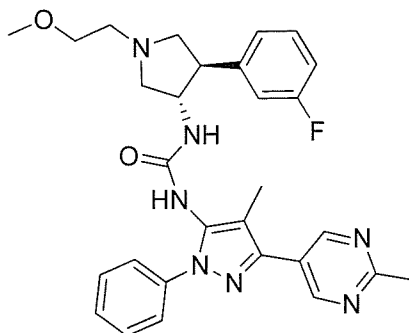


CLAIMS

1. A Compound



1-((3S,4R)-4-(3-fluorophenyl)-1-(2-methoxyethyl)pyrrolidin-3-yl)-3-(4-methyl-3-(2-methylpyrimidin-5-yl)-1-phenyl-1H-pyrazol-5-yl)urea, or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein the compound is a dihydrochloride salt of 1-((3S,4R)-4-(3-fluorophenyl)-1-(2-methoxyethyl)pyrrolidin-3-yl)-3-(4-methyl-3-(2-methylpyrimidin-5-yl)-1-phenyl-1H-pyrazol-5-yl)urea.

3. A pharmaceutical composition, which comprises a compound of claim 1 or 2, and a pharmaceutically acceptable diluent or carrier.

4. The pharmaceutical composition according to claim 3, wherein said pharmaceutical composition is formulated for oral administration.

5. The pharmaceutical composition according to claim 4, wherein said pharmaceutical composition is in the form of a tablet or capsule.

6. The compound according to claim 1 or 2 for use in the treatment of a disease or disorder selected from the group consisting of pain, cancer, inflammation or an inflammatory diseases, neurodegenerative diseases, certain infectious diseases, Sjogren's syndrome, endometriosis, diabetic peripheral neuropathy, prostatitis, pelvic pain syndrome,

diseases related to an imbalance of the regulation of bone remodeling, and diseases resulting from Connective Tissue Growth Factor aberrant signaling.

7. The compound for use according to claim 6, wherein the disorder is pain.
8. The compound for use according to claim 7, wherein said pain is chronic pain.
9. The compound for use according to claim 8, wherein said chronic pain is chronic back pain.
10. The compound for use according to claim 7, wherein said pain is acute pain.
11. The compound for use according to claim 7, wherein said pain is selected from the group consisting of neuropathic pain, inflammatory pain, pain associated with cancer, pain associated with bone fracture, and pain associated with surgery.
12. The compound for use according to claim 11, wherein said pain is neuropathic pain.
13. The compound for use according to claim 12, wherein said neuropathic pain is pain associated with diabetic peripheral neuropathy.
14. The compound for use according to claim 11, wherein said pain is inflammatory pain.
15. The compound for use according to claim 14, wherein said inflammatory pain is pain associated with osteoarthritis.
16. The compound for use according to claim 11, wherein said pain is pain associated with cancer.

17. The compound for use according to claim 11, wherein said pain is pain associated with bone fracture.

18. The compound for use according to claim 11, wherein said pain is pain associated with surgery.

19. The compound for use according to any one of claims 7-18, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered in combination with an effective amount of at least one additional therapeutic agent selected from the group consisting of anti-inflammatory compounds, steroids, analgesics, opioids, calcitonin gene-related peptide receptor antagonists, subtype-selective ion channel modulators, anticonvulsants, dual serotonin-norepinephrine reuptake inhibitors, JAK family kinase inhibitors, and tricyclic antidepressants.

20. The compound for use according to claim 19, wherein the analgesic is an NSAID.

21. The compound for use according to claim 6, wherein said disease is an inflammatory disease.

22. The compound for use according to claim 21, wherein the inflammatory disease is selected from the group consisting of inflammatory lung diseases, interstitial cystitis, painful bladder syndrome, inflammatory bowel diseases, and inflammatory skin diseases.

23. The compound for use according to claim 22, wherein the inflammatory disease is interstitial cystitis.

24. The compound for use according to claim 22, wherein the inflammatory disease is painful bladder syndrome.

25. The compound for use according to any one of claims 21-24, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered in combination with an effective amount of one or more additional agents selected from the group consisting of anti-TNF agents, antimetabolite and antifolate drugs, and targeted kinase inhibitors.

26. The compound for use according to claim 25, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered in combination with an effective amount of one or more additional agents selected from the group consisting of infliximab, adalimumab, certolizumab pegol, golimumab, etanercept, Methotrexate, Ruxolitinib, Tofacitinib, CYT387, Lestaurtinib, Pacritinib and TG101348.

27. The compound for use according to claim 6, wherein the disease is a disease resulting from Connective Tissue Growth Factor aberrant signaling.

