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- *Zhang, Liu, et al. "Methyltransferase-like 3 silenced inhibited the ferroptosis development via regulating the glutathione peroxidase 4 levels in the intracerebral hemorrhage progression." Bioengineered 13.6 (2022): 14215-14226.*
- *Wu, Xun, et al. "The m6A methyltransferase METTL3 drives neuroinflammation and neurotoxicity through stabilizing BATF mRNA in microglia." Cell Death & Differentiation (2024): 1-18.*
- *Chen, Xuechai, et al. "Down-regulation of m6A mRNA methylation is involved in dopaminergic neuronal death." ACS chemical neuroscience 10.5 (2019): 2355-2363.*
- *Xu, Huan, et al. "m6A mRNA methylation is essential for oligodendrocyte maturation and CNS myelination." Neuron 105.2 (2020): 293-309.*
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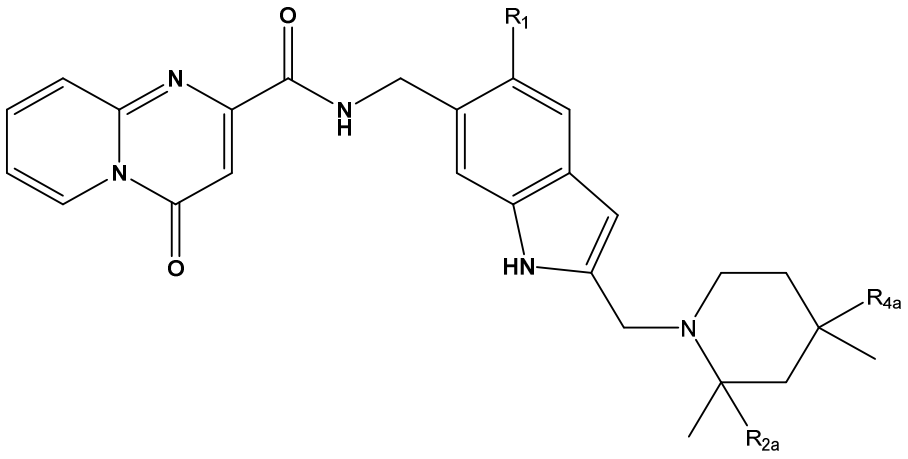
SUMMARY

[0033] In one example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof. In one aspect, the present disclosure provides a compound of formula (I) shown below, or a pharmaceutically acceptable salt thereof:



(I)

wherein: R_1 is selected from hydrogen, chloro or fluoro; R_{2a} is hydrogen or methyl; and R_{4a} is hydrogen or methyl; wherein only one of R_{2a} and R_{4a} may be methyl. In another aspect, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from any one of the following: N-((2-(((2R,4R)-2,4-dimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2S,4S)-2,4-

dimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (R)-4-oxo-N-((2-((2,2,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (S)-4-oxo-N-((2-((2,2,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2R,4R)-4-methyl-2-(methyl-d3)piperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2S,4S)-4-methyl-2-(methyl-d3)piperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (R)-4-oxo-N-((2-((2,4,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (S)-4-oxo-N-((2-((2,4,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2R,4R)-2,4-dimethylpiperidin-1-yl)methyl)-5-fluoro-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2S,SR)-2,4-dimethylpiperidin-1-yl)methyl)-5-fluoro-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (R)-N-((5-fluoro-2-((2,4,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (S)-N-((5-fluoro-2-((2,4,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (S)-N-((5-fluoro-2-((2,2,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((2-(((2S,4S)-2,4-dimethylpiperidin-1-yl)methyl)-5-fluoro-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; (R)-N-((5-fluoro-2-((2,2,4-trimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((5-fluoro-2-(((2R,4R)-4-methyl-2-(methyl-d3)piperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; N-((5-fluoro-2-(((2S,4S)-4-methyl-2-(methyl-d3)piperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; or N-((5-chloro-2-(((2S,4S)-2,4-dimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide. In yet another aspect, the present disclosure provides a compound which is N-((2-(((2S,4S)-2,4-dimethylpiperidin-1-yl)methyl)-1H-indol-6-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide, or a pharmaceutically acceptable salt thereof.

[0034] In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients. In another example, the present disclosure provides a pharmaceutical composition as defined herein which comprises a compound as defined herein, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

[0035] In another aspect, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in therapy.

[0036] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a proliferative condition.

[0037] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of cancer. In a particular example, the cancer is a human cancer.

[0038] In particular example, the cancer is a cancer of the CNS. Cancers of the CNS include but are not limited to Glioma, Glioblastoma Multiforme (GBM), Astrocytomas, Oligodendrogliomas, Ependyomas, Meningiomas, other brain neoplasms or secondary tumours that have metastasized to the brain.

[0039] In another particular example, the cancer is leukaemia (e.g. acute myeloid leukaemia (AML), acute lymphocytic leukaemia (ALL), chronic myeloid leukaemia or chronic lymphocytic leukaemia (CLL)).

[0040] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the inhibition of METTL3 activity.

[0041] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of disorder of the CNS.

[0042] The disorder of the CNS may be a neurodegenerative disorder, for example a tauopathy, a motor neuron disease (including ALS), a repeat expansion disease (such as Huntington's Disease), dementia (including frontotemporal dementia, vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease), Parkinson's Disease or multiple sclerosis.

[0043] The disorder of the CNS may be epilepsy.

[0044] Tauopathies are progressive neurodegenerative disorders that are pathologically defined by tau-positive deposits in the brain. Tauopathies include but are not limited to Alzheimer's disease, progressive supranuclear palsy, corticobasal syndrome, frontotemporal dementias, Pick's disease, globular glial tauopathy, argyrophilic grain disease, aging-related tau astrogliopathy, primary age-related tauopathy and chronic traumatic encephalopathy.

[0045] Motor neuron diseases (MNDs) are a group of progressive neurological disorders that destroy motor neurons, the cells that control skeletal muscle activity such as walking, breathing, speaking, and swallowing. This group includes diseases such as amyotrophic lateral sclerosis, progressive bulbar palsy, primary lateral sclerosis, progressive muscular atrophy, spinal muscular atrophy, Kennedy's disease, and post-polio syndrome. MNDs are also linked to frontotemporal dementia. The term "motor neuron disease" is often used interchangeably with amyotrophic lateral sclerosis because ALS is the most common adult-onset presentation of this disease.

[0046] Suitably, the motor neuron disease is selected from amyotrophic lateral sclerosis, progressive bulbar palsy, primary lateral sclerosis, progressive muscular atrophy, spinal muscular atrophy, Kennedy's disease, and post-polio syndrome. In the context of the present disclosure, the treatment of a motor neuron disease also encompasses the treatment of frontotemperal dementia linked to motor neuron disease.

[0047] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a motor neuron disease (including ALS).

[0048] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a repeat expansion disease. Suitably, the repeat expansion disease is Huntington's Disease.

[0049] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of dementia. