-(1-(azetidin-3-yl)-1H-pyrazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

tert-butyl 4-(4-(3-cyano-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridin-6-yl)-1H-pyrazol-1-yl)piperidine-1-carboxylate;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

(R)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-(1-(2-methoxyethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-6-(1-(3-hydroxy-2-methylpropyl)-5-methyl-1H-pyrazol-3-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(2-hydroxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(S)-4-(6-(4-(2-methoxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(2-methoxy-2-phenylacetyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methyloxazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(2-methyloxazol-5-yl)-4-(6-(4-(pyridin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

(R)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methylthiazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(2-methylthiazol-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

6-(2,4-dimethylthiazol-5-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-1,2,3-triazol-4-yl)-4-(6-(piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

(R)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-1,2,3-triazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

tert-butyl 4-(5-(3-cyano-6-(1-isopropyl-1H-1,2,3-triazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)piperazine-1-carboxylate;

(R)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-isopropyl-1H-1,2,3-triazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

6-(1-isopropyl-1H-1,2,3-triazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-

yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 6-(1-isopropyl-1H-1,2,3-triazol-4-yl)-4-(6-(4-(pyridin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 6-(1-isopropyl-1H-1,2,3-triazol-4-yl)-4-(6-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);
 6-(1-(2-methoxyethyl)-1H-1,2,3-triazol-4-yl)-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 (R)-4-(6-(4-(2-hydroxy-3-methylbutanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-(2-methoxyethyl)-1H-1,2,3-triazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(5-(3-cyano-6-(1-(2-methoxyethyl)-1H-1,2,3-triazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-isobutylpiperazine-1-carboxamide;
 4-(5-fluoro-6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(2-(4-(pyridin-2-ylmethyl)piperazin-1-yl)pyrimidin-5-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(4-(4-(pyridin-2-ylmethyl)piperazin-1-yl)phenyl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 6-(1-methyl-1H-pyrazol-4-yl)-4-(4-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)phenyl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 4-(4-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)phenyl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;
 3-chloro-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;
 3-chloro-4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine;
 3-methyl-6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyrimidin-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine;
 4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine;
 or a pharmaceutically acceptable salt thereof.

42. The compound of claim 41, selected from the following compounds:

((S)-4-(6-(4-(2-hydroxy-3-phenylpropanoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(2-(pyridin-2-yl)acetyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2,6-difluorobenzoyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile 2,2,2-trifluoroacetate;

4-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N,N-diethylpiperazine-1-carboxamide;

1-(5-(3-cyano-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-4-yl)pyridin-2-yl)-N-(2-methoxy-3-methylbutyl)piperidine-4-carboxamide;

4-(6-(4-(2-(5-fluoropyridin-2-yl)acetyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile bis(2,2,2-trifluoroacetate);

4-(6-(4-(2,6-difluorobenzyl)piperazin-1-yl)pyridine-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

4-(6-(4-(2-methoxybenzyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

6-(1-methyl-1H-pyrazol-4-yl)-4-(6-(4-(pyridine-2-ylmethyl)piperazin-1-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

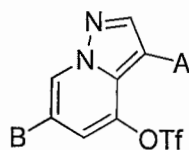
4-(6-(4-((6-methoxypyridin-3-yl)methyl)piperazin-1-yl)pyridin-3-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile;

or a pharmaceutically acceptable salt thereof.

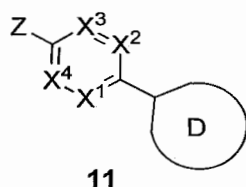
43. A pharmaceutical composition, comprising a compound according to any one of claims 1-42, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier or excipient.

44. A process for the preparation of a compound of General Formula I according to claim 1, comprising:

(a) for a compound of claim 1 where E is H and A, B, X¹, X², X³, X⁴, and D are as defined in claim 1, coupling a corresponding compound having the formula



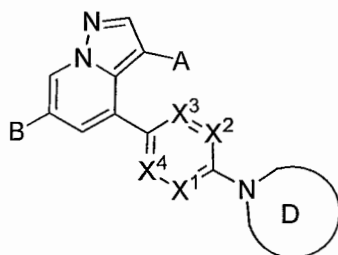
where A and B are as defined in claim 1, with a compound having the formula **11**

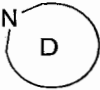


in the presence of a palladium catalyst and optionally a ligand and in the presence of a base, where Z is -B(OR^a)(OR^b) and R^a and R^b are H or (1-6C)alkyl, or R^a and R^b together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents

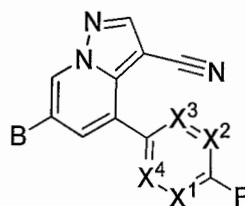
selected from (C1-C3 alkyl), the  ring is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I, and X¹, X², X³ and X⁴ are as defined for Formula B, followed by removal of a protecting group on the D ring if present; or

(b) for a compound of claim 1 where A, B, X¹, X², X³, X⁴, D and E are as defined in claim 1 with the exception that E is not hydrogen, functionalizing a corresponding compound having the formula



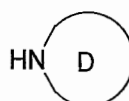
wherein the  moiety is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I, and A, B, X¹, X², X³ and X⁴ are as defined for General Formula I; or

(c) for a compound of claim 1 where A is CN, D is as defined in claim 1 provided that the D ring is coupled to the ring defined by X¹, X², X³ and X⁴ through a ring nitrogen atom in the D ring, X¹, X², X³, X⁴ are as defined for claim 1 provided that at least one of X¹ and X² is nitrogen, and E is as defined in claim 1, reacting a corresponding compound having the formula **15**



15

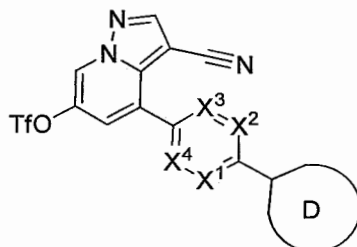
where B, X¹, X², X³ and X⁴ are as defined in claim 1 provided that at least one of X¹ and X² is nitrogen, with a corresponding compound having the formula **17**



17

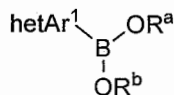
in the presence of a base, wherein the  ring is as defined for hetCyc¹, hetCyc² and hetCyc³ of Formula I; or

(d) for a compound of claim 1 where A is CN, E is H, and B, X¹, X², X³, X⁴, and D are as defined in claim 1, reacting a corresponding compound having the formula **22**



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where X¹, X², X³, X⁴ and D are as defined in claim 1, with a boronic ester having the formula



where hetAr¹ is as defined in claim 1 and R^a and R^b are H or (1-6C)alkyl, or R^a and R^b together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents selected from (C1-C3 alkyl), in the presence of a palladium catalyst and optionally a ligand and in the presence of a base; and

removing any protecting groups and optionally forming a pharmaceutically acceptable salt thereof or isolating a solvate of a free base or salt thereof.

45. Use of a compound of any one of claims 1-42 or a pharmaceutical composition according to claim 43 for the manufacture of a medicament for treating cancer.

46. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a RET-associated cancer in a subject.

47. The use of claim 46, wherein the RET-associated cancer is a cancer having a dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same.

48. The use of claim 47, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is one or more point mutations in the RET gene.

49. The use of claim 48, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 2, 3, 4, 5, 6, 7, 8, 11, 12, 13, 20, 32, 34, 40, 64, 67, 114, 136, 145, 180, 200, 292, 294, 321, 330, 338, 360, 373, 393, 432, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 633, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 802, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 882, 883, 884, 886, 891, 897, 898, 900, 901, 904, 905, 907, 908, 911, 912, 919, 919, 921, 922, 930, 961, 972, 981, 982, 1009, 1015, 1017, 1041, 1062, 1064, and 1096.

50. The use of claim 49, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 32, 34, 40, 64, 67, 114, 145, 292, 321, 330, 338, 360, 393, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 883, 884, 886, 891, 897, 898, 901,

904, 907, 908, 911, 912, 918, 919, 921, 922, 930, 961, 972, 982, 1009, 1017, 1041, and 1064.

51. The use of claim 50, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more of the following amino acid substitutions: S32L, D34S, L40P, P64L, R67H, R114H, V145G, V292M, G321R, R330Q, T338I, R360W, F393L, A510V, E511K, C515S, C531R, G533C, G533S, G550E, V591I, G593E, R600Q, I602V, K603Q, K603E, Y606C, C609Y, C609S, C609G, C609R, C609F, C609W, C611R, C611S, C611G, C611Y, C611F, C611W, C618S, C618Y, C618R, C618Y, C618G, C618F, C618W, F619F, C620S, C620W, C620R, C620G, C620L, C620Y, C620F, E623K, D624N, C630A, C630R, C630S, C630Y, C630F, D631N, D631Y, D631A, D631G, D631V, D631E, E632K, E632G, C634W, C634Y, C634S, C634R, C634F, C634G, C634L, C634A, C634T, R635G, T636P, T636M, A640G, A641S, A641T, V648I, S649L, A664D, H665Q, K666E, K666M, K666N, S686N, G691S, R694Q, M700L, V706M, V706A, E713K, G736R, G748C, A750P, S765P, P766S, P766M, E768Q, E768D, L769L, R770Q, D771N, N777S, V778I, Q781R, L790F, Y791F, V804L, V804M, V804E, E805K, Y806E, Y806F, Y806S, Y806G, Y806C, E818K, S819I, G823E, Y826M, R833C, P841L, P841P, E843D, R844W, R844Q, R844L, M848T, I852M, A866W, R873W, A876V, L881V, A883F, A883S, A883T, E884K, R886W, S891A, R897Q, D898V, E901K, S904F, S904C, K907E, K907M, R908K, G911D, R912P, R912Q, M918T, M918V, M918L, A919V, E921K, S922P, S922Y, T930M, F961L, R972G, R982C, M1009V, D1017N, V1041G, and M1064T.

52. The use of claim 48, wherein the one or more point mutations in a RET gene occur in one or more of exons 10, 11, 13, 14, 15, and 16 of a human RET gene.

53. The use of claim 47, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is a RET gene fusion.

54. The use of claim 53, wherein the RET gene fusion is selected from the group consisting of: BCR-RET, CLIP1-RET, KIF5B-RET, CCDC6-RET, NCOA4-RET, TRIM33-RET, ERC1-RET, ELKS-RET, RET-ELKS, FGFR1OP-RET, RET-MBD1, RET-RAB61P2, RET-PCM1, RET-PPKAR1A, RET-TRIM24, RET-RFG9, RFP-RET, RET-GOLGA5, HOOK3-RET, KTN1-RET,

TRIM27-RET, AKAP13-RET, FKBP15-RET, SPECC1L-RET, TBL1XR1/RET, CEP55-RET, CUX1-RET, KIAA1468-RET, PPKAR1A-RET, RFG8/RET, RET/RFG8, H4-RET, ACBD5-RET, PTCex9-RET, MYH13-RET, PIBF1-RET, KIAA1217-RET, and MPRIP-RET.

55. The use of any one of claims 46-54, wherein the RET-associated cancer is selected from the group consisting of: lung cancer, papillary thyroid cancer, medullary thyroid cancer, differentiated thyroid cancer, recurrent thyroid cancer, refractory differentiated thyroid cancer, multiple endocrine neoplasia type 2A or 2B (MEN2A or MEN2B, respectively), pheochromocytoma, parathyroid hyperplasia, breast cancer, colorectal cancer, papillary renal cell carcinoma, ganglioneuromatosis of the gastroenteric mucosa, and cervical cancer.

56. The use of claim 55, wherein the cancer is RET fusion lung cancer or medullary thyroid cancer.

57. The use of claim 55, wherein the lung cancer is small cell lung carcinoma, non-small cell lung cancer, bronchioles lung cell carcinoma, or lung adenocarcinoma.

58. The use of any one of claims 46-57, wherein the medicament is formulated for oral administration.

59. A compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for use in treating a patient identified or diagnosed as having a RET-associated cancer.

60. The compound of claim 59, wherein the RET-associated cancer is a cancer having a dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same.

61. The compound of claim 60, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is one or more point mutations in the RET gene.

62. The compound of claim 61, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 2, 3, 4, 5, 6, 7, 8, 11, 12, 13, 20, 32, 34, 40, 64, 67, 114, 136, 145, 180, 200, 292, 294, 321, 330, 338, 360, 373, 393, 432, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 633, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 802, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 882, 883, 884, 886, 891, 897, 898, 900, 901, 904, 905, 907, 908, 911, 912, 919, 919, 921, 922, 930, 961, 972, 981, 982, 1009, 1015, 1017, 1041, 1062, 1064, and 1096.

63. The compound of claim 62, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 32, 34, 40, 64, 67, 114, 145, 292, 321, 330, 338, 360, 393, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 883, 884, 886, 891, 897, 898, 901, 904, 907, 908, 911, 912, 918, 919, 921, 922, 930, 961, 972, 982, 1009, 1017, 1041, and 1064.

64. The compound of claim 63, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more of the following amino acid substitutions: S32L, D34S, L40P, P64L, R67H, R114H, V145G, V292M, G321R, R330Q, T338I, R360W, F393L, A510V, E511K, C515S, C531R, G533C, G533S, G550E, V591I, G593E, R600Q, I602V, K603Q, K603E, Y606C, C609Y, C609S, C609G, C609R, C609F, C609W, C611R, C611S, C611G, C611Y, C611F, C611W, C618S, C618Y, C618R, C618Y, C618G, C618F, C618W, F619F, C620S, C620W, C620R, C620G, C620L, C620Y, C620F, E623K, D624N, C630A, C630R, C630S, C630Y, C630F, D631N, D631Y, D631A, D631G, D631V, D631E, E632K, E632G, C634W, C634Y, C634S, C634R, C634F, C634G, C634L, C634A, C634T, R635G, T636P, T636M, A640G, A641S, A641T, V648I, S649L, A664D, H665Q, K666E,

K666M, K666N, S686N, G691S, R694Q, M700L, V706M, V706A, E713K, G736R, G748C, A750P, S765P, P766S, P766M, E768Q, E768D, L769L, R770Q, D771N, N777S, V778I, Q781R, L790F, Y791F, V804L, V804M, V804E, E805K, Y806E, Y806F, Y806S, Y806G, Y806C, E818K, S819I, G823E, Y826M, R833C, P841L, P841P, E843D, R844W, R844Q, R844L, M848T, I852M, A866W, R873W, A876V, L881V, A883F, A883S, A883T, E884K, R886W, S891A, R897Q, D898V, E901K, S904F, S904C, K907E, K907M, R908K, G911D, R912P, R912Q, M918T, M918V, M918L, A919V, E921K, S922P, S922Y, T930M, F961L, R972G, R982C, M1009V, D1017N, V1041G, and M1064T.

65. The compound of claim 61, wherein the one or more point mutations in a RET gene occur in one or more of exons 10, 11, 13, 14, 15, and 16 of a human RET gene.

66. The compound of claim 60, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is a RET gene fusion.

67. The compound of claim 66, wherein the RET gene fusion is selected from the group consisting of: BCR-RET, CLIP1-RET, KIF5B-RET, CCDC6-RET, NCOA4-RET, TRIM33-RET, ERC1-RET, ELKS-RET, RET-ELKS, FGFR1OP-RET, RET-MBD1, RET-RAB61P2, RET-PCM1, RET-PPKAR1A, RET-TRIM24, RET-RFG9, RFP-RET, RET-GOLGA5, HOOK3-RET, KTN1-RET, TRIM27-RET, AKAP13-RET, FKBP15-RET, SPECC1L-RET, TBL1XR1/RET, CEP55-RET, CUX1-RET, KIAA1468-RET, PPKAR1A-RET, RFG8/RET, RET/RFG8, H4-RET, ACBD5-RET, PTCex9-RET, MYH13-RET, PIBF1-RET, KIAA1217-RET, and MPRIP-RET.

68. The compound of any one of claims 59-67, wherein the RET-associated cancer is selected from the group consisting of: lung cancer, papillary thyroid cancer, medullary thyroid cancer, differentiated thyroid cancer, recurrent thyroid cancer, refractory differentiated thyroid cancer, multiple endocrine neoplasia type 2A or 2B (MEN2A or MEN2B, respectively), pheochromocytoma, parathyroid hyperplasia, breast cancer, colorectal cancer, papillary renal cell carcinoma, ganglioneuromatosis of the gastroenteric mucosa, and cervical cancer.

69. The compound of claim 68, wherein the cancer is RET fusion lung cancer or medullary thyroid cancer.

70. The compound of claim 68, wherein the lung cancer is small cell lung carcinoma, non-small cell lung cancer, bronchiolus lung cell carcinoma, or lung adenocarcinoma.

71. An *in vitro* method for inhibiting RET kinase activity in a mammalian cell, the method comprising contacting the mammalian cell with a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof.

72. The method of claim 71, wherein the mammalian cell is a mammalian cancer cell.

73. The method of claim 72, wherein the mammalian cancer cell is a mammalian RET-associated cancer cell.

74. The method of any one of claims 71-73, wherein the cell has dysregulation of a RET gene, a RET kinase protein, or expression or activity or level of any of the same.

75. The method of claim 74, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is one or more point mutations in the RET gene.

76. The method of claim 75, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 2, 3, 4, 5, 6, 7, 8, 11, 12, 13, 20, 32, 34, 40, 64, 67, 114, 136, 145, 180, 200, 292, 294, 321, 330, 338, 360, 373, 393, 432, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 633, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 802, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 882, 883, 884, 886, 891, 897, 898, 900, 901, 904, 905, 907, 908, 911, 912, 919, 919, 921, 922, 930, 961, 972, 981, 982, 1009, 1015, 1017, 1041, 1062,

1064, and 1096.

77. The method of claim 76, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more amino acid substitutions at one or more of the following amino acid positions: 32, 34, 40, 64, 67, 114, 145, 292, 321, 330, 338, 360, 393, 510, 511, 515, 531, 532, 533, 550, 591, 593, 600, 602, 603, 606, 609, 611, 618, 619, 620, 623, 624, 630, 631, 632, 634, 635, 636, 640, 641, 648, 649, 664, 665, 666, 686, 691, 694, 700, 706, 713, 736, 748, 750, 765, 766, 768, 769, 770, 771, 777, 778, 781, 790, 791, 804, 805, 806, 818, 819, 823, 826, 833, 841, 843, 844, 848, 852, 866, 873, 876, 881, 883, 884, 886, 891, 897, 898, 901, 904, 907, 908, 911, 912, 918, 919, 921, 922, 930, 961, 972, 982, 1009, 1017, 1041, and 1064.

78. The method of claim 77, wherein the one or more point mutations in a RET gene results in the translation of a RET protein having one or more of the following amino acid substitutions: S32L, D34S, L40P, P64L, R67H, R114H, V145G, V292M, G321R, R330Q, T338I, R360W, F393L, A510V, E511K, C515S, C531R, G533C, G533S, G550E, V591I, G593E, R600Q, I602V, K603Q, K603C, Y606C, C609Y, C609S, C609G, C609R, C609F, C609W, C611R, C611S, C611G, C611Y, C611F, C611W, C618S, C618Y, C618R, C618Y, C618G, C618F, C618W, F619F, C620S, C620W, C620R, C620G, C620L, C620Y, C620F, E623K, D624N, C630A, C630R, C630S, C630Y, C630F, D631N, D631Y, D631A, D631G, D631V, D631E, E632K, E632G, C634W, C634Y, C634S, C634R, C634F, C634G, C634L, C634A, C634T, R635G, T636P, T636M, A640G, A641S, A641T, V648I, S649L, A664D, H665Q, K666E, K666M, K666N, S686N, G691S, R694Q, M700L, V706M, V706A, E713K, G736R, G748C, A750P, S765P, P766S, P766M, E768Q, E768D, L769L, R770Q, D771N, N777S, V778I, Q781R, L790F, Y791F, V804L, V804M, V804E, E805K, Y806E, Y806F, Y806S, Y806G, Y806C, E818K, S819I, G823E, Y826M, R833C, P841L, P841P, E843D, R844W, R844Q, R844L, M848T, I852M, A866W, R873W, A876V, L881V, A883F, A883S, A883T, E884K, R886W, S891A, R897Q, D898V, E901K, S904F, S904C, K907E, K907M, R908K, G911D, R912P, R912Q, M918T, M918V, M918L, A919V, E921K, S922P, S922Y, T930M, F961L, R972G, R982C, M1009V, D1017N, V1041G, and M1064T.

79. The method of claim 75, wherein the one or more point mutations in a RET gene occur in one or more of exons 10, 11, 13, 14, 15, and 16 of a human RET gene.

80. The method of claim 74, wherein the dysregulation in a RET gene, a RET kinase protein, or expression or activity or level of any of the same is a RET gene fusion.

81. The method of claim 80, wherein the RET gene fusion is selected from the group consisting of: BCR-RET, CLIP1-RET, KIF5B-RET, CCDC6-RET, NCOA4-RET, TRIM33-RET, ERC1-RET, ELKS-RET, RET-ELKS, FGFR1OP-RET, RET-MBD1, RET-RAB61P2, RET-PCM1, RET-PPKAR1A, RET-TRIM24, RET-RFG9, RFP-RET, RET-GOLGA5, HOOK3-RET, KTN1-RET, TRIM27-RET, AKAP13-RET, FKBP15-RET, SPECC1L-RET, TBL1XR1/RET, CEP55-RET, CUX1-RET, KIAA1468-RET, PPKAR1A-RET, RFG8/RET, RET/RFG8, H4-RET, ACBD5-RET, PTCex9-RET, MYH13-RET, PIBR1-RET, KIAA1217-RET, and MPRIP-RET.

82. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating irritable bowel syndrome in a patient in need thereof.

83. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for reducing pain associated with irritable bowel syndrome in a patient in need thereof.

84. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for inhibiting metastasis of a cancer in a patient in need thereof.

85. The use of claim 96, wherein the compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof is used in combination with another chemotherapeutic agent.

86. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a subject having a cancer,

wherein (a) prior to such treating, the subject has been administered one or more doses of a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof for a period of time and (b) a determination has been made whether a cancer cell in a sample obtained from the subject following such administration has at least one RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a);
and wherein

(c) a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof is to be administered in monotherapy or in conjunction with another anticancer agent to the subject if the subject has a cancer cell that has at least one RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a),
or

(d) additional doses of the RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a) are to be administered to the subject if the subject has a cancer cell that does not have a RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a).

87. The use of claim 86, wherein the anticancer agent in (c) is another RET inhibitor.

88. The use of claim 87, wherein the anticancer agent in (c) is the same RET inhibitor administered in step (a).

89. The use of claim 86, wherein the subject is to be administered additional doses of the RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a), and the subject is to be administered another anticancer agent.

90. The use of claim 89, wherein the anticancer agent is another RET inhibitor.

91. The use of claim 89, wherein the anticancer agent is a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof.

92. Use of a compound of any one of claims 1-42 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating a subject having a cancer, wherein (a) after the subject has been administered one or more doses of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof for a period of time, (b) a determination has been made whether a cancer cell in a sample obtained from the subject has one or more RET inhibitor resistance mutations that confer increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a); and wherein

(c) a different RET inhibitor is to be administered as a monotherapy or in conjunction with another anticancer agent to a subject having a cancer cell that has one or more RET inhibitor resistance mutations that confer increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a); or

(d) additional doses of a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a) are to be administered to a subject having a cancer cell that does not have a RET inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a).

93. The use of claim 92, wherein the different RET inhibitor of (c) is a compound that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof.

94. The use of claim 92, wherein the different RET inhibitor of (c) is a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof that is different from that administered in step (a).

95. The use of claim 92, wherein the anticancer agent of (c) is a different RET inhibitor.

96. The use of claim 92, wherein the anticancer agent of (c) is a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof.

97. The use of claim 96, wherein the anticancer agent of (c) is the same compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof administered in (a).

98. The use of claim 92, wherein the subject is to be administered additional doses of the compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof of (a), and the subject is to be administered another anticancer agent.

99. The use of claim 98, wherein the anticancer agent is another RET inhibitor.

100. The use of claim 99, wherein the anticancer agent is a RET inhibitor that is not a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof.

101. The use of claim 99, wherein the anticancer agent is a compound of General Formula I or a pharmaceutically acceptable salt or solvate thereof that is different from the compound of step (a).