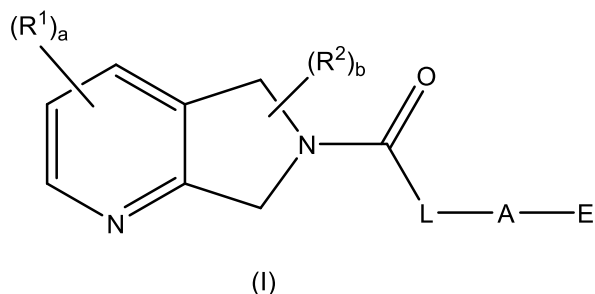


Claims

1. A compound of Formula (I):



or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein:

each R^1 , when present, is independently selected from the group consisting of halogen, cyano, hydroxy, $-SF_5$, nitro, 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) alkylthio, optionally substituted (C_1-C_6) alkoxy, optionally substituted (C_3-C_6) cycloalkyl, optionally substituted $-O-(C_3-C_6)$ cycloalkyl, $-N(R^3)(R^4)$, $-N(R^3)(C(=O)(R^4))$, $-C(=O)N(R^3)(R^4)$, $-O-C(=O)-N(R^3)(R^4)$, $-C(=O)-R^3$, and $-C(=O)-OR^3$;

a is an integer selected from 0, 1, 2, and 3;

each R^2 , when present, is independently selected from the group consisting of hydroxy, $-SF_5$, nitro, 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) alkylthio, optionally substituted (C_1-C_6) alkoxy, $-N(R^3)(R^4)$, $-N(R^3)(C(=O)(R^4))$, $-C(=O)N(R^3)(R^4)$, $-O-C(=O)-N(R^3)(R^4)$, $-C(=O)-R^3$, and $-C(=O)-OR^3$;

b is an integer selected from 0, 1, 2, 3, and 4;

L is selected from $-(CH_2)_m-$ and $-O-$, wherein m is an integer selected from 1 and 2;

A is absent or selected from the group consisting of (C_3-C_6) cycloalkyl and (4- to 10-membered)heterocycloalkyl, wherein said cycloalkyl and heterocycloalkyl are each optionally substituted with one to five substituents independently selected from the group consisting of halogen, cyano, hydroxy, $-SF_5$, nitro, 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)alkylthio, optionally substituted (C₁-C₆)alkoxy, -N(R³)(R⁴), -N(R³)(C(=O)(R⁴), -C(=O)N(R³)(R⁴), -O-C(=O)-N(R³)(R⁴), -C(=O)-R³, and -C(=O)-OR³;

E is selected from (C₃-C₁₂)cycloalkyl, (C₆-C₁₀)aryl and (5- to 10-membered)heteroaryl, wherein said cycloalkyl, aryl, and heteroaryl are optionally substituted with one to five substituents independently selected from the group consisting of halogen, cyano, hydroxy, -SF₅, nitro, optionally substituted (C₁-C₆)alkyl, optionally substituted (C₂-C₆)alkenyl, optionally substituted (C₂-C₆)alkynyl, optionally substituted (C₁-C₆)alkylthio, optionally substituted (C₁-C₆)alkoxy, optionally substituted (C₃-C₆)cycloalkyl, methyloxetanyl, -N(R³)(R⁴), -N(R³)(C(=O)R⁴), -C(=O)N(R³)(R⁴), -O-C(=O)-N(R³)(R⁴), -C(=O)-R³, and -C(=O)-OR³;

R³ and R⁴ at each occurrence are each independently selected from hydrogen and optionally substituted (C₁-C₆)alkyl; or R³ and R⁴ taken together with the nitrogen to which they are attached form an optionally substituted (4- to 6-membered)heterocycloalkyl.

wherein each occurrence of optionally substituted (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)alkylthio, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkyl, -O-(C₃-C₆)cycloalkyl and (4- to 6-membered)heterocycloalkyl is independently optionally substituted with a substituent selected from the group consisting of halogen, oxo, cyano, hydroxy, -SF₅, nitro, (C₁-C₆)alkyl, -(C₁-C₆)alkoxy, -N(R³)(R⁴), -N(R³)(C(=O)R⁴), -N(R³)C(=O)-OR⁴, -C(=O)-N(R³)(R⁴), -O-C(=O)-N(R³)(R⁴), -C(=O)-R³, -C(=O)-OR³, and (C₃-C₈)cycloalkyl; and

wherein each occurrence of optionally substituted (C₁-C₆)alkyl is independently optionally substituted with a substituent selected from the group consisting of halogen, oxo, cyano, hydroxy, -SF₅, nitro, -(C₁-C₆)alkoxy, -N(R³)(R⁴), -N(R³)(C(=O)R⁴), -N(R³)C(=O)-OR⁴, -C(=O)-N(R³)(R⁴), -O-C(=O)-N(R³)(R⁴), -C(=O)-R³, -C(=O)-OR³, and (C₃-C₈)cycloalkyl.

2. The compound according to claim 1, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein L is -(CH₂)_m- and m is an integer selected from 1 and 2.

3. The compound according to any one of claims 1-2, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein A is a (C₃-C₈)cycloalkyl selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, wherein said cycloalkyl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, -N(R³)(R⁴), optionally substituted (C₁-C₆)alkyl, and optionally substituted (C₁-C₆)alkoxy.

4. The compound according to claim 3, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein A is cyclopropyl.

5. The compound according to any one of claims 1-2, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein A is a (4- to 6-membered)heterocycloalkyl selected from the group consisting of azetidiny, dihydrofuranyl, dihydrothiophenyl, tetrahydrothiophenyl, tetrahydrofuranyl, tetrahydrotriazinyl, tetrahydropyrazolyl, tetrahydrooxazinyl, tetrahydropyrimidinyl, imidazolidinyl, pyrrolidinyl, piperidinyl, piperazinyl, oxazolidinyl, thiazolidinyl, pyrazolidinyl, tetrahydropyranyl, tetrahydrothiazinyl, tetrahydrothiadiazinyl, tetrahydrooxazolyl, oxetanyl, dioxetanyl, dioxolanyl, dioxanyl, oxazinyl, and oxathiazinyl, wherein said heterocycloalkyl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, -N(R³)(R⁴), optionally substituted (C₁-C₆)alkyl, and optionally substituted (C₁-C₆)alkoxy.

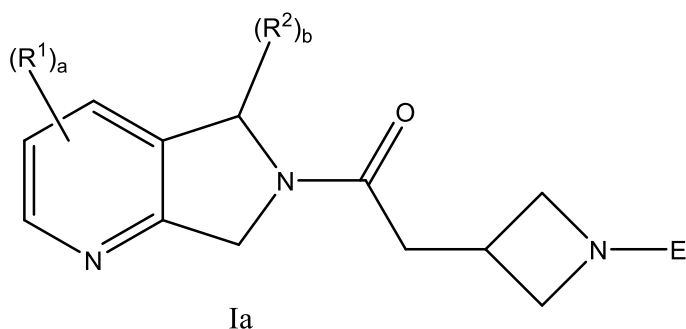
6. The compound according to claim 5, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein A is a (4- to 6-membered)heterocycloalkyl and the heterocycloalkyl is azetidiny.

7. The compound according to any one of claims 1-6, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein E is a (5- to 10-membered)heteroaryl selected from the group consisting of triazolyl, imidazolyl, furanyl, isoxazolyl, isothiazolyl, 1,2,3-, 1,2,4, 1,2,5-, or 1,3,4-oxadiazolyl,

oxazolyl, thiophenyl, thiazolyl, isothiazolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, benzofuranyl, benzimidazolyl, benzothienyl, benzoxadiazolyl, benzothiazolyl, isobenzothiofuranyl, benzothiofuranyl, benzisoxazolyl, benzoxazolyl, benzodioxolyl, furanopyridinyl, purinyl, imidazopyridinyl, imidazopyrimidinyl, pyrrolopyridinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, thienopyridinyl, triazolopyrimidinyl, triazolopyridinyl, anthranilyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, oxochromanyl, and 1,4-benzoxazinyl, wherein said heteroaryl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, $-N(R^3)(R^4)$, optionally substituted (C_1-C_6) alkyl, and optionally substituted (C_1-C_6) alkoxy.

8. The compound according to claim 7, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein the heteroaryl is a (5- to 6-membered)nitrogen-containing heteroaryl selected from the group consisting of triazolyl, imidazolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, and pyridazinyl, wherein said nitrogen-containing heteroaryl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, $-N(R^3)(R^4)$, optionally substituted (C_1-C_6) alkyl, and optionally substituted (C_1-C_6) alkoxy.

9. The compound according to claim 1, wherein the compound has a structure according to Formula Ia:



or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein:

each R^1 , when present, is independently selected from the group consisting of halogen, optionally substituted (C_1-C_6) alkyl, and optionally substituted (C_1-C_6) alkoxy;

a is an integer selected from 1, 2 and 3;

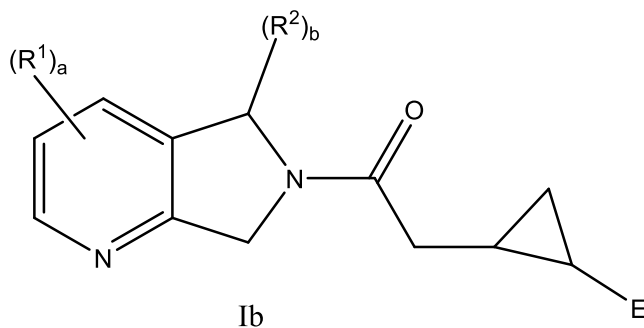
R^2 , when present, is an optionally substituted (C_1-C_6) alkyl;

b is an integer selected from 0 and 1;

E is a (5- to 6-membered)heteroaryl, wherein said heteroaryl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, optionally substituted (C_1-C_6) alkyl, optionally substituted (C_1-C_6) alkoxy, and $-N(R^3)(R^4)$, wherein R^3 and R^4 at each occurrence are each independently selected from hydrogen and optionally substituted (C_1-C_6) alkyl.

10. The compound according to claim 9, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein, E is a (5- to 6-membered)nitrogen-containing heteroaryl selected from the group consisting of pyrazolyl, thiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, and pyrazinyl.

11. The compound according to claim 1, wherein the compound has a structure according to Formula Ib:



or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein:

each R^1 , when present, is independently selected from the group consisting of halogen, optionally substituted (C_1-C_6) alkyl, and optionally substituted (C_1-C_6) alkoxy;

a is an integer selected from 1, 2 and 3;

R^2 , when present, is an optionally substituted (C_1-C_6) alkyl;

b is an integer selected from 0 and 1;

E is a (5- to 6-membered)heteroaryl, wherein said heteroaryl is optionally substituted with one to three substituents independently selected from the group consisting of halogen, cyano, hydroxy, optionally substituted (C₁-C₆)alkyl, optionally substituted (C₁-C₆)alkoxy, and -N(R³)(R⁴), wherein R³ and R⁴ at each occurrence are each independently selected from hydrogen and optionally substituted (C₁-C₆)alkyl.

12. The compound according to claim 11, or an *N*-oxide thereof, or a pharmaceutically acceptable salt of the compound or the *N*-oxide, wherein, E is a (5- to 6-membered)nitrogen-containing heteroaryl selected from the group consisting of pyrazolyl, thiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, and pyrazinyl.

13. The compound according to claim 1, wherein the compound is selected from the group consisting of 1-(2,4-Dimethyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl)-2-[1-(pyridin-3-yl)azetidin-3-yl]ethanone,

1-[2-(Methoxymethyl)-4-methyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl]-2-{1-[2-(trifluoromethyl)pyridin-4-yl]azetidin-3-yl}ethenone,

1-(2,4-Dimethyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl)-2-{1-[2-(trifluoromethyl)pyridin-4-yl]azetidin-3-yl}ethenone,

1-(3-Chloro-2,4-dimethyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl)-2-{1-[2-(difluoromethyl)pyridin-4-yl]azetidin-3-yl}ethenone,

1-[3-chloro-2-(methoxymethyl)-4-methyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl]-2-{1-[2-(difluoromethyl)pyridin-4-yl]azetidin-3-yl}ethenone,

1-(3-chloro-2,4-dimethyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl)-2-[trans-2-(pyrimidin-5-yl)cyclopropyl]ethanone, and

1-[2-(hydroxymethyl)-4-methyl-5,7-dihydro-6H-pyrrolo[3,4-*b*]pyridin-6-yl]-2-{1-[2-(trifluoromethyl)pyridin-4-yl]azetidin-3-yl}ethanone

or an *N*-oxide thereof, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt of the *N*-oxide.

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound, or *N*-oxide, or pharmaceutically acceptable salt of any one of claims 1 to 13, and a pharmaceutically acceptable carrier.

15. A compound, or *N*-oxide, or pharmaceutically acceptable salt of any one of claims 1 to 13, or the pharmaceutical composition according to claim 14 for use in the treatment of an M4-mediated (or M4-associated) disease or disorder.

16. Use of a compound, or *N*-oxide, or pharmaceutically acceptable salt of any one of claims 1 to 13, or the pharmaceutical composition according to claim 14 in the manufacture of a medicament for the treatment of an M4-mediated (or M4-associated) disease or disorder.

17. The use of claim 16, wherein the M4-mediated (or M4-associated) disease or disorder is a disease or disorder selected from the group consisting of Alzheimer's Disease, schizophrenia or psychosis, pain, addiction, a sleep disorder, a cognitive disorder (e.g. mild cognitive impairment), Parkinson's Disease, Parkinson's Disease-levodopa-induced dyskinesia, Huntington's Disease, dyskinesia, dry mouth, pulmonary hypertension, chronic obstructive pulmonary disease (COPD), asthma, urinary incontinence, glaucoma, Trisomy 21 (Down Syndrome), cerebral amyloid angiopathy, dementia, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type (HCHWA-D), Creutzfeld-Jakob disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stroke, pancreatitis, inclusion body myositis, other peripheral amyloidoses, diabetes, autism, and atherosclerosis.

18. The use of claim 16, wherein the M4-mediated (or M4-associated) disease or disorder is a disease or disorder selected from the group consisting of Alzheimer's Disease, schizophrenia, pain, addiction, and a sleep disorder.