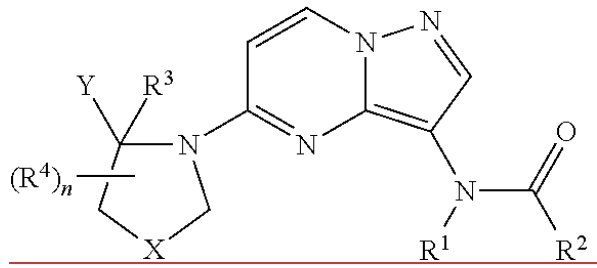
SUMMARY

[0016a] In one aspect, the present disclosure refers to use of a compound of Formula (I):

I



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^c;

NR^bR^c forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring formed by NR^bR^c is optionally substituted with one or two substituents independently selected from OH, F, NH_2, CO_2H, CO_2Et, $NHCO_2C(CH_3)_3$, CF_3, methyl, ethyl, isopropyl, $CO_2C(CH_3)_3$ and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2;

X is —CH_2—;

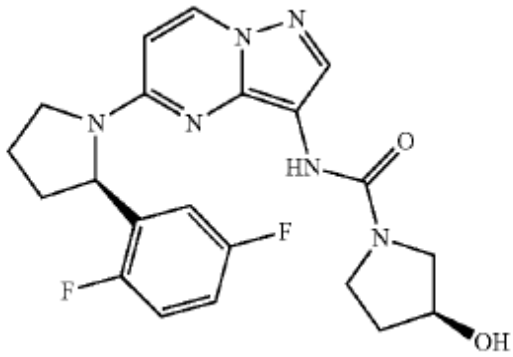
R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and

n is 0, 1, or 2,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a cancer in a mammal in need thereof.

[0016b] In one aspect, the present disclosure refers to use of a compound:

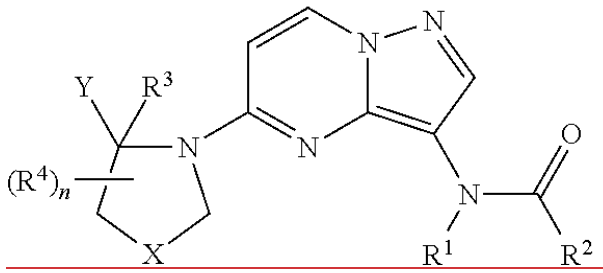


(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide, or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a cancer in a mammal.

[0016c] In one aspect, the present disclosure refers to use of a compound of Formula (I):

I



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^c;

NR^bR^c forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring formed by NR^bR^c is optionally substituted with one or two substituents independently selected from OH, F, NH_2, CO_2H, CO_2Et, $NHCO_2C(CH_3)_3$, CF_3, methyl, ethyl, isopropyl, $CO_2C(CH_3)_3$, and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3, and CHF_2;

X is —CH_2—;

R^3 is H or (1-4C alkyl);

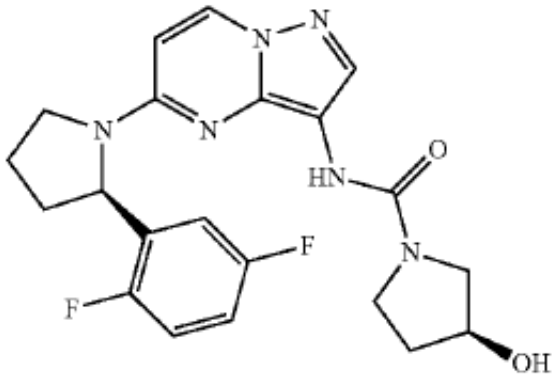
each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4C)alkoxy, NH_2,

NH(1-4C alkyl), and CH_2OH; and

n is 0, 1, or 2,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a lung cancer that exhibits one or more of an overexpression, activation, amplification and mutation of a Trk kinase in a mammal in need thereof.

[0016d] In one aspect, the present disclosure refers to use of a compound:

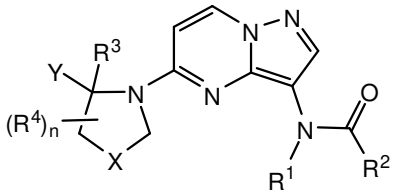


(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide, or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for treating a lung cancer that exhibits one or more of an overexpression, activation, amplification and mutation of a Trk kinase in a mammal in need thereof.

DETAILED DESCRIPTION

[0017] Accordingly, one embodiment of this invention provides a compound of the general Formula **I**:



I

[0018] or a pharmaceutically acceptable salt thereof, wherein:

[0019] R^1 is H or (1-6C alkyl);

[0020] R^2 is NR^bR^c, (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C)hydroxyalkyl, -(1-4C alkyl)hetAr^1, -(1-4C alkyl)NH_2, -(1-4C alkyl)NH(1-4C alkyl), -(1-4C alkyl)N(1-4C alkyl)$_2$,

$hetAr^2$, $hetCyc^1$, $hetCyc^2$, phenyl which is optionally substituted with $NHSO_2$(1-4C alkyl), or (3-6C)^{e}cycloalkyl which is optionally substituted with (1-4C alkyl), CN, OH, OMe, NH_2, NHMe, $N(CH_3)_2$, F, CF_3, CO_2(1-4C alkyl), CO_2H, $C(=O)NR^eR^f$ or $C(=O)OR^g$;

[0021] R^b is H or (1-6C alkyl);

[0022] R^c is H, (1-4C)alkyl, (1-4C)hydroxyalkyl, $hetAr^3$, or phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from halogen, CN, CF_3 and -O(1-4C alkyl),

[0023] or NR^bR^c forms a 4 membered heterocyclic ring having a ring nitrogen atom wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from halogen, OH, (1-4C alkyl), (1-4 C)alkoxy, -OC(=O)(1-4C alkyl), NH_2, -NHC(=O)O(1-4C alkyl) and (1-4C)hydroxyalkyl,

[0024] or NR^bR^c forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring is optionally substituted with one or more substituents independently selected from OH, halogen, CF_3, (1-4C)alkyl, CO_2(1-4C alkyl), CO_2H, NH_2, NHC(=O)O(1-4C alkyl) and oxo,

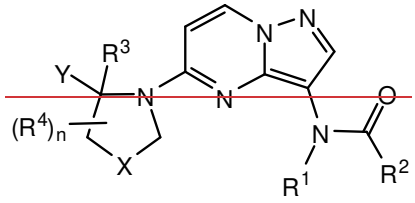
[0025] or NR^bR^c forms a 7-8 membered bridged heterocyclic ring having a ring nitrogen atom and optionally having a second ring heteroatom selected from N and O, wherein said ring is optionally substituted with CO_2(1-4C alkyl);

[0026] $hetAr^1$ is a 5-membered heteroaryl ring having 1-3 ring nitrogen atoms;

[0027] $hetAr^2$ is 5-6 membered heteroaryl ring having at least one nitrogen ring atom and optionally having a second ring heteroatom independently selected from N and S,

What is claimed is:

1. A compound having the general formula **I**



I

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^e, (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C)hydroxyalkyl, (1-4C alkyl)$hetAr^1$, (1-4C alkyl)NH_2, (1-4C alkyl)NH(1-4C alkyl), (1-4C alkyl)N(1-4C alkyl)$_2$, $hetAr^2$, $hetCyc^1$, $hetCyc^2$, phenyl which is optionally substituted with $NHSO_2$(1-4C alkyl), or (3-6C)cycloalkyl which is optionally substituted with (1-4C alkyl), CN, OH, OMe, NH_2, NHMe, $N(CH_3)_2$, F, CF_3, CO_2(1-4C alkyl), CO_2H, $C(=O)NR^eR^f$ or $C(=O)OR^g$;

R^b is H or (1-6C alkyl);

R^e is H, (1-4C)alkyl, (1-4C)hydroxyalkyl, $hetAr^3$, or phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from halogen, CN, CF_3 and O(1-4C alkyl),

or NR^bR^e forms a 4 membered heterocyclic ring having a ring nitrogen atom, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from halogen, OH, (1-4C alkyl), (1-4C)alkoxy, OC(=O)(1-4C alkyl), NH_2, NHC(=O)O(1-4C alkyl) and (1-4C)hydroxyalkyl,

or NR^bR^e forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring is optionally substituted with one or more substituents independently selected from OH, halogen, CF_3, (1-4C)alkyl, CO_2(1-4C alkyl), CO_2H, NH_2, NHC(=O)O(1-4C alkyl) and oxo,

or NR^bR^e forms a 7-8 membered bridged heterocyclic ring having a ring nitrogen atom and optionally having a second ring heteroatom selected from N and O, wherein said ring is optionally substituted with CO_2(1-4C alkyl);

$hetAr^1$ is a 5-membered heteroaryl ring having 1-3 ring nitrogen atoms;

~~hetAr^2 is 5-6 membered heteroaryl ring having at least one nitrogen ring atom and optionally having a second ring heteroatom independently selected from N and S, wherein said heteroaryl ring is optionally substituted with one or more substituents independently selected from (1-4C alkyl), halogen, (1-4 C)alkoxy and NH(1-4C alkyl);~~

~~hetCyc^1 is a carbon linked 4-6 membered azacyclic ring optionally substituted with one or more substituents independently selected from (1-4C alkyl), and CO_2(1-4C alkyl);~~

~~hetCyc^2 is a pyridinone or pyridazinone ring which is optionally substituted with a substituent selected from (1-4C)alkyl;~~

~~hetAr^3 is a 5-6 membered heteroaryl ring having 1-2 ring heteroatoms independently selected from N and O and optionally substituted with one or more substituents independently selected from (1-4C)alkyl;~~

~~R^e is H or (1-4C)alkyl;~~

~~R^f is H, (1-4C)alkyl, or (3-6C)cycloalkyl;~~

~~or NR^{e}R^f forms a 4-6 membered azacyclic ring optionally having an additional ring heteroatom selected from N and O, wherein the azacyclic ring is optionally substituted with OH;~~

~~R^g is H or (1-6C)alkyl;~~

~~Y is (i) phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2, or (ii) a 5-6 membered heteroaryl ring having a ring heteroatom selected from N and S, wherein said heteroaryl ring is optionally substituted with one or more halogen atoms;~~

~~X is null, CH_2, CH_2CH_2, CH_2O, or CH_2NR^d;~~

~~R^d is H or (1-4C alkyl);~~

~~R^3 is H or (1-4C alkyl);~~

~~each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4 C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and~~

~~n is 0, 1, 2, 3, 4, 5 or 6.~~

~~2. A compound of claim 1, wherein R^2 is NR^{b}R^e, (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C)hydroxyalkyl, (1-4C alkyl)hetAr^1, (1-4C alkyl)NH_2, (1-4C alkyl)NH(1-4C alkyl), (1-4C alkyl)N(1-4C alkyl)$_2$, hetAr^2, hetCyc^1, hetCyc^2, phenyl which is optionally substituted with $NHSO_2$(1-4C alkyl), or (3-6C)cycloalkyl which is~~

optionally substituted with (1-4C alkyl), CN, OH, OMe, NH_2, NHMe, $N(CH_3)_2$, F, CF_3, CO_2(1-4C alkyl) or CO_2H.

3. A compound of claim 1 or 2, wherein R^2 is NR^bR^e.

4. A compound according to any of claims 1-3, wherein:

NR^bR^e forms a 4-membered heterocyclic ring having a ring nitrogen atom, wherein said ring is optionally substituted with one or more substituents independently selected from halogen, OH, (1-4C alkyl), (1-4C)alkoxy, OC(=O)(1-4C alkyl), NH_2, NHC(=O)O(1-4C alkyl) and (1-4C)hydroxyalkyl,

or NR^bR^e forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring is optionally substituted with one or more substituents independently selected from OH, halogen, CF_3, (1-4C)alkyl, CO_2(1-4C alkyl), CO_2H, NH_2, NHC(=O)O(1-4C alkyl) and oxo,

or NR^bR^e forms a 7-8 membered bridged heterocyclic ring having a ring nitrogen atom and optionally having a second ring heteroatom selected from N and O, wherein said ring is optionally substituted with CO_2(1-4C alkyl).

5. A compound according to any of claims 1-3, wherein:

R^e is H, (1-4C)alkyl, (1-4C)hydroxyalkyl, $hetAr^3$, or phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from halogen, CN, CF_3 and O(1-4C alkyl).

6. A compound of claim 1 or 2, wherein R^2 is (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C alkyl)$hetAr^1$ or (1-4C alkyl)NH(1-4C alkyl).

7. A compound of claim 1 or 2, wherein R^2 is $hetAr^2$, $hetCyc^1$ or $hetCyc^2$.

8. A compound of claim 1or 2, wherein R^2 is phenyl optionally substituted with $NHSO_2$(1-4C alkyl).

9. A compound of claim 1 or 2, wherein R^2 is (3-6C)cycloalkyl which is optionally substituted with (1-4C alkyl), CN, OH, CF_3, CO_2(1-4C alkyl) or CO_2H.

10. A compound of claim 1, wherein R^2 is $C(=O)NR^eR^f$ or $C(=O)OR^g$.

11. A compound according to any of claims 1-10, wherein X is null, CH_2 or CH_2CH_2.

12. A compound according to claim 11, wherein X is CH^2.

13. A compound according to any of claims 1-10, wherein X is CH_2O.

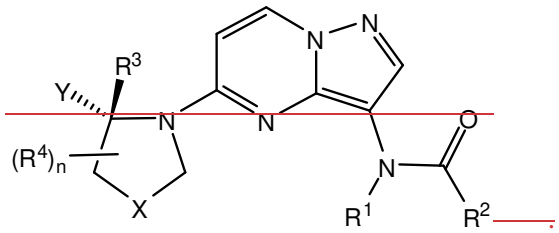
14. A compound according to any of claims 1-10, wherein X is CH_2NR^d.

15. A compound according to any of claims 1-14, wherein Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2.

16. A compound according to claim 15, wherein Y is phenyl, 3-fluorophenyl, 2,5-difluorophenyl, 2-chloro-5-fluorophenyl, 2-methoxyphenyl, 2-methoxy-5-fluorophenyl, 2-trifluoromethyl-5-fluorophenyl, 2-difluoromethyl-5-fluorophenyl or 3-chloro-5-fluorophenyl.

17. A compound according to any of claims 1-14, wherein Y is a 5-6 membered heteroaryl ring having a ring heteroatom selected from N and S, wherein said ring is optionally substituted with one or more halogen atoms.