28. The compound for use according to claim 27, wherein the disease is selected from the group consisting of Raynaud's Syndrome, Idiopathic pulmonary fibrosis, scarring (hypertrophic, keloid and others), cirrhosis, endomyocardial fibrosis, atrial fibrosis, myelofibrosis, progressive massive fibrosis (lung), nephrogenic systemic fibrosis, scleroderma, systemic sclerosis, arthrofibrosis, and ocular fibrosis.

29. The compound for use according to claim 6, wherein said disease is cancer.

30. The compound for use according to claim 29, wherein said cancer is a cancer having a dysregulation of TrkA.

31. The compound for use according to claim 30, wherein the dysregulation of TrkA comprises one or more chromosome translocations or inversions resulting in TrkA gene fusions.

32. The compound for use according to claim 31, wherein the TrkA gene fusion is LMNA-TrkA, TFG-TrkA, TPM3-TrkA, CD74-TrkA, NFASC-TrkA, MPRIP-TrkA, BCAN-

TrkA, TP53-TrkA, RNF213-TrkA, RABGAP1L-TrkA, IRF2BP2-TrkA, SQSTM1-TrkA, SSBP2-TrkA, or TPR-TrkA.

33. The compound for use according to claim 32, wherein said cancer is non-small cell lung cancer, papillary thyroid carcinoma, glioblastoma multiforme, colorectal carcinoma, melanoma, cholangiocarcinoma, or sarcoma.

34. The compound for use according to claim 30, wherein the dysregulation of TrkA comprises one or more deletions, insertions or mutations in the TrkA protein.

35. The compound for use according to claim 34, wherein said cancer is acute myeloid leukemia, large cell neuroendocrine carcinoma, or neuroblastoma.

36. The compound for use according to claim 30, wherein the dysregulation of TrkA is overexpression of wild-type TrkA (autocrine activation).

37. The compound for use according to claim 36, wherein the cancer is prostate carcinoma, neuroblastoma, pancreatic carcinoma, melanoma, head and neck squamous cell carcinoma, or gastric carcinoma.

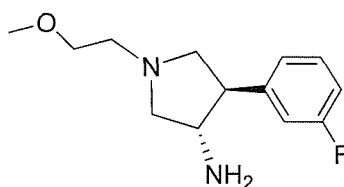
38. The compound for use according to any one of claims 29-37, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered in combination with an effective amount of at least one additional therapeutic agent selected from one or more additional therapy or chemotherapeutic agent.

39. The compound for use according to claim 38, wherein said additional therapy or chemotherapeutic agent is selected from radiotherapy, cytotoxic chemotherapeutics, tyrosine kinase targeted-therapeutics, apoptosis modulators, signal transduction inhibitors, immune-targeted therapies and angiogenesis-targeted therapies.

40. The compound for use according to claim 39 wherein said chemotherapeutic agent is selected from tyrosine kinase targeted-therapeutics.

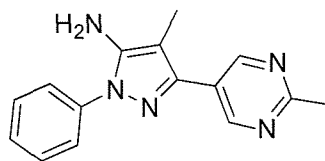
41. Use of the compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating pain, cancer, inflammation/inflammatory diseases, neurodegenerative diseases, certain infectious diseases, Sjogren's syndrome, endometriosis, diabetic peripheral neuropathy, prostatitis, pelvic pain syndrome, diseases related to an imbalance of the regulation of bone remodeling, or diseases resulting from Connective Tissue Growth Factor aberrant signaling.

42. A process for the preparation of a compound of claim 1 or 2, which comprises:
(a) reacting a compound having the formula **II-A**



II-A

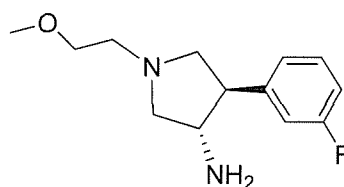
with a compound having the formula **III**



III

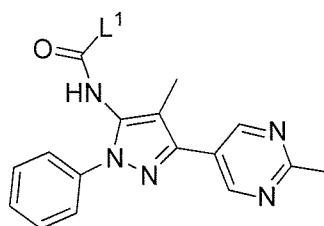
in the presence carbonyldiimidazole or triphosgene and a base; or

(b) reacting a compound having the formula **II-A**



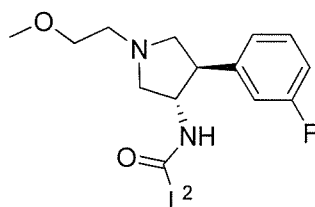
II-A

with a compound having the formula **IV**

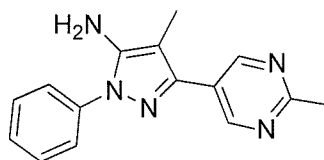
**IV**

where L^1 is a leaving group, in the presence of a base; or

(c) reacting a compound having the formula **V**

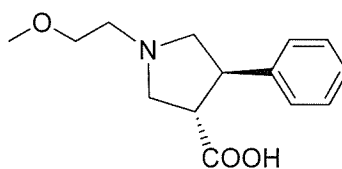
**V**

where L^2 is a leaving group, with a compound having the formula **III**

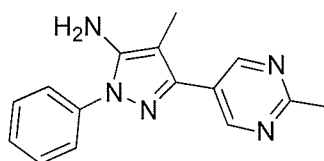
**III**

in the presence of a base; or

(d) reacting a compound having the formula **VI**

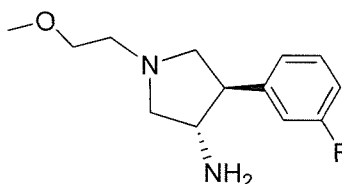
**VI**

with diphenylphosphoryl azide to form an intermediate, followed by reacting the intermediate with a compound having the formula **III**

**III**

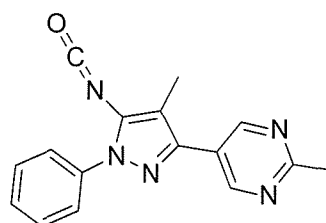
in the presence a base; or

(e) reacting a compound having the formula **II-A**



II-A

with a compound having the formula **VII**

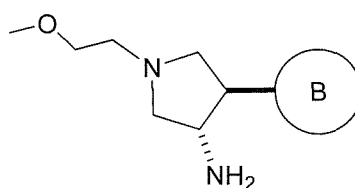


VII

in the presence of a base; and

removing and protecting groups if present and optionally preparing a pharmaceutically acceptable salt thereof.

43. A process for preparing a racemic mixture of a compound of Formula **II**



II

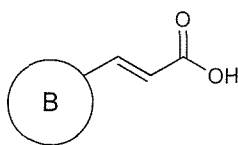
wherein:

Ring B is Ar¹ or hetAr¹;

Ar¹ is phenyl optionally substituted with one or more substituents independently selected from halogen, CF₃, CF₃O-, (1-4C)alkoxy, hydroxy(1-4C)alkyl, (1-6C)alkyl and CN; and

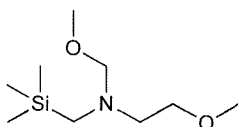
hetAr¹ is a 5-6 membered heteroaryl having 1-3 ring heteroatoms independently selected from N, S and O, and optionally substituted with 1-2 groups independently selected from (1-6C)alkyl, halogen, OH, CF₃, NH₂ and hydroxy(1-2C)alkyl, said process comprising:

(a) reacting a compound of formula **(a)**

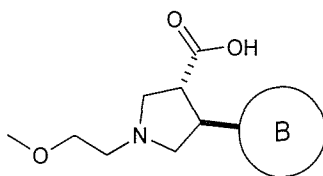


(a)

where Ring B is as defined for Formula **II**, with 2-methoxy-N-(methoxymethyl)-N-((trimethylsilyl)methyl)ethanamine having the formula



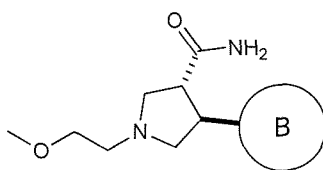
in the presence of a catalytic amount of acid, to provide a compound of formula (b)



(b)

where Ring B is as defined for Formula **II**;

(b) reacting said compound of formula (b) with carbonyl diimidazole in the presence of a catalytic amount of imidazole hydrochloride, followed by treatment with ammonia, to provide a compound having formula (c)



(c)

where Ring B is as defined for Formula **II**; and

(c) reacting said compound of formula (c) with sodium hypochlorite, followed by treatment with KOH, followed by treatment with HCl, to provide said compound of Formula **II** as a racemic mixture of *trans* Formula **II**.

44. The method according to claim 43, further comprising isolating enantiomer **1** of *trans* Formula **II** as the di-*p*-toluoyl-D-tartaric acid salt or as the free base, comprising:

treating racemic *trans* Formula **II** with di-*p*-toluoyl-D-tartaric acid to provide the di-*p*-toluoyl-D-tartaric acid salt of racemic *trans* **II**;

recrystallizing the di-p-toluoyl-D-tartaric acid salt of *trans* **II** to provide the di-p-toluoyl-D-tartaric acid salt of enantiomer **1** of *trans* **II**; and optionally

treating the di-p-toluoyl-D-tartaric acid salt of enantiomer **1** of *trans* **II** with an inorganic base to provide free base of enantiomer **1** of *trans* **II** having the absolute configuration as illustrated:

