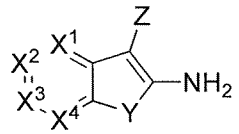
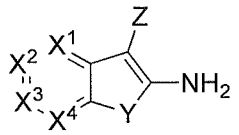
SUMMARY ~~OF THE INVENTION~~

~~In one aspect, t~~The present ~~invention~~ disclosure provides a compound of formula **(I)** or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof, wherein X^1-X^4, Y, and Z are defined herein.



(I)

Hence, in one aspect, the present disclosure provides a compound of formula **(I)**:



(I)

wherein:

X^1 is CR^1, N, or NO;

X^2 is CR^2, N, or NO;

X^3 is CR^3, N, or NO;

X^4 is CR^4, N, or NO;

Y is O, S, or NR^8;

Z is OR^5, SR^5 or NR^5R^6;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_1-C_6 alkoxy, mono or bicyclic optionally substituted C_6-C_{14} aryl, mono or bicyclic optionally substituted heteroaryl, optionally substituted (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, aminoalkyl, alkylcarboxyl, (alkyl)carboxyamido, optionally substituted (aryl)amino, hydroxyl, halogen, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl)-, optionally substituted heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted C_3-C_8 cycloalkoxy, $N(R^7)_2$, CN, NO_2, CO_2H, $CONR^AR^B$, $S(O)_nR^7$, and optionally substituted heterocyclyloxy having 1 to 2 heteroatoms selected from the group consisting of O, $S(O)_n$, and NR^7;

n is 0 to 2;

R^A and R^B are independently selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic C_3-C_8 cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl;

R^7 is H, C_1-C_6 alkyl, mono or bicyclic C_6-C_{14} aryl, mono or bicyclic heteroaryl, (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, mono or bicyclic cycloalkyl, mono or bicyclic heterocyclyl, alkylcarboxyl, heterocyclyl(alkyl), heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, aryloxy, heteroaryloxy, C_3-C_6 cycloalkoxy, or heterocyclyloxy having 1 to 2 heteroatoms selected from the group consisting of O, $S(O)_n$, and NR^A;

R^A is H, C_1-C_6 alkyl, mono or bicyclic C_6-C_{14} aryl, mono or bicyclic heteroaryl, (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, mono or bicyclic cycloalkyl, mono or bicyclic heterocyclyl, alkylcarboxyl, heterocyclyl(alkyl), heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, aryloxy, heteroaryloxy, C_3-C_6 cycloalkoxy, or optionally substituted heterocyclyloxy;

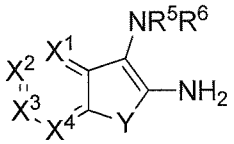
R^5 and R^6 are independently selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl; and

R^8 is H or optionally substituted C_1-C_6 alkyl;

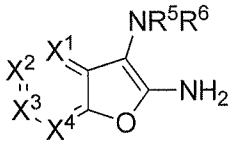
or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof;

wherein thieno[2,3-b]pyrimidine-2,3-diamine HCl salt is excluded.

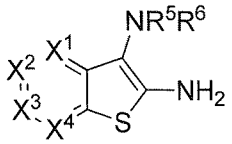
~~In another aspect, c~~Compounds of formulae **(I-A)**, **(I-AA)**, **(I-AAA)**, **(I-B)**, **(I-BB)**, **(I-BBB)**, **(I-BBBB)**, **(I-BBBBB)**, **(I-BBBBBB)**, **(I-C)**, **(I-CC)**, **(I-D)**, **(I-DD)**, **(I-E)**, **(I-EE)**, **(I-F)**, **(I-FF)**, **(I-G)** and **(I-GG)** are also provided, wherein X^1-X^4, R^1, R^2, R^3, R^4, R^5 and R^6 are defined herein.



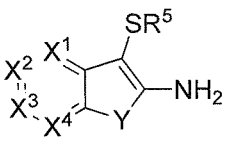
(I-A)



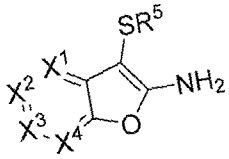
(I-AA)



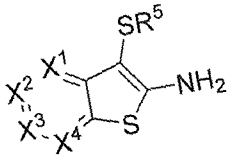
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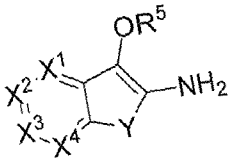
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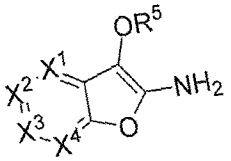
(I-BB)



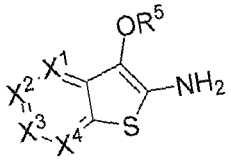
(I-BBB)



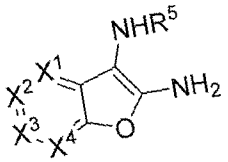
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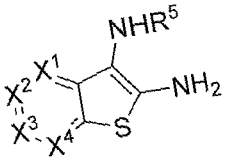
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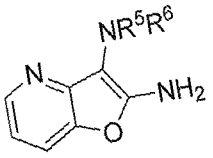
(I-BBBBBB)



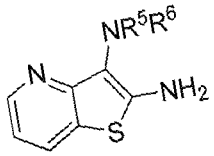
(I-C)



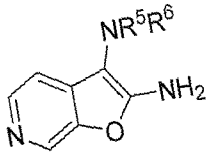
(I-CC)



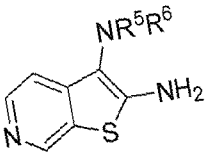
(I-D)



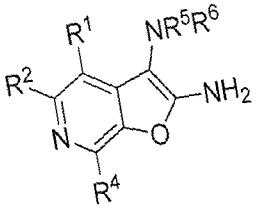
(I-DD)



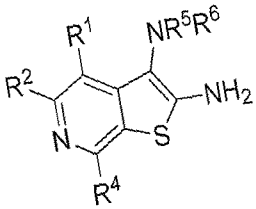
(I-E)



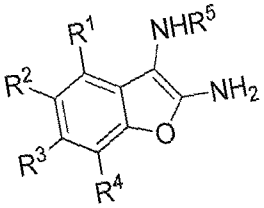
(I-EE)



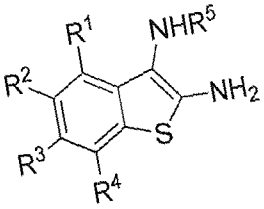
(I-F)



(I-FF)

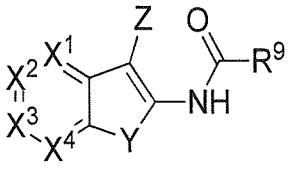


(I-G)

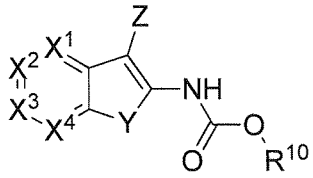


(I-GG)

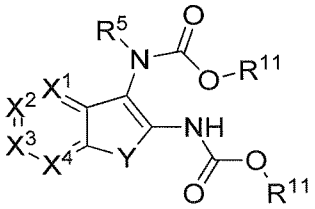
~~In another aspect, t~~The ~~invention~~ disclosure also relates to prodrugs of compounds of formula (**I**) having a formula (**II**), (**III**) or (**IV**) are provided, wherein R^9-R^{11} are defined herein



(**II**)

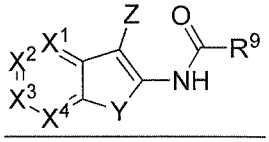


(**III**)



(**IV**)

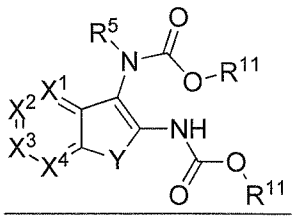
In another aspect, the disclosure relates to a prodrug of a compound as defined herein, wherein the prodrug is an acylated compound which has a formula (**II**):



(**II**)

wherein R^9 is optionally-substituted C_1-C_6 alkyl.

In another aspect, the disclosure relates to a prodrug of a compound as defined herein, wherein the prodrug is a dicarbamate compound which has a formula (**IV**):



(**IV**)

wherein R^{11} is optionally-substituted C_1-C_6 alkyl, aryl, (aryl)alkyl, heteroaryl, or (heteroaryl)alkyl.

~~In one aspect, t~~The disclosure also ~~invention~~ relates to a metabolite of a compound of formula (**I**) – (**IV**) or a prodrug of said compound of formula (**I**), or a pharmaceutically acceptable salt or a prodrug thereof.

The disclosure also relates to ~~In a further aspect,~~ a composition comprising a compound or prodrug thereof as described herein and a pharmaceutically acceptable carrier is provided.

The disclosure also relates to ~~In another aspect,~~ a composition comprising a metabolite of a compound of formula (**I**) – (**IV**) or prodrug thereof as described herein and a pharmaceutically acceptable carrier is provided~~,~~. In another aspect, the present disclosure relates to a composition comprising a compound as defined herein and a pharmaceutically acceptable carrier.

The disclosure also relates to ~~In yet another aspect,~~ a kit comprising a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein is provided.

The disclosure also relates to ~~In another aspect,~~ a method for treating a disease treatable by inhibiting a kynurenine pathway ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof to a subject in need thereof. The disclosure also relates to ~~In another aspect,~~ a method for regulating a kynurenine pathway ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In another aspect,~~ a method of regulating one or more of a indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof. In another ~~aspect~~embodiment, the regulating is inhibiting the kynurenine pathway or one or more of the enzymes.

The disclosure also relates to ~~In still a further aspect,~~ a method of regulating the kynurenine pathway by inhibiting indoleamine 2,3-dioxygenase-1 and/or indoleamine 2,3-dioxygenase-2 and/or tryptophan 2,3-dioxygenase ~~is provided~~ and includes administering a compound or a metabolite thereof, or or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In one aspect,~~ a method of reducing kynurenine pathway metabolites ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to~~In another aspect,~~ a method of altering tryptophan levels in a subject and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein ~~is provided~~. In one ~~aspect~~embodiment, the tryptophan levels are increased. In another ~~aspect~~embodiment, kynurenine/tryptophan ratio is decreased.

The disclosure also relates to ~~In one aspect,~~ a method of treating a disease associated with or resulting from dysregulation of a kynurenine pathway ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In another aspect,~~ a method for treating a disease caused by the dysregulation of the kynurenine pathway by inhibiting indoleamine 2,3-dioxygenase-1 and/or indoleamine 2,3-dioxygenase-2 and/or tryptophan 2,3-dioxygenase ~~is provided~~ and includes administering a compound or a pharmaceutically acceptable salt or prodrug thereof described herein to a subject in need thereof.

The disclosure also relates to ~~In yet another aspect,~~ a method for treating a disease caused by activation of indoleamine 2,3-dioxygenase-1 or tryptophan 2,3-dioxygenase or both enzymes ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof. The disclosure also relates to ~~In yet another aspect,~~ a method for treating a disease caused by activation of indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes or both ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In yet another aspect,~~ a method for treating a disease caused by activation of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or both ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In another aspect,~~ a method of inhbiting activation of one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In another aspect,~~ a method for treating a disease associated with one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes ~~is provided~~ and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a subject in need thereof.

The disclosure also relates to ~~In yet a further aspect,~~ a method ~~is provided~~ for treating a disease characterized by abnormal immune suppression resulting from dysregulation of a kynurenine pathway and includes administering a compound of formula (**I**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a subject in need thereof.

The disclosure also relates to ~~In a further aspect,~~ a method for regulating a disease characterized by abnormal immune suppression resulting from a dysregulated kynurenine due to activation any one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzyme ~~is provided~~ and includes administering a compound, a metabolite thereof or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof.

The disclosure also relates to ~~In one aspect,~~ a method of treating immune suppression ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof as described herein to a subject in need thereof. In another ~~aspect~~embodiment, the immune suppression is associated with increased kynurenine metabolite levels or enzymatic activity of one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes. The disclosure also relates to ~~In yet another aspect,~~ a method ~~is provided~~ for treating immune suppression associated with one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof to a subject in need thereof. Thus, the disclosure also relates to ~~in an aspect,~~ compounds of the ~~invention~~ disclosure for use in treatment of immunosuppression associated with one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes ~~are provided~~.

The disclosure also relates to ~~In yet another aspect,~~ a method for treating immune suppression through inhibiting enzymatic activity of indoleamine 2,3-dioxygenase and/or tryptophan 2,3-dioxygenase ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a subject in need thereof.

The disclosure also relates to ~~In yet another aspect,~~ a method of reducing or eliminating an immune mediated disorder ~~is provided~~ and includes administering a compound of formula (**I**) – (**IV**) or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a patient.

The disclosure also relates to ~~In yet another aspect,~~ a method of inhibiting an autoimmune reaction or autoimmune antibody production in a subject ~~is provided~~ and includes administering a compound or a metabolite thereof, or a pharmcetucially acceptable salt or prodrug thereof as described to a subject in need thereof. The disclosure also relates to ~~In another aspect,~~ a method of inhibiting autoimmune reaction or autoimmune antibody production is inhibited by (i) inhibiting indoleamine 2,3-dioxygenase-2 or (ii) reducing kynurenine metabolites, and includes administering a compound or a metabolite thereof, or a pharmcetucially acceptable salt or prodrug thereof as described to a subject in need thereof. In one ~~aspect~~embodiment, the foregoing reduction in autoimmune reaction or autoimmune antibody production is associated with inflammatory diseases, cancer or autoimmine disorders.

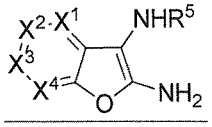
In one ~~aspect~~embodiment, the list of diseases comprise cancer, bacterial infection, viral infection, parasitic infection, immune-mediated disorder, autoimmune disorder, inflammatory disease, central nervous system disease, peripheral nervous system disease, neurodegenerative disease, mood disorder, sleep disorder, cerebrovascular disease, peripheral artery disease, or cardiovascular disease. In another ~~aspect~~embodiment, all foregoing methods comprise administration of one or more therapeutic agent or therapy. In one embodiment~~aspect~~, the therapeutic agent is a chemotherapeutic agent selected from a group further comprising a cancer vaccine, a targeted drug, a targeted antibody, an antibody fragment, an antimetabolite, an antineoplastic, an antifolate, a toxin, an alkylating agent, a DNA strand breaking agent, a DNA minor groove binding agent, a pyrimidine analog, a purine analog, a ribonucleotide reductase inhibitor, a tubulin interactive agent, an anti-hormonal agent, an immunomoldulator, an anti-adrenal agent, a cytokine, a radiation therapy, a cell therapy, or a hormone therapy.

The disclosure also relates to ~~In another aspect,~~ a method of treating depression, Alzheimer's disease, dementia, schizophrenia, HIV inection, malaria, rheumatoid arthritis, insomnia or multiple sclierosis ~~is provided~~ and include administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a patient.

In one ~~aspect~~embodiment, the disease is cancer. In another ~~aspect~~embodiment, cancer disease is a cancer of squamous cell, peritoneum, prostate, head, neck, eye, mouth, throat, esophagus, bronchus, larynx, pharynx, thyroid cancer, chest, bone, lungs, colon, rectum, stomach, urinary bladder, gall bladder, uterus, cervix, breast, ovaries, uterus, vagina, vulva, testicles, penis, anus, skin, thyroid, blood, lymph nodes, kidney, liver, intestines, salivary gland, pancreas, brain, spine, adrenal gland, skin or leukemia. The disclosure also relates to ~~In another aspect,~~ a method of treating tumor resistance ~~is provided~~ comprising administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a patient.

In another ~~aspect~~embodiment, the viral infection is HIV infection. In another ~~aspect~~embodiment, parasite infection is malaria or Leishmaniasis.

The disclosure also relates to ~~In another aspect,~~ a method of preparing a compound of formula (**I-C**) ~~is provided~~ as described herein. In another aspect, the present disclosure relates to a method of preparing a compound of formula (**I-C**), said method comprising:



(**I-C**)

wherein:

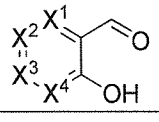
X^1 is CR^1, N, or NO;

X^2 is CR^2, N, or NO;

X^3 is CR^3, N, or NO;

X^4 is CR^4, N, or NO; and

R^5 is selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl;

(i) reacting  with an an amine (R^5-NH_2);

(ii) reacting the product of step (i) with a cyanide salt; and

(iii) reacting the product of step (ii) with a Lewis acid.

In another aspect, the present disclosure relates to a compounds obtainable by the method of preparing a compound of formula (**I-C**) ~~are provided~~.

The disclosure also relates to ~~In yet another aspect,~~ a method for diagnosing and treating a disease associated with kynurenine pathway or one or more of indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a subject ~~is provided~~ and includes: (i) assaying a blood and/or tissue sample from a subject; (ii) determining the subject's blood and/or tissue tryptophan or Kynurenine concentration or both in the sample; (iii) optionally determining the subject's Kynurnine/tryptophan ratio; and (iv) administering a compound or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof described herein to a subject.

The disclosure also relates to ~~In still another aspect,~~ a method of monitoring a disease associated with kynurenine pathway or one or more of indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a subject ~~is provided~~ and includes (i) dosing a subject having a disease associated with kynurenine pathway with a compound, (ii) analyzing a blood or tissue samples or both at one or more time points or continuously during a treatment regimen, (iii) determining a tryptophan and a kynurenine concentration in the blood or the tissue sample or both, (iv) optionally determining the subject's kynurnine/tryptophan ratio, and (v) adjusting the treatment regimen or dosage of the compound.

The disclosure also relates to ~~In a further aspect,~~ a method for diagnosing and treating a disease associated with kynurenine pathway or one or more of indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a patient ~~is provided~~ and includes (i) analyzing a patient sample for the presence or absence of altered kynurenin/tryptophan ratio, wherein the patient is diagnosed with a disease associated with kynurenine pathway if altered kynurenine/tryptophan ratio is detected and (ii) administering a compound to the diagnosed patient.

The disclosure also relates to ~~In still a further aspect,~~ a method for treating a disease associated with kynurenine pathway or one or more of an indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzyme in a patient and includes (i) requesting a test providing the results of an analysis to determine whether the patient's kynurnine levels are altered, and (ii) administering a compound to the patient if the patient's kynurenine levels are altered.

The disclosure also relates to ~~In yet another aspect,~~ a use of foregoing methods ~~is provided~~ wherein the disease is cancer, bacterial infection, viral infection, parasitic infection, immune-mediated disorder, autoimmune

disorder, inflammatory disease, central nervous system disease, peripheral nervous system disease, neurodegenerative disease, mood disorder, sleep disorder, cerebrovascular disease, peripheral artery disease, or cardiovascular disease.

Other aspects and advantages of the ~~invention~~ disclosure will be readily apparent from the following detailed description ~~of the invention~~.

heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl;

R^7 is H, C_1-C_6 alkyl, mono or bicyclic C_6-C_{14} aryl, mono or bicyclic heteroaryl, (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, mono or bicyclic cycloalkyl, mono or bicyclic heterocyclyl, alkylcarboxyl, heterocyclyl(alkyl), heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, aryloxy, heteroaryloxy, C_3-C_6 cycloalkoxy, or heterocyclyloxy having 1 to 2 heteroatoms selected from the group consisting of O, $S(O)_n$, and NR^A;

R^A is H, C_1-C_6 alkyl, mono or bicyclic C_6-C_{14} aryl, mono or bicyclic heteroaryl, (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, mono or bicyclic cycloalkyl, mono or bicyclic heterocyclyl, alkylcarboxyl, heterocyclyl(alkyl), heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, aryloxy, heteroaryloxy, C_3-C_6 cycloalkoxy, or optionally substituted heterocyclyloxy;

R^5 and R^6 are independently selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl; and

R^8 is H or optionally substituted C_1-C_6 alkyl;

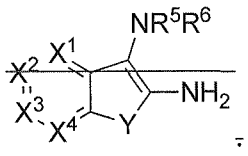
or a metabolite thereof, or a pharmaceutically acceptable salt or prodrug thereof; wherein thieno[2,3-b]pyrimidine-2,3-diamine HCl salt is excluded.

2. The compound according to claim 1, wherein one or two of X^1, X^2, X^3 and X^4 is N.

3. The compound according to claim 1, wherein X^1 is CR^1, X^2 is CR^2, X^3 is CR^3, and X^4 is CR^4.

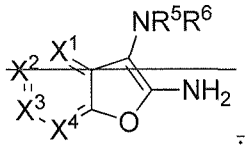
~~4. The compound according to claim 1, wherein X^3 is NO.~~

~~5. The compound according to claim 1 having formula (I-A):~~



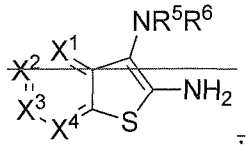
~~(I-A).~~

~~6. The compound according to claim 1 having formula (I-AA):~~



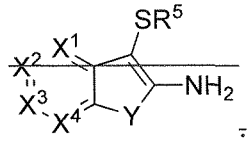
~~(I-AA).~~

~~7. The compound according to claim 1 having formula (I-AAA):~~



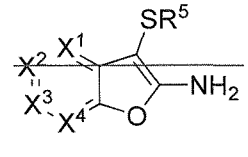
~~(I-AAA).~~

~~8. The compound according to claim 1, having formula (I-B):~~



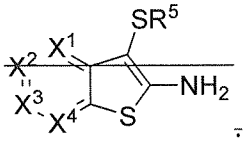
~~(I-B).~~

~~9. The compound according to claim 1, having formula (I-BB):~~



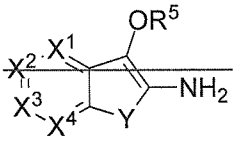
~~(I-BB).~~

~~10. The compound according to claim 1, having formula (I-BBB):~~



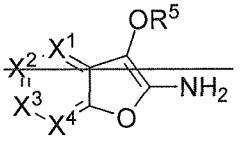
~~(I-BBB).~~

~~11. The compound according to claim 1 having formula (I-BBBB):~~



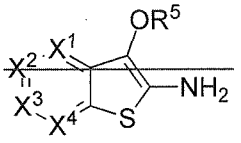
~~(I-BBBB).~~

~~12. The compound according to claim 1 having formula (I-BBBBB):~~



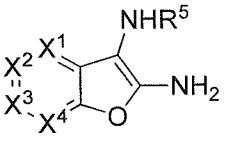
~~(I-BBBBB).~~

~~13. The compound according to claim 1 having formula (I-BBBBBB):~~



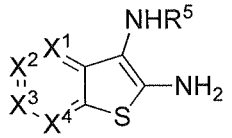
~~(I-BBBBBB).~~

~~14~~. The compound according to claim 1, having formula (**I-C**):



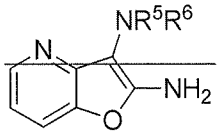
(**I-C**).

~~15~~. The compound according to claim 1 having formula (**I-CC**):



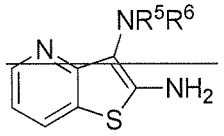
(**I-CC**).

~~16. The compound according to claim 1 having formula (I-D):~~



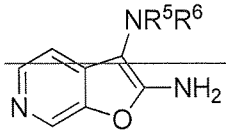
~~(I-D).~~

~~17. The compound according to claim 1 having formula (I-DD):~~



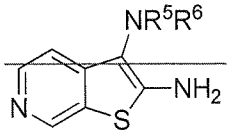
~~(I-DD).~~

~~18. The compound according to claim 1 having formula (I-E):~~



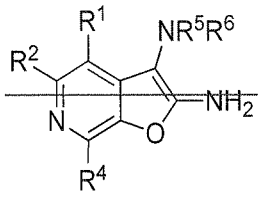
~~(I-E).~~

~~19. The compound according to claim 1 having formula (I-EE):~~



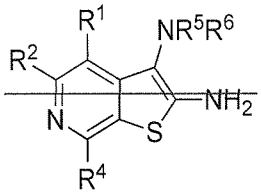
~~(I-EE).~~

~~20. The compound according to claim 1 having formula (I-F):~~



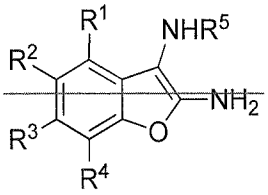
~~(I-F).~~

~~21. The compound according to claim 1 having formula (I-FF):~~



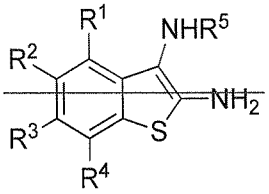
~~(I-FF).~~

~~22. The compound according to claim 1 having formula (I-G):~~



~~(I-G).~~

~~23. The compound according to claim 1 having formula (I-GG):~~



~~(I-GG).~~

~~24~~6. The compound according to claim 1, wherein R^1 is H, halogen, CN, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, or C_1-C_6 alkyl.

~~25. The compound according to claim 23, wherein R^1 is H or CN.~~

~~26~~7. The compound according to claim 1, wherein R^2 is H, halogen, hydroxyl, CN, $N(R^7)_2$, mono or bicyclic optionally substituted C_6-C_{14} aryl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_1-C_6 alkyl, or optionally substituted aryloxy.

~~27. The compound according to claim 26, wherein R^2 is H or optionally substituted C_1-C_6 alkyl.~~

~~28. The compound according to claim 26, wherein R^2 is halogen.~~

~~29. The compound according to 28, wherein R^2 is Cl, F, Br or I.~~

~~30. The compound according to claim 26, wherein R^2 is optionally substituted C_1-C_6 alkoxy or optionally substituted aryloxy.~~

~~31~~8. The compound according to claim 26 wherein R^2 is $N(R^7)_2$ or mono or bicyclic optionally substituted $C_6 - C_{14}$ aryl.

~~32~~9. The compound according to claim 1, wherein R^3 is H, halogen, NO_2, or CN.

~~33. The compound according to claim 1, wherein R^3 is H.~~

~~34~~10. The compound according to claim 1, wherein R^4 is:
H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C1-C6 alkoxy, mono or bicyclic optionally substituted C_6-C_{14} aryl, CH_2-aryl, mono or bicyclic optionally substituted heteroaryl, optionally substituted (aryl)alkyl, (alkoxy)carbonyl, (alkyl)amido, (alkyl)amino, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, aminoalkyl, alkylcarboxyl, (alkyl)carboxyamido, optionally substituted (aryl)amino, hydroxyl, halogen, C1-C6 haloalkyl, optionally substituted heterocyclyl(alkyl)-, optionally substituted heteroaryl(alkyl), hydroxyalkyl, perfluoroalkyl, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted C_3-C_8 cycloalkoxy,

$N(R^7)_2$, CN, NO_2, CO2H, $CONR^AR^B$, $S(O)nR^7$, and optionally substituted heterocyclyloxy having 1 to 2 heteroatoms selected from the group consisting of O, S(O)n, and NR^7, and n is 0 to 2.

~~35~~11. The compound according to claim ~~34~~10, wherein R^4 is H, halogen, or CN.

~~36. The compound according to claim 35, wherein R^4 is Cl, F, Br or I.~~

~~37. The compound according to claim 34, wherein R^4 is optionally substituted alkyl, optionally substituted cycloalkyl, or optionally substituted arylalkyl.~~

~~38. The compound according to claim 34, wherein R^4 is optionally substituted arylalkenyl, or optionally substituted arylalkynyl.~~

~~39. The compound according to claim 34, wherein R^4 is $N(R^7)_2$.~~

~~40~~12. The compound according to claim ~~39~~10, wherein R^4 is optionally substituted diarylamine or optionally substituted diphenylamine.

~~41. The compound according to claim 34, wherein R^4 is optionally substituted aryl, optionally substituted bicylic aryl, heteroaryl, optionally substituted heteroaryl, or bicyclic heteroaryl,~~

~~42. The compound according to claim 34, wherein R^4 is optionally substituted heterocyclyl.~~

~~43~~13. The compound according to claim ~~41~~10, wherein R^4 is optionally substituted pyridine, optionally substituted picolyl, or optionally substituted picolinamide.

~~44~~14. The compound according to claim ~~34 or 41~~10, wherein R^4 is optionally substituted phenyl.

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4515. The compound according to claim 4414, wherein R^4 is phenyl substituted with one or more C_1-C_6 alkoxy or halogen.

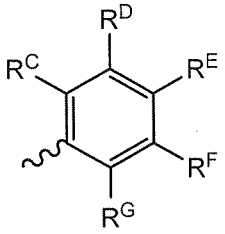
4616. The compound according to claim 3410, wherein R^4 is optionally substituted pyridine.

~~47. The compound according to claim 34, wherein R^4 is optionally substituted (alkyl)carboxyamido, (aryl)carboxyamido, (alkyl)amido, alkylcarboxyl, (alkoxy)carbonyl, COOH, C1-C6 cyclyloxy, heterocyclyloxy, aryloxy, heteroaryloxy, perfluoroalkyl, $S(O)_nN(R^7)_2$, or pyrimidine.~~

4817. The compound according to claim 1, wherein R^5 or R^6 is H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, or perfluoroalkyl.

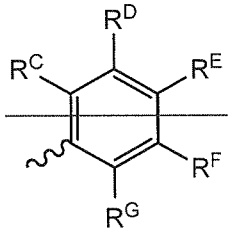
~~49. The compound according to claim 1, wherein R^5 or R^6 is optionally substituted phenyl.~~

5018. The compound according to claim 491, wherein R^5 or R^6 is:



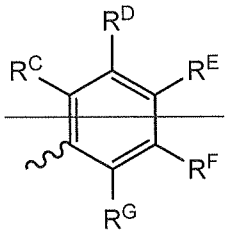
wherein, R^C to R^G are independently selected from the group consisting of H, halogen, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, heterocycle, optionally substituted C_1-C_6 alkyl, C_3-C_8 cycloalkyl, CN, -O(aryl), C_2-C_6 alkynyl, C(O)C_1-C_6 alkyl, -O-C_1-C_6 haloalkyl, and optionally substituted aryl.

~~51. The compound according to claim 49, wherein R^5 or R^6 is:~~



~~wherein, R^C to R^G are independently selected from the group consisting of H, halogen, CHF_2, $C(CH_3)F_2$, OCF_3, OCH_3, $OCH(CH_3)_2$, morpholine, piperidine, CH_3, $C(CH_3)_3$, CH_2CH_3, $CH(CH_3)_2$, cyclopropyl, cyclohexyl, CH_2-cyclopropyl, CH_2-cyclobutyl, benzyl, CN, phenoxy, ethynyl, $C(O)CH_3$, and phenyl.~~

~~52. The compound according to claim 49, wherein R^5 or R^6 is:~~



~~wherein, R^C to R^G are independently selected from the group consisting of H and optionally substituted aryl.~~

~~53. The compound according to claim 52, wherein R^C to R^G are independently selected from the group consisting of H and aryl substituted with one or more of halogen.~~

~~54. The compound according to claim 53, wherein R^C to R^G are independently selected from the group consisting of H and aryl substituted with one or more Cl or F.~~

~~55~~19. The compound according to claim ~~49~~1, wherein R^5 or R^6 is phenyl, 2-Br-4-F-phenyl, 2,3,4-tri-Cl-phenyl, 2,3-di-Cl-4-F-phenyl, 2,4-di-Cl-phenyl, 2-Cl-4-F-phenyl, 2-Cl-phenyl, 2-Et-phenyl, 2,4-di-F-3-Cl-phenyl, 2-F-3-CN-phenyl, 2,4-di-F-phenyl, 2-tetralin, 2,3-di-Me-phenyl, 2-Me-4-Br-phenyl, 2,4-di-Me-phenyl, 2,4-di-OMe-phenyl, 2-piperidine-phenyl, 3-Br-4,5-di-F-phenyl, 3-Br-4-F-phenyl, 3-Br-4-Me-phenyl, 3-Br-phenyl, 3-acetylene-4-F-phenyl, 3-acetylene-phenyl, 3-CF2Me-4-F-phenyl, 3-CF3-4-Br-phenyl, 3-CF3-4-Cl-phenyl, 3-CF3-4-F-phenyl, 3-CF3-phenyl, 3-CH2-cyclobutyl-phenyl, 3-CH2-cyclopropyl-phenyl, 3-CH2Ph-phenyl, 3-CHF2-phenyl, 3,4-di-Cl-phenyl, 3,5-di-Cl-4-F-phenyl, 3-Cl-4,6-di-F-phenyl, 3-Cl-4-F-phenyl, 3-Cl-4-I-phenyl, 3-Cl-4-Me-phenyl, 3-Cl-5-Me-phenyl, 3,6-di-Cl-phenyl, 3-Cl-6-F-phenyl, 3-Cl-6-OMe-phenyl, 3-Cl-phenyl, 3-CN-phenyl, 3-cyclohexyl-phenyl, 3-cyclopropyl-phenyl, 3-Et-phenyl, 3,4,6-tri-F-phenyl, 3,4-di-F-phenyl, 3,5-di-F-phenyl, 3-F-phenyl, 3-tetralin, 3-I-phenyl, 3-iPr-phenyl, 3-Me-4-Cl-phenyl, 3-Me-4-F-phenyl, 3,4-di-Me-phenyl, 3,5-di-Me-phenyl, 3-Me-phenyl, 3-OCF3-4-F-phenyl, benzo[d]dioxolane, 3-OiPr-

phenyl, 3-OMe-4-Cl-phenyl, 3,5-di-OMe-phenyl, 3-OMe-phenyl, 3-Ph-phenyl, 3-chloropyridyl, 3-pyridyl, 3,5-di-tBu-phenyl, 3-tBu-phenyl, 4-Br-phenyl, 4-acetylene-phenyl, 4-CF3-phenyl, 4-CH2Ph-phenyl, 4-Cl-phenyl, 4-CN-phenyl, 4-COMe-phenyl, 4-F-phenyl, 4-Me-phenyl, 4-morpholine-phenyl, 4-OCF3-phenyl, 4-OPh-phenyl, or 5-Cl-6-F-phenyl.

~~56. The compound according to claim 1, wherein R^5 or R^6 is optionally substituted heteroaryl.~~

~~57. The compound according to claim 56, wherein R^5 or R^6 is pyridine optionally substituted with one or more halogen.~~

~~58. The compound according to claim 57, wherein each halogen is independently selected from a group of F, Cl, Br and I.~~

~~59. The compound according to claim 58, wherein the halogen is Cl or F.~~

~~60. The compound according to claim 56, wherein R^5 or R^6 is benzo[d]dioxolane.~~

~~61. The compound according to claim 56, wherein R^5 or R^6 is tetrahydronaphthalene.~~

~~62. The compound according to claim 56, wherein R^5 or R^6 is pyrrolyl, indolyl, pyrimidinyl, alkyl, benzyl, cycloalkylyl, heterocycloalkylyl, or heterocycloalkylylalkyl.~~

~~63~~20. The compound according to claim 1, which is selected from the group consisting of:

N^3-(3-Chloro-4-fluorophenyl)furo[3,2-b]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-Phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(2-Chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-(Trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,4-Dichlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Chloro-3-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2-Bromo-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(4-Morpholinophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2,4,5-Trifluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2,4,5-Trifluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3,4-Dimethylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3,5-Dimethylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3,4-Dichlorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(4-Bromophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(4-Chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-iodophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Ethylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Iodophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Bromo-4-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Bromo-4,5-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(4-Benzylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2-(Piperidin-1-yl)phenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(5-Chloro-2-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-(Trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(4-Fluoro-3-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,
3-((2-Aminofuro[2,3-c]pyridin-3-yl)amino)-2-fluorobenzonitrile,
N^3-(4-Phenoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2-Chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2,3,4-Trichlorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3,5-Di-*tert*-butylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(2,4-Dimethoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(Benzo[d][1,3]dioxol-5-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Ethynylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,5-Dimethoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

4-((2-Aminofuro[2,3-c]pyridin-3-yl)amino)benzonitrile,

N^3-(*p*-tolyl)Furo[2,3-c]pyridine-2,3-diamine,

1-(4-((2-Aminofuro[2,3-c]pyridin-3-yl)amino)phenyl)ethanone,

N^3-(3-Cyclopropylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Isopropylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-2,4-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,3-Dichloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,5-Dichloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(*m*-tolyl)Furo[2,3-c]pyridine-2,3-diamine,

N^3-(Pyridin-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-(Trifluoromethoxy)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5-Chloro-2,4-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5-Chloropyridin-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-([1,1'-Biphenyl]-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,4-Dimethylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,5-Dichlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

(2-Amino-3-((3-chloro-4-fluorophenyl)amino)-7-methylfuro[2,3-c]pyridin-4-yl)methanol,

4-Chloro-N^3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Bromo-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluoro-3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-(*tert*-Butyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluoro-3-(trifluoromethoxy)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5,6,7,8-Tetrahydronaphthalen-1-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-methoxyfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-(Difluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-methylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-4-methoxyfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Ethynylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-(1,1-Difluoroethyl)-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Chloro-3-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5,6,7,8-Tetrahydronaphthalen-2-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-4,7-dimethylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-ethylfuro[2,3-c]pyridine-2,3-diamine,

7-Ethyl-N^3-(4-fluoro-3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Benzylphenyl)furo[2,3-c]pyridine-2,3-diamine,

7-Ethyl-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-propylfuro[2,3-c]pyridine-2,3-diamine,

7-Propyl-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluoro-3-(trifluoromethyl)phenyl)-7-propylfuro[2,3-c]pyridine-2,3-diamine,

7-Methyl-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

7-Phenyl-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-isopropylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-(Cyclopropylmethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-methoxy-7-methylfuro[2,3-c]pyridine-2,3-diamine,

7-Benzyl-N^3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-5-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Cyclohexylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-(Cyclobutylmethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(3-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(4-chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Ethynylphenyl)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-ethynylphenyl)-7-methylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(pyridin-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

7-Ethyl-N^3-(3-ethynylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

3-((2-Aminofuro[2,3-c]pyridin-3-yl)amino)benzonitrile,

N^3-(3-Chloro-4-fluorophenyl)-7-(3-chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(4-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

5-Butoxy-N^3-(3-chloro-4-fluorophenyl)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridine-7-carbonitrile,

N^3-(3-Chloro-4-fluorophenyl)-5-phenoxy-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-ethoxy-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

5-(*tert*-Butoxy)-N^3-(3-chloro-4-fluorophenyl)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-isopropoxy-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-cyclohexylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-ethyl-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Ethynyl-4-fluorophenyl)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Ethynyl-4-fluorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)benzofuran-6-carbonitrile,

2-Amino-3-((3-(trifluoromethyl)phenyl)amino)benzofuran-6-carbonitrile,

2-Amino-3-(m-tolylamino)benzofuran-6-carbonitrile,

2-Amino-3-((3-bromophenyl)amino)benzofuran-6-carbonitrile,

2-Amino-3-((2-chlorophenyl)amino)benzofuran-6-carbonitrile,

N^3-(3-Chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine,

N^3-Phenylbenzo[b]thiophene-2,3-diamine,

N^3-(3-(Trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Fluorophenyl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)thieno[2,3-c]pyridine-2,3-diamine,

3-((3-Chlorophenyl)thio)benzo[b]thiophen-2-amine,

5-Bromo-N^3-(3-chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine,

N^3-(4-Chloro-3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine,

3-((3-Chlorophenyl)thio)benzo[b]thiophen-2-amine hydrochloride,

N^3-(4-Bromo-3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine,

3-(3-Chlorophenoxy)benzo[b]thiophen-2-amine hydrochloride,

N^3-(4-Fluoro-3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine,

5-Chloro-N^3-(3-chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine hydrochloride,

5-Chloro-N^3-phenylbenzo[b]thiophene-2,3-diamine,

5-Chloro-N^3-(4-fluorophenyl)benzo[b]thiophene-2,3-diamine,

5-Chloro-N^3-(4-fluoro-3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine,

5-Chloro-N^3-(3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine hydrochloride,

N^3-(3-Chloro-4-fluorophenyl)-5-phenylbenzo[b]thiophene-2,3-diamine,

N^3-Methyl-N^3-phenylbenzo[b]thiophene-2,3-diamine hydrochloride,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)benzo[b]thiophene-6-carbonitrile,

N^3-(3-Ethynylphenyl)-1-benzothiophene-2,3-diamine,

N^3-(2,3-Dimethylphenyl)-1-benzothiophene-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(pyridin-2-yl)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)-7-(pyridine-2-yl)furo[2,3-c]pyridine-5-carbonitrile,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)-7-phenylfuro[2,3-c]pyridine-5-carbonitrile,

N^3-(3-Methoxy-5-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^7-(3-Chloro-4-fluorophenyl)furo[3,2-d]pyrimidine-6,7-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridine-7-carboxylic acid,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridine-7-carboxamide,

N^3-(3-Chloro-4-fluorophenyl)-N5,N5-dimethyl-7-phenylfuro[2,3-c]pyridine-2,3,5-triamine,

N^3-(3-Cyclobutylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Cyclopentylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(trifluoromethyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-1H-pyrrolo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-phenoxyfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(pyridine-2-yloxy)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-N^7-phenylfuro[2,3-c]pyridine-2,3,7-triamine,

N^3-(3-Chloro-4-fluorophenyl)-N^7-(pyridine-3-yl)furo[2,3-c]pyridine-2,3,7-triamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(phenylethynyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-(2-(dimethylamino)ethoxy)-7-(pyridine-2-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-(3-dimethylamino)ethoxy)-7-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(1-methyl-1H-pyrazol-5-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(piperidin-1-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(4-methylpiperazin-1-yl)furo[2,3-c]pyridine-2,3-diamine,
2-Amino-3-((3-chloro-4-fluorophenyl)amino)-N-phenylfuro[2,3-c]pyridine-7-carboxamide,
N^3-(3-Chloro-4-fluorophenyl)-7-(4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-(1-methyl-1H-pyrazol-4-yl)furo[2,3-c]pyridine-2,3-diamine,
4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)benzonitrile,
4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)benzamide,
Methyl 4-(2-amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)benzoate,
N^3-(3-Chloro-4-fluorophenyl)-7-iodofuro[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-(2-morpholinopyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,
7-Bromo-N^3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-(2,6-dimethylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,
7-Chloro-N3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-iodo-5-methoxyfuro[2,3-c]pyridine-2,3-diamine,
4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(2-methoxyethyl)benzamide,
N^3-(3-chloro-4-fluorophenyl)-7-(3,4-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-7-(2,3,4-trifluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
7-Bromo-N^3-(3-chloro-4-fluorophenyl)-5-methoxyfuro[2,3-c]pyridine-2,3-diamine,
4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)-5-methoxyfuro[2,3-c]pyridin-7-yl)benzonitrile,
N^3-(3-chloro-4-fluorophenyl)-7-(4-fluorophenyl)-5-methoxyfuro[2,3-c]pyridine-2,3-diamine,
4-(2-amino-3-((3-chloro-4-fluorophenyl)amino)-5-methoxyfuro[2,3-c]pyridin-7-yl) benzamide,
N^3-(3-chloro-4-fluorophenyl)-7-fluorofuro[2,3-c]pyridine-2,3-diamine,
5-Chloro-N^3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-chloro-4-fluorophenyl)-6-nitrobenzofuran-2,3-diamine,
N^3-(3-Chloro-4-fluorophenyl)-5-fluoro-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,
N^3-(3-chloro-4-fluorophenyl)-5-fluorofuro[2,3-c]pyridine-2,3-diamine,
2-Amino-3-((2-chlorophenyl)amino)furo[2,3-c]pyridine-7-carbonitrile,

2-Amino-3-((4-fluoro-3-(trifluoromethyl)phenyl)amino)furo[2,3-c]pyridine-7-carbonitrile,

N^3-(3,4-difluorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3,4-difluorophenyl)amino)furo[2,3-c]pyridine-7-carbonitrile,

2-Amino-3-((3,5-difluorophenyl)amino)furo[2,3-c]pyridine-7-carbonitrile,

N^3-(3,5-Difluorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-5-fluoro-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-Fluoro-N^3-(4-fluoro-3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5,7-difluorofuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2,6-difluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluoro-3-(trifluoromethyl)phenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

N^3-(3,4-Difluorophenyl)-7-(2-methoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Chlorophenyl)-N^3-(3,4-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-N7,N7-diphenylfuro[2,3-c]pyridine-2,3,7-triamine,

N^3-(4-Fluorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2-Chlorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(Pyridin-4-yl)-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(naphthalen-1-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-fluoro-3-(trifluoromethyl)phenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2-chlorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-methylpyridin-4-yl)-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-Bromo-N^3-(3-chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine hydrochloride,

N^3-(3,4-Difluorophenyl)benzo[b]thiophene-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)benzo[b]thiophen-7-yl)benzonitrile,

N^3-(3-Chloro-4-fluorophenyl)-7-(pyridin-4-yl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-methylbenzo[b]thiophene-2,3-diamine,

N^3-(3,4-difluorophenyl)-5-methylbenzo[b]thiophene-2,3-diamine,

N^3-(3,4-difluorophenyl)-5-fluorofuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chlorophenyl)-7-(pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2-Chlorophenyl)-5-fluorofuro[2,3-c]pyridine-2,3-diamine,

4-(2-Amino-3-((2-chlorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

N^3-(3-Chlorophenyl)-5-fluorofuro[2,3-c]pyridine-2,3-diamine,

5-Fluoro-N^3-(3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

5-Fluoro-N^3-(4-fluoro-3-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

4-(2-Amino-3-((3,4-difluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-Amino-3-((4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-Amino-3-((3-chlorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-Amino-3-((3-(trifluoromethyl)phenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-amino-3-((4-fluoro-3-(trifluoromethyl)phenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

5-Fluoro-N^3-(4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methoxypyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Bromophenyl)benzo[b]thiophene-2,3-diamine,

N^3-(4-Fluorophenyl)benzo[b]thiophene-2,3-diamine,

N^3-(2-Ethylphenyl)benzo[b]thiophene-2,3-diamine hydrochloride,

N^3-(3-Chloro-4-fluorophenyl)-7-phenylbenzo[b]thiophene-2,3-diamine,

N^3-(3-Chlorophenyl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Methoxyphenyl)benzo[b]thiophene-2,3-diamine,

N^3-(benzo[d][1,3]dioxol-5-yl)benzo[b]thiophene-2,3-diamine,

N^3-(4-Bromo-2-methylphenyl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Chlorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N3-phenylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methylpyridin-4-yl)benzo[b]thiophene-2,3-diamine,

5-Fluoro-N^3-(4-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-(2-(piperidin-1-yl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-fluoro-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-morpholinofuro[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-5-fluoro-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(naphthalen-2-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chlorophenyl)-7-(2-methylpyridin-4-yl)benzo[b]thiophene-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-phenylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-butylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(*tert*-butyl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-isobutylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-propylpicolinamide,

N^3-(3-Ahlorophenyl)-5-fluoro-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,4-Difluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-cyclohexylpicolinamide,

N^3-(3-Chloro-4-fluorophenyl)-7-(3,5-dichlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-(*tert*-Butyl)pyridin-4-yl)-N^3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridine 6-oxide,

7-(Benzo[d][1,3]dioxol-5-yl)-N3-(3-chloro-4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-ethylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5-Chloro-2-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-2-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-phenylbenzo[b]thiophene-2,3-diamine,

N^3-(4-Fluorophenyl)-7-(2-methylpyridin-4-yl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-5-methyl-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-(trifluoromethyl)pyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

(4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)pyridin-2-yl)(piperidin-1-yl)methanone,

(4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(pyridin-2-yl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(2-morpholinoethyl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-pentylpicolinamide,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-chloro-5-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(3,5-dimethylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(3,5-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-styrylfuro[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(isoquinolin-4-yl)benzo[b]thiophene-2,3-diamine,

N^3-(3-Bromo-4-methylphenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-([1,1'-Biphenyl]-3-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Bromo-4-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-2,4-difluorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-(4-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-(4-(trifluoromethoxy)phenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-(pyridin-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluoro-3-(trifluoromethoxy)phenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-(Difluoromethyl)phenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

3-((2-Amino-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridin-3-yl)amino)benzonitrile,

N^3-(4-Chlorophenyl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-Hexyl-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-Benzyl-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-Cyclohexyl-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-(tetrahydro-2H-pyran-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N^3-((tetrahydro-2H-pyran-4-yl)methyl)furo[2,3-c]pyridine-2,3-diamine,

(E)-N^3-(4-Fluorophenyl)-7-styrylfuro[2,3-c]pyridine-2,3-diamine,

(E)-N^3-(3,4-Difluorophenyl)-7-styrylfuro[2,3-c]pyridine-2,3-diamine,

(E)-N^3-(4-Fluoro-3-(trifluoromethyl)phenyl)-7-styrylfuro[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3,4-difluorophenyl)amino)-N-methylfuro[2,3-c]pyridine-7-carboxamide,

7-(Aminomethyl)-N^3-(3-chlorophenyl)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl acetate,

N-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)acetamide,

N^3-(2-Chlorophenyl)-7-(piperidin-4-ylmethyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(pyridin-4-ylmethyl)furo[2,3-c]pyridine-2,3-diamine,

(2-Amino-3-((3,4-difluorophenyl)amino)furo[2,3-c]pyridin-7-yl)methanol,

N^3-(3-Chlorophenyl)-7-(trifluoromethyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(cyclohexyloxy)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-((tetrahydro-2H-pyran-4-yl)oxy)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)-N-methylfuro[2,3-c]pyridine-7-sulfonamide,

2-Amino-3-((3,4-difluorophenyl)amino)-N-phenylfuro[2,3-c]pyridine-7-sulfonamide,,

N^3-(4-Fluorophenyl)-5-(trifluoromethyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2-Chlorophenyl)-5-(trifluoromethoxy)furo[2,3-c]pyridine-2,3-diamine,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-5-carbonitrile,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N,N-dimethylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-ethylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-isopropylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(2-methoxyethyl)picolinamide,

N-(3-(1*H*-Imidazol-1-yl)propyl)-4-(2-amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(pyridin-3-yl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(pyridin-4-yl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(4-methylpiperazin-1-yl)picolinamide,

N^3-(3-Chloro-4-fluorophenyl)thieno[3,2-b]pyridine-2,3-diamine,

3-((3-Chloro-4-fluorophenyl)thio)furo[2,3-c]pyridin-2-amine,

3-((3-Chloro-4-fluorophenyl)thio)benzofuran-2-amine,

3-(3-Chloro-4-fluorophenoxy)furo[2,3-c]pyridin-2-amine,

3-(3-Chloro-4-fluorophenoxy)benzofuran-2-amine,

N^3-(3-Chloro-4-fluorophenyl)benzofuran-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methylpyridin-4-yl)benzofuran-2,3-diamine,

N3-(3-Chloro-4-fluorophenyl)-7-(2,6-difluoropyridin-4-yl)benzofuran-2,3-diamine,

N3-(3-Chloro-4-fluorophenyl)-7-(2,6-difluoropyridin-4-yl)benzo[b]thiophene-2,3-diamine,

N3-(3-Chloro-4-fluorophenyl)-7-(2-fluoropyridin-4-yl)benzofuran-2,3-diamine,

N3-(3-Chloro-4-fluorophenyl)-7-(2-fluoropyridin-4-yl)benzo[b]thiophene-2,3-diamine,,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)benzofuran-7-yl)-N-methylpicolinamide,

2-Amino-3-((3-chloro-4-fluorophenyl)amino)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridin-5-ol,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-fluoropyridin-4-yl)benzofuran-2,3-diamine,

N^3-(3-chlorophenyl)-7-(2-fluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Fluorophenyl)-7-(2-fluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(2-fluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4-Fluorophenyl)-7-(2-fluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-1H-indole-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methylpyridin-4-yl)-1H-pyrrolo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(2-methylpyridin-4-yl)-1H-indole-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)-1H-pyrrolo[2,3-c]pyridin-7-yl)-N methylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)-1H-indol-7-yl)-N-methylpicolinamide,

N^3-(3-Chloro-4-fluorophenyl)-7-(4-methylpyrimidin-2-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(imidazo[1,2-a]pyridin-5-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-7-(imidazo[1,2-a]pyridin-2-yl)furo[2,3-c]pyridine-2,3-diamine,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methyl-1H-imidazole-1-carboxamide,

N^3-(1-Methyl-1H-pyrrol-3-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Methylpyridin-4-yl)-N3-(1H-pyrrol-3-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(1-Methyl-1H-pyrrol-2-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(1-Methyl-1H-indol-2-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(6-Chloropyrimidin-4-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(6-Fluoropyrimidin-4-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2-Fluoropyrimidin-5-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(4,5-difluoropyrimidin-2-yl)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chlorophenyl)-7-(2,6-difluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(2,6-difluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

7-(2,6-Difluoropyridin-4-yl)-N3-(4-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(5-chloro-2-fluorophenyl)-7-(2,6-difluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(4-(methoxymethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Chloro-6-fluorophenyl)-N3-(3,4-difluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N-(4-(2-Amino-3-((3,4-difluorophenyl)amino)furo[2,3-c]pyridin-7-yl)phenyl)pyrrolidine-1 carboxamide,

N^3-(3,4-Difluorophenyl)-7-(4-fluoro-2-methylphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(4-propoxyphenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3,4-Difluorophenyl)-7-(4-morpholinophenyl)furo[2,3-c]pyridine-2,3-diamine,

5-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-2-fluorophenol,

Methyl 5-(2-amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-2-chlorobenzoate,

3-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylbenzamide,

4-(4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)picolinamido)butanoic acid,

7-(2,6-Difluoropyridin-4-yl)-N^3-(4-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

7-(2-Fluoropyridin-4-yl)-N^3-(4-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

5-Fluoro-7-(2-methylpyridin-4-yl)-N3-(4-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3diamine,

4-(2-Amino-3-((4-(trifluoromethyl)phenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-Amino-5-fluoro-3-((4-(trifluoromethyl)phenyl)amino)furo[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)-5-fluorofuro[2,3-c]pyridin-7-yl)-N-methylpicolinamide,

5-Fluoro-N^3-(4-(trifluoromethyl)phenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-6-fluorobenzo[b]thiophene-2,3-diamine,

N^3-(3-Chloro-4-fluorophenyl)-1-methyl-1H-indole-2,3-diamine,

7-(2,6-Difluoropyridin-4-yl)-N^3-(3-fluorophenyl)furo[2,3-c]pyridine-2,3-diamine,

N^3-(2,5-Ddifluorophenyl)-7-(2,6-difluoropyridin-4-yl)furo[2,3-c]pyridine-2,3-diamine,

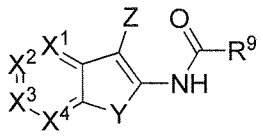
4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N-(2-hydroxyethyl)picolinamide,

4-(2-Amino-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-7-yl)-N,N diethylpicolinamide,

N^3-(3-Chloro-4-fluorophenyl)-7-(2,3-dichlorophenyl)furo[2,3-c]pyridine-2,3-diamine, or

N^3-(3-Chloro-4-fluorophenyl)-7-(naphthalen-2-yl)benzo[b]thiophene-2,3-diamine.

~~64~~21. A prodrug of a compound of claim 1, wherein the prodrug is an acylated compound which has a formula (**II**):

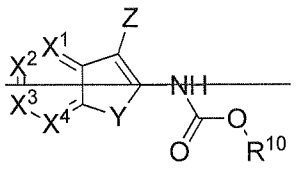


(**II**)

wherein R^9 is optionally-substituted C_1-C_6 alkyl.

~~65. A compound of claim 64, wherein R^9 is methyl.~~

~~66. A prodrug of a compound of claim 1, wherein the prodrug is a carbamate compound which has a formula (III):~~

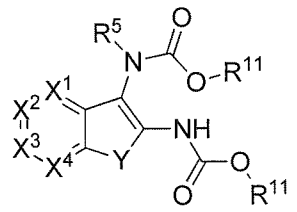


~~(III)~~

~~wherein R^{10} is optionally-substituted C_1-C_6 alkyl, aryl, (aryl)alkyl, heteroaryl, or (heteroaryl)alkyl.~~

~~67. A compound of claim 66, wherein R^{10} is selected from methyl, ethyl, benzyl, (C_1-C_6 alkoxy)methyl, and 1-(C_1-C_6 alkoxy)ethyl.~~

~~68~~22. A prodrug of a compound of claim 1, wherein the prodrug is a dicarbamate compound which has a formula (**IV**):



(**IV**)

wherein R^{11} is optionally-substituted C_1-C_6 alkyl, aryl, (aryl)alkyl, heteroaryl, or (heteroaryl)alkyl.

~~69. A compound of claim 68, wherein R^{11} is selected from methyl, ethyl, benzyl, (C_1-C_6 alkoxy)methyl, and 1-(C_1-C_6 alkoxy)ethyl.~~

~~70. The compound according to claims 64 to 69, wherein R^9-R^{11} is optionally substituted C_1-C_6 alkyl or mono or bicyclic C_6-C_{14} aryl or heteroaryl.~~

~~71~~23. The compound according to any one of claims 1 to ~~70~~22, which is:

Benzyl (3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-2-yl)carbamate,

Benzyl (2-(((benzyloxy)carbonyl)amino)furo[2,3-c]pyridin-3-yl)(3-chloro-4-fluorophenyl)carbamate,

Ethyl (3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-2-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)carbamate,

Methyl (3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-2-yl)carbamate,

Methyl (3-chloro-4-fluorophenyl)(2-((methoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(7-cyano-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(7-(3-cyanophenyl)-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)carbamate,

Benzyl (3-((3-chloro-4-fluorophenyl)amino)-7-cyanofuro[2,3-c]pyridin-2-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(2-((ethoxycarbonyl)amino)-7-iodofuro[2,3-c]pyridin-3-yl)carbamate,

Ethyl (7-(4-carbamoylphenyl)-3-((3-chloro-4-fluorophenyl)amino)furo[2,3-c]pyridin-2-yl)carbamate,

Ethyl (7-((4-carbamoylphenyl)ethynyl)-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)(3-chloro-4-fluorophenyl)carbamate,

Ethyl (7-bromo-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)(3-chloro-4-fluorophenyl)carbamate,

Ethyl (3-((3-chloro-4-fluorophenyl)amino)-7-phenylfuro[2,3-c]pyridin-2-yl)carbamate,

Ethyl (3-((3-chloro-4-fluorophenyl)amino)-7-(2,6-dimethylpyridin-4-yl)furo[2,3-c]pyridin-2-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(7-(2,6-dimethylpyridin-4-yl)-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(6-cyano-2-((ethoxycarbonyl)amino)benzofuran-3-yl) carbamate,

Ethyl (2-((ethoxycarbonyl)amino)-7-(pyridin-4-yl)furo[2,3-c]pyridin-3-yl)(4-fluoro-3-(trifluoromethyl)phenyl)carbamate,

Ethyl (7-cyano-2-((ethoxycarbonyl)amino)furo[2,3-c]pyridin-3-yl)(4-fluoro-3-(trifluoromethyl)phenyl)carbamate,

Ethyl (3-((3-chloro-4-fluorophenyl)amino)benzo[b]thiophen-2-yl)carbamate,

Ethyl (3-chloro-4-fluorophenyl)(2-((ethoxycarbonyl)amino)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridin-3-yl)carbamate, or

Ethyl (3,4-difluorophenyl)(2-((ethoxycarbonyl)amino)-7-(2-methylpyridin-4-yl)furo[2,3-c]pyridin-3-yl)carbamate.

~~72. The compound according to any one of claims 1 to 67 or 70, which is an acetylated prodrug.~~

~~73. The compound according to any one of claims 1 to 72, which is a salt of an acid or base.~~

~~74. The compound according to any one of claims 1 to 73, wherein the salt is an acetate, an accinate, an aspartate, a benzenesulfonate, a benzoate, a bicarbonate, a bisulfate, a bitartrate, a bromide, a butyrate, a citrate, a camphorsulfonate, an edisylate, an ethanesulfonate, a formate, a fumarate, a gluconate, a glucuronate, a glutamate, a hydrobromide, a hydrochloride, an iodide, an isonicotinate, a lactate, a lauryl sulfate, a malate, a maleate, a malonate, a mandelate, a methylsufonate, a mesylate, a nitrate, a oleate, an oxalate, a palmitate, a pantothenate, a phosphate, an acid phosphate, a propionate, a p-toluenesulfonate, a tartarate, a trifluoracetate, a salicylate, a stearate, a succinate, a sulfate, a tannate, or a pyridinium salt.~~

~~75~~24. The compound according to any one of claims 1 or ~~74~~23, which is:
7-Bromo-N^3-(3-chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine hydrochloride,
3-((3-chlorophenyl)thio)benzo[b]thiophen-2-amine hydrochloride,
3-(3-chlorophenoxy)benzo[b]thiophen-2-amine hydrochloride,
5-chloro-N^3-(3-chloro-4-fluorophenyl)benzo[b]thiophene-2,3-diamine hydrochloride,
5-chloro-N^3-(3-(trifluoromethyl)phenyl)benzo[b]thiophene-2,3-diamine hydrochloride,
N^3-methyl-N^3-phenylbenzo[b]thiophene-2,3-diamine hydrochloride, or
N3-(2-Ethylphenyl)benzo[b]thiophene-2,3-diamine hydrochloride.

~~76. The compound according to claims 1 to 75, wherein the compound is a metabolite of compounds of formulae (I), (II), (III) or (IV), and a pharmaceutically acceptable carrier or prodrug thereof.~~

~~77~~25. A composition comprising a compound of any one of claims 1 to ~~76~~24 and a pharmaceutically acceptable carrier.

~~78. A kit comprising a compound of any one of claims 1 to 77.~~

~~79. The kit according to claim 78, further comprising one or more additional medications comprising a chemotherapeutic, vaccine, targeted antibody, adoptive T-cell transfer, B-cell therapy, targeted drug, and hormone therapy.~~

~~80. A method for regulating a kynurenine pathway, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.~~

~~81. A method of regulating any one or more of one or more of indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.~~

82. The method according to claim 80 or 81, wherein said regulating comprises inhibiting the kynurenine pathway or one or more of the enzymes.

83. A method of reducing kynurenine pathway metabolites, said method comprising administering a compound of claims 1 to 77 to a subject in need thereof.

84. A method of altering tryptophan levels in a subject, said method comprising administering a therapeutic amount of a compound of claims 1 to 77 to a subject in need thereof.

85. A method according to claim 84, wherein the tryptophan levels are increased.

86. A method of treating immune suppression, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

87. The method according to claim 86, wherein the immune suppression is associated with increased kynurenine levels or enzymatic activity of one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase.

88. A method of reducing or eliminating an immune mediated disorder, said method comprising administering a compound of any one of claims 1 to 77 to a patient in need thereof.

89. A method of inhibiting activation of a indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

90. A method of treating a disease resulting from dysregulation of the kynurenine pathway, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

91. A method of treating a disease is associated with one or more of indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase

enzyme, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

92. A method of treating a disease caused by activation of indoleamine 2,3-dioxygenase-1 or tryptophan 2,3-dioxygenase enzyme or both, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

93. A method of treating a disease caused by activation of indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzyme or both, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

94. A method of treating a disease caused by activation of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 enzyme or both, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

95. A method for treating a disease treatable by inhibiting a kynurenine pathway, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

96. A method for regulating a disease characterized by abnormal immune suppression resulting from a dysregulated kynurenine pathway due to activation of one or more of indoleamine 2,3-dioxygenase-1 or indoleamine 2,3-dioxygenase-2 or tryptophan 2,3-dioxygenase enzymes, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

97. A method of inhibiting an autoimmune antibody production, said method comprising administering a compound of any one of claims 1 to 77 to a subject in need thereof.

98. A method according to claim 98, wherein (i) indoleamine 2,3-dioxygenase-2 is inhibited, (ii) a KYN level is reduced, or (ii) said autoimmune antibody production is associated with an autoimmune disorder, an inflammatory disorder, or cancer.

99. The method according to any one of claims 80 to 98, wherein said disease is cancer, bacterial infection, viral infection, parasitic infection, immune-mediated disorder, autoimmune disorder, inflammatory disease, central nervous system disease, peripheral nervous system disease, neurodegenerative disease, mood disorder, sleep disorder, cerebrovascular disease, peripheral artery disease, or cardiovascular disease.

100. The method according to any of claims 80 to 99, wherein the disease is depression, Alzheimer's disease, dementia, schizophrenia, HIV infection, malaria, rheumatoid arthritis, insomnia or multiple sclerosis.

101. The method according to any of claims 80 to 99, wherein the cancer is a cancer of squamous cell, peritoneum, prostate, head, neck, eye, mouth, throat, esophagus, bronchus, larynx, pharynx, thyroid cancer, chest, bone, lungs, colon, rectum, stomach, urinary bladder, gall bladder, uterus, cervix, breast, ovaries, uterus, vagina, vulva, testicles, penis, anus, skin, thyroid, blood, lymph nodes, kidney, liver, intestines, salivary gland, pancreas, brain, spine, adrenal gland, skin, or leukemia.

102. The method according to any of claims 80 to 101, said method further comprising one or more therapeutic agent or therapy.

103. The method according to any of claim 80 to 99, 101 or 102, wherein said therapeutic agent or therapy is a chemotherapeutic agent selected from a group further comprising a cancer vaccine, a targeted drug, a targeted antibody, an antibody fragment, an antimetabolite, an antineoplastic, an antifolate, a toxin, an alkylating agent, a DNA strand breaking agent, a DNA minor groove binding agent, a pyrimidine analog, a purine analog, a ribonucleotide reductase inhibitor, a tubulin interactive agent, an anti-hormonal agent, an immunomoldulator, an anti-adrenal agent, a cytokine, a radiation therapy, a cell therapy, or a hormone therapy.

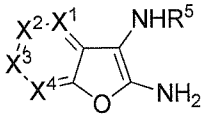
104. The method according to claim 105, wherein said chemotherapeutic agent is selected from the group consisting of doxorubicin, epirubicin, methotrexate, paclitaxel or derivative thereof, cyclophosphamide, 5-FU, cisplatin, gemcitabine, dactinomycin, levamisole,

~~etoposide, topotecan, thiotepa, vinblastine, and docetaxel and carboplatin or a derivative thereof.~~

~~105. The method according to claim 102, wherein said therapeutic agent is a cancer vaccine, a targeted antibody, an adoptive T-cell transfer, a targeted drug, and a hormone therapy.~~

~~106. The method according to claim 105, wherein said targeted antibody is anti-CTLA4, anti-PD1, or anti-PD-L1.~~

~~107~~26. A method of preparing a compound of formula (**I-C**), said method comprising:



(**I-C**)

wherein:

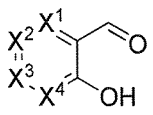
X^1 is CR^1, N, or NO;

X^2 is CR^2, N, or NO;

X^3 is CR^3, N, or NO;

X^4 is CR^4, N, or NO; and

R^5 is selected from the group consisting of H, optionally substituted C_1-C_6 alkyl, optionally substituted mono or bicyclic C_6-C_{14} aryl, optionally substituted mono or bicyclic heteroaryl, optionally substituted (aryl)alkyl, optionally substituted mono or bicyclic cycloalkyl, optionally substituted mono or bicyclic heterocyclyl, C_1-C_6 haloalkyl, optionally substituted heterocyclyl(alkyl), optionally substituted heteroaryl(alkyl), hydroxyalkyl, and perfluoroalkyl;

(i) reacting  with an an amine (R^5-NH_2);

(ii) reacting the product of step (i) with a cyanide salt; and

(iii) reacting the product of step (ii) with a Lewis acid.

~~108~~27. The method according to claim ~~107~~26, wherein said Lewis acid is selected from trimethylsilyl trifluoromethanesulfonate, $Sc(OTf)_3$, $Fe(OTf)_2$, $Ni(OTf)_2$, and $In(OTf)_3$.

~~109~~28. The method according to claim ~~107~~26, wherein said cyanide salt is selected from a group consisting of a trialkyl silyl cyanide, NaCN, KCN, and $Zn(CN)_2$.

~~110~~29. The method according to claim ~~109~~28, wherein said trialkyl silyl cyanide is TMSCN.

~~111~~30. The method according to claim ~~108~~27, wherein the product of step (i) is an imine intermediate.

~~112. A compound obtainable by a method according to claims 107 to 111.~~

~~113. A method for diagnosing and treating a disease associated with kynurenine pathway or one or more of a indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a subject, said method comprising:~~

~~assaying a blood and/or tissue sample from a subject;~~

~~determining the subject's blood and/or tissue tryptophan or Kynurenine concentration or both in the sample;~~

~~optionally determining the subject's Kynurnine/tryptophan ratio; and~~

~~administering a compound of any one of the claims 1 to 77.~~

~~114. A method of monitoring a disease associated with kynurenine pathway or one or more of a indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a subject, said method comprising:~~

~~dosing a subject having a disease associated with kynurenine pathway with a compound of any of claims 1 to 77;~~

~~analyzing a blood or tissue samples or both at one or more time points or continuously during a treatment regimen;~~

~~determining a tryptophan and a Kynurenine concentration in the blood or the tissue sample or both;~~

~~optionally determining the subject's Kynurnine/tryptophan ratio; and~~

adjusting the treatment regimen or dosage of the compound.

115. A method for diagnosing and treating a disease associated with Kynurenine pathway or one or more of a indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a patient comprising:

analyzing a patient sample for the presence or absence of altered Kynurenin/tryptophan ratio, wherein the patient is diagnosed with a disease associated with Kynurenine pathway if altered Kynurenine/ratio is detected; and

administering a compound of any of claims 1 to 77 to the diagnosed patient.

116. A method for treating a disease associated with kynurenine pathway or one or more of a indoleamine 2,3-dioxygenase-1 or an indoleamine 2,3-dioxygenase-2 or a tryptophan 2,3-dioxygenase enzymes in a patient comprising:

requesting a test providing the results of an analysis to determine whether the patient's kynurnine levels are altered; and

administering a compound of any of claims 1 to 77 to the patient if the patient's kynurenine levels are altered.

117. A method according to claims 113 to 116, wherein the disease is cancer, bacterial infection, viral infection, parasitic infection, immune-mediated disorder, autoimmune disorder, inflammatory disease, central nervous system disease, peripheral nervous system disease, neurodegenerative disease, mood disorder, sleep disorder, cerebrovascular disease, peripheral artery disease, or cardiovascular disease.