18. A compound according to any of claims 1-17, wherein Y has the absolute configuration of Figure **Ia**:



Ia

19. A compound according to any of claims 1-18, wherein R^3 is H.

20. A compound according to claim 1, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^e;

NR^bR^e forms a 4-membered heterocyclic ring having a ring nitrogen atom, wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from halogen, OH, (1-4C alkyl), (1-4C)alkoxy, OC(=O)(1-4C alkyl), NH_2, NHC(=O)O(1-4C alkyl) and (1-4C)hydroxyalkyl,

or NR^bR^e forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring is optionally substituted with one or more substituents independently selected from OH, halogen, CF_3, (1-4C)alkyl, CO_2(1-4C alkyl), CO_2H, NH_2, NHC(=O)O(1-4C alkyl) and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2;

X is null, CH_2, or CH_2CH_2;

R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4-C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and

n is 0, 1, or 2.

21. A compound according to claim 20, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^e;

NR^bR^e forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring is optionally substituted with one or more substituents independently selected from OH, halogen, CF_3, (1-4C)alkyl, CO_2(1-4C alkyl), CO_2H, NH_2, NHC(=O)O(1-4C alkyl) and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2;

X is CH_2;

R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4-C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and

n is 0, 1, or 2.

22. A compound according to claim 21, wherein the heterocyclic ring formed by NR^bR^e is optionally substituted with one or two substituents independently selected from OH, F, NH_2, CO_2H, CO_2Et, $NHCO_2C(CH_3)_3$, CF_3, methyl, ethyl, isopropyl, $CO_2C(CH_2)_3$ and oxo.

23. A compound according to claim 22, wherein Y is phenyl optionally substituted with one or more halogen atoms.

24. A compound according to claim 23, wherein Y is phenyl optionally substituted with one or two fluorine atoms.

25. A compound according claim 20, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^e;

NR^bR^e forms a 4-membered heterocyclic ring having a ring nitrogen atom, wherein said ring is optionally substituted with one or more substituents independently

selected from halogen, OH, (1-4C alkyl), (1-4C)alkoxy, OC(=O)(1-4C alkyl), NH_2, NHC(=O)O(1-4C alkyl) and (1-4C)hydroxyalkyl;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2;

X is CH_2;

R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and

n is 0, 1, or 2.

26. A compound according to claim 25, wherein the heterocyclic ring formed by NR^bR^c is optionally substituted with one or two substituents independently selected from F, OH, methyl, OMe, $OC(=O)C(CH_3)_2$, NH_2, $NHC(=O)OC(CH_3)_3$ and CH_2OH.

27. A compound according to claim 26, wherein Y is phenyl optionally substituted with one or more halogen atoms.

28. A compound according to claim 27, wherein Y is phenyl optionally substituted with one or two fluorine atoms.

29. A compound according to any of claims 20-28, wherein n is zero or one.

30. A compound according to claim 29, wherein R^3 is hydrogen.

31. A compound according to claim 30, wherein R^1 is hydrogen.

32. A compound according to claim 1, which is a trifluoroacetate salt, a sulfate salt or a hydrochloride salt.

33. A pharmaceutical composition, which comprises a compound of Formula **I** as defined in any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

34. A method for treating pain, cancer, inflammation, neurodegenerative disease or Typanosoma cruzi infection in a mammal, which comprises administering to said mammal a therapeutically effective amount of a compound of Formula **I** as defined in any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof.

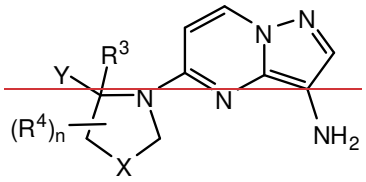
35. A method for treating osteolytic disease in a mammal, which comprises administering to said mammal a therapeutically effective amount of a compound of Formula **I** as defined in any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof.

36. A compound of Formula **I** as defined in any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, for use in the treatment of pain, cancer, inflammation, neurodegenerative disease or Typanosoma cruzi infection in a mammal.

37. A compound of Formula **I** as defined in any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, for use in the treatment of osteolytic disease in a mammal.

38. A process for the preparation of a compound of claim 1, which comprises:

(a) for a compound of Formula **I** wherein R^2 is NR^bR^e, reacting a corresponding compound of formula **II**



II

with a compound having the formula HNR^bR^e in the presence of a coupling reagent; or

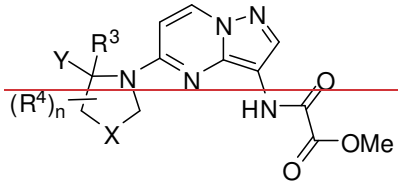
(b) for a compound of Formula **I** wherein R^2 is NR^bR^e and R^b is H, reacting a corresponding compound of formula **II** with a compound having the formula $O=C=N-R^e$; or

(c) for a compound of Formula **I** wherein R^2 is $hetAr^2$ or a phenyl ring which is optionally substituted with $NHSO_2$(1-4C alkyl) , reacting a corresponding compound of Formula **II** with a corresponding compound having the formula $HOC(=O)R^2$ in the presence of a coupling reagent and a base; or

(d) for a compound of Formula **I** wherein R^2 is (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C)hydroxyalkyl, or (3-6C)cycloalkyl which is optionally substituted with (1-4C alkyl), CN, OH, CF_3, CO_2(1-4C alkyl) or CO_2H, reacting a corresponding compound of Formula **II** with a corresponding compound having the formula $(R^2CO)_2O$ in the presence of a base; or

(e) for a compound of Formula **I** wherein R^2 is (1-4C)alkyl, (1-4C)fluoroalkyl, CF_3, (1-4C)hydroxyalkyl, or (3-6C)cycloalkyl which is optionally substituted with (1-4C alkyl), CN, OH, CF_3, CO_2(1-4C alkyl) or CO_2H, reacting a corresponding compound of Formula **II** with a corresponding compound having the formula $HOC(=O)R^2$ in the presence of a coupling reagent and a base;

~~(f) for a compound of Formula I wherein R^2 is $C(=O)NR^eR^f$, reacting a compound of formula VII~~



~~VII~~

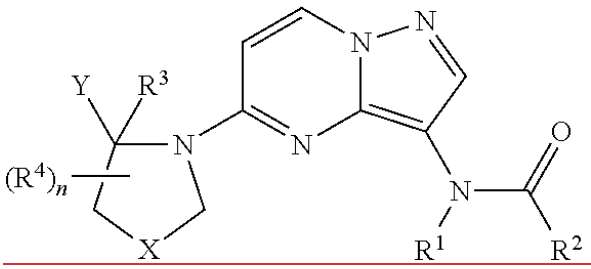
~~with a compound having the formula HNR^eR^f in the presence of a base; or~~

~~(g) for a compound of Formula I wherein R^2 is $C(=O)OR^g$, reacting a compound of Formula II with methyl 2-chloro-2-oxoacetate, and treating with an alkali hydroxide to prepare a compound of formula I where R^g is H; and~~

~~removing or adding any protecting groups if desired, and forming a salt if desire~~

1. Use of a compound of Formula (I):

I



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^c;

NR^bR^c forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring formed by NR^bR^c is optionally substituted with one or two substituents independently selected from OH, F, NH_2, CO_2H, CO_2Et, $NHCO_2C(CH_3)_3$, CF_3, methyl, ethyl, isopropyl, $CO_2C(CH_3)_3$ and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3 and CHF_2;

X is —CH_2—;

R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4C)alkoxy, NH_2, NH(1-4C alkyl) and CH_2OH; and

n is 0, 1, or 2,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a cancer in a mammal in need thereof.

2. The use of claim 1, wherein the cancer exhibits one or more of overexpression, activation, amplification, and mutation of a Trk kinase.

3. The use of claim 2, wherein the Trk kinase is TrkA.

4. The use of claim 2, wherein the Trk kinase is TrkB.

5. The use of claim 2, wherein the Trk kinase is TrkA and TrkB.

6. The use of claim 2, wherein the Trk kinase is selected from one or more of: TrkA, TrkB, and TrkC.

7. The use of claim 1, wherein the cancer exhibits overexpression of a Trk kinase.

8. The use of claim 1, wherein the cancer exhibits activation of a Trk kinase.

9. The use of claim 1, wherein the cancer exhibits amplification of a Trk kinase.

10. The use of claim 1, wherein the cancer exhibits mutation of a Trk kinase.

11. The use of claim 1, wherein the cancer is a hematological malignancy.

12. The use of claim 12, wherein the cancer is selected from the group consisting of myeloma and lymphoma.

13. The use of claim 1, wherein the cancer is a solid tumor.

14. The use of claim 13, wherein the cancer is selected from the group consisting of a breast

cancer, a lung cancer, a renal cancer, a thyroid cancer, an ovarian cancer, a prostate cancer, a pancreatic cancer, and a colorectal cancer.

15. The use of claim 1, wherein the cancer is selected from the group consisting of a neuroblastoma, a multiple myeloma, an astrocytoma, a medulloblastoma, a glioma, a melanoma, a thyroid carcinoma, a lung adenocarcinoma, a bone metastasis, and a large cell neuroendocrine tumor.

16. The use of claim 15, wherein the cancer is a lung adenocarcinoma.

17. The use of claim 1, wherein the mammal is to be further treated with a second therapy selected from the group consisting of surgery, radiotherapy, chemotherapy, a signal transduction inhibitor, or a monoclonal antibody.

18. The use of claim 1, wherein the medicament is to be further administered with a second agent selected from the group consisting of a mitotic inhibitor, an alkylating agent, an anti-metabolite, an antisense DNA, an antisense RNA, an intercalating antibiotic, a growth factor inhibitor, a signal transduction inhibitor, a cell cycle inhibitor, an enzyme inhibitor, a retinoid receptor modulator, a proteasome inhibitor, a topoisomerase inhibitor, a biological response modifier, an anti-hormone, an angiogenesis inhibitor, a cytostatic agent, an anti-androgen, a targeted antibody, a HMG-CoA reductase inhibitor, and a prenyl-protein transferase inhibitor.

19. The use of claim 1, wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered orally.

20. The use of claim 1, wherein Y is phenyl optionally substituted with one or more halogen atoms.

21. The use of claim 20, wherein Y is phenyl optionally substituted with one or two fluorine atoms.

22. The use of claim 1, wherein n is zero or one.

23. The use of claim 22, wherein R^3 is hydrogen.

24. The use of claim 23, wherein R^1 is hydrogen.

25. The use of claim 1, wherein the compound of Formula (I) is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

26. The use of claim 25, wherein the compound of Formula (I) is a sulfate salt.

27. The use of claim 1, wherein the compound of Formula (I) is selected from the group consisting of:

(R)-N-(5-(2-(3-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(3R,4R)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3,4-dihydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(S)-tert-butyl 4-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-ylcarbamoyl)-2-methylpiperazine-1-carboxylate;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-methylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-isopropylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-ethylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-

methylpiperazine-1-carboxamide;

N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3,5-dimethylpiperazine-1-carboxamide;

(S)-tert-butyl 4-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-ylcarbamoyl)-2-methylpiperazine-1-carboxylate;

(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-methylpiperazine-1-carboxamide hydrochloride;

(S)-N-(5-((R)-2-(3-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)ppyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-y1)-4-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-

a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-methoxyphenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5((R)-2-(5-fluoro-2-methoxypheny)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

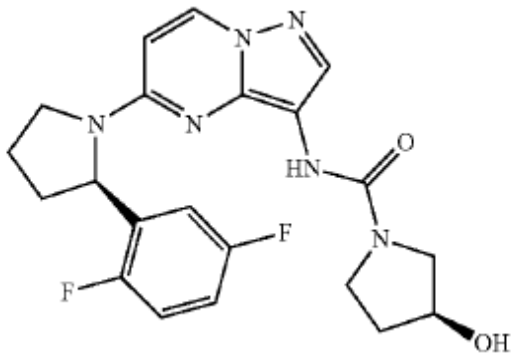
(R)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

or a pharmaceutically acceptable salt thereof.

28. The use of claim 27, wherein the compound of Formula (I) is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

29. The use of claim 28, wherein the compound of Formula (I) is a sulfate salt.

30. Use of a compound:

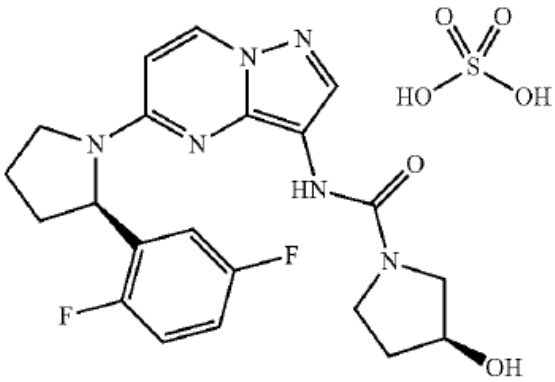


(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide, or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a cancer in a mammal.

31. The use of claim 30, wherein the compound is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

32. The use of claim 31, wherein the compound is:



(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide sulfate.

33. The use of claim 30, wherein the cancer is associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase.

34. The use of claim 32, wherein the Trk kinase is TrkA.

35. The use of claim 33, wherein the Trk kinase is TrkB.

36. The use of claim 33, wherein the Trk kinase is TrkA and TrkB.

37. The use of claim 33, wherein the Trk kinase is selected from one or more of: TrkA, TrkB, and TrkC.

38. The use of claim 30, wherein the cancer exhibits overexpression of a Trk kinase.

39. The use of claim 30, wherein the cancer exhibits activation of a Trk kinase.

40. The use of claim 30, wherein the cancer exhibits amplification of a Trk kinase.

41. The use of claim 30, wherein the cancer exhibits mutation of a Trk kinase.

42. The use of claim 30, wherein the cancer is a hematological malignancy.

43. The use of claim 42, wherein the cancer is selected from the group consisting of: myeloma and lymphoma.

44. The use of claim 30, wherein the cancer is a solid tumor.

45. The use of claim 44, wherein the cancer is selected from the group consisting of: a breast cancer, a lung cancer, a renal cancer, a thyroid cancer, an ovarian cancer, a prostate cancer, a pancreatic cancer, and a colorectal cancer.

46. The use of claim 30, wherein the cancer is selected from the group consisting of: a neuroblastoma, a multiple myeloma, an astrocytoma, a medulloblastoma, a glioma, a melanoma, a thyroid carcinoma, a lung adenocarcinoma, a brain metastasis, and a large cell neuroendocrine tumor.

47. The use of claim 46, wherein the cancer is a lung adenocarcinoma.

48. The use of claim 30, wherein the mammal is to be further treated with a second therapy selected from the group consisting of surgery, radiotherapy, chemotherapy, a signal transduction inhibitor, or a monoclonal antibody.

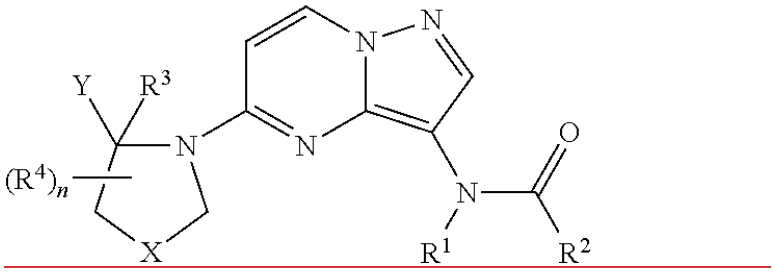
49. The use of claim 30, wherein the medicament is to be further administered with a second agent selected from the group consisting of a mitotic inhibitor, an alkylating agent, an anti-metabolite, an antisense DNA, an antisense RNA, an intercalating antibiotic, a growth factor inhibitor, a signal transduction inhibitor, a cell cycle inhibitor, an enzyme inhibitor, a retinoid receptor modulator, a proteasome inhibitor, a topoisomerase inhibitor, a biological response modifier, an anti-hormone, an angiogenesis inhibitor, a cytostatic agent, an anti-androgen, a targeted antibody, a HMG-CoA reductase inhibitor, and a

prenyl-protein transferase inhibitor.

50. The use of claim 30, wherein the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally.

51. Use of a compound of Formula (I):

I



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H or (1-6C alkyl);

R^2 is NR^bR^c;

NR^bR^c forms a 5-6 membered heterocyclic ring having a ring heteroatom which is nitrogen and optionally having a second ring heteroatom or group selected from N, O and SO_2, wherein the heterocyclic ring formed by NR^bR^c is optionally substituted with one or two substituents independently selected from OH, F, NH_2, CO_2H, CO_2Et, $NHCO_2C(CH_3)_3$, CF_3, methyl, ethyl, isopropyl, $CO_2C(CH_3)_3$, and oxo;

Y is phenyl optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkoxy, CF_3, and CHF_2;

X is —CH_2—;

R^3 is H or (1-4C alkyl);

each R^4 is independently selected from halogen, (1-4C)alkyl, OH, (1-4C)alkoxy, NH_2, NH(1-4C alkyl), and CH_2OH; and

n is 0, 1, or 2,

in the manufacture of a medicament for attenuating or ameliorating one or more symptoms of a lung cancer that exhibits one or more of an overexpression, activation, amplification and mutation of a Trk kinase in a mammal in need thereof.

52. The use of claim 51, wherein the Trk kinase is TrkA.

53. The use of claim 51, wherein the Trk kinase is TrkB.

54. The use of claim 51, wherein the Trk kinase is TrkA and TrkB.

55. The use of claim 51, wherein the Trk kinase is selected from one or more of: TrkA, TrkB, and TrkC.

56. The use of claim 51, wherein the cancer exhibits overexpression of a Trk kinase.

57. The use of claim 51, wherein the cancer exhibits activation of a Trk kinase.

58. The use of claim 51, wherein the cancer exhibits amplification of a Trk kinase.

59. The use of claim 51, wherein the cancer exhibits mutation of a Trk kinase.

60. The use of claim 51, wherein the lung cancer is a lung adenocarcinoma.

61. The use of claim 51, wherein the mammal is to be further treated with a second therapy selected from the group consisting of: surgery, radiotherapy, chemotherapy, a signal transduction inhibitor, or a monoclonal antibody.

62. The use of claim 51, wherein the medicament is to be further administered with a second agent selected from the group consisting of: a mitotic inhibitor, an alkylating agent, an anti-metabolite, an antisense DNA, an antisense RNA, an intercalating antibiotic, a growth factor inhibitor, a signal transduction inhibitor, a cell cycle inhibitor, an enzyme inhibitor, a retinoid receptor modulator, a proteasome inhibitor, a topoisomerase inhibitor, a biological response modifier, an anti-hormone, an angiogenesis inhibitor, a cytostatic agent, an anti-androgen, a targeted antibody, a HMG-CoA reductase inhibitor, and a prenyl-protein transferase inhibitor.

63. The use of claim 51, wherein the compound of Formula (I), or a pharmaceutically

acceptable salt thereof, is to be administered orally.

64. The use of claim 51, wherein Y is phenyl optionally substituted with one or more halogen atoms.

65. The use of claim 64, wherein Y is phenyl optionally substituted with one or two fluorine atoms.

66. The use of claim 51, wherein n is zero or one.

67. The use of claim 66, wherein R^3 is hydrogen.

68. The use of claim 67, wherein R^1 is hydrogen.

69. The use of claim 51, wherein the compound of Formula (I) is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

70. The use of claim 69, wherein the compound of Formula (I) is a sulfate salt.

71. The use of claim 51, wherein the compound of Formula (I) is selected from the group consisting of:

(R)-N-(5-(2-(3-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(3R,4R)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3,4-dihydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)morpholine-4-carboxamide;

(S)-tert-butyl 4-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-

a]pyrimidin-3-ylcarbamoyl)-2-methylpiperazine-1-carboxylate;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-methylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-isopropylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-ethylpiperazine-1-carboxamide;

(R)-N-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-methylpiperazine-1-carboxamide;

N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3,5-dimethylpiperazine-1-carboxamide;

(S)-tert-butyl 4-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-ylcarbamoyl)-2-methylpiperazine-1-carboxylate;

(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-methylpiperazine-1-carboxamide hydrochloride;

(S)-N-(5-((R)-2-(3-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)ppyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-y1)-4-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-(difluoromethyl)-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-(2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-4-hydroxypiperidine-1-carboxamide;

(R)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-

3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(2-chloro-5-fluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(R)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-(trifluoromethyl)phenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

(S)-N-(5-((R)-2-(5-fluoro-2-methoxyphenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

(S)-N-(5((R)-2-(5-fluoro-2-methoxypheny)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypiperidine-1-carboxamide;

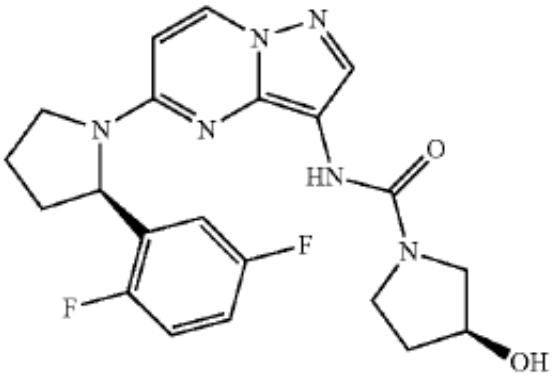
(R)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide;

or a pharmaceutically acceptable salt thereof.

72. The use of claim 71, wherein the compound of Formula (I) is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

73. The use of claim 72, wherein the compound of Formula (I) is a sulfate salt.

74. Use of a compound:

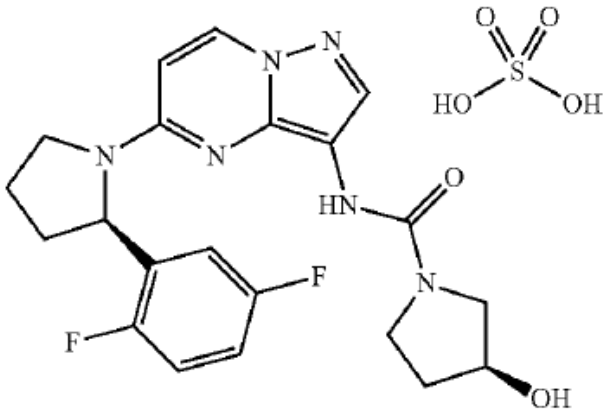


(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide, or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for treating a lung cancer that exhibits one or more of an overexpression, activation, amplification and mutation of a Trk kinase in a mammal in need thereof.

75. The use of claim 74, wherein the compound is a trifluoroacetate salt, a sulfate salt, or a hydrochloride salt.

76. The use of claim 75, wherein the compound is:



(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide sulfate.

77. The use of claim 74, wherein the Trk kinase is TrkA.

78. The use of claim 74, wherein the Trk kinase is TrkB.

79. The use of claim 74, wherein the Trk kinase is TrkA and TrkB.

80. The use of claim 74, wherein the lung cancer is a lung adenocarcinoma.

81. The use of claim 74, wherein the mammal is to be further treated with a second therapy selected from the group consisting of: surgery, radiotherapy, chemotherapy, a signal transduction inhibitor, or a monoclonal antibody.

82. The use of claim 74, wherein the medicament is to be further administered with a second agent selected from the group consisting of: a mitotic inhibitor, an alkylating agent, an anti-metabolite, an antisense DNA, an antisense RNA, an intercalating antibiotic, a growth factor inhibitor, a signal transduction inhibitor, a cell cycle inhibitor, an enzyme inhibitor, a retinoid receptor modulator, a proteasome inhibitor, a topoisomerase inhibitor, a biological response modifier, an anti-hormone, an angiogenesis inhibitor, a cytostatic agent, an anti-androgen, a targeted antibody, a HMG-CoA reductase inhibitor, and a prenyl-protein transferase inhibitor.

83. The use of claim 74, wherein the compound, or a pharmaceutically acceptable salt thereof, is to be administered orally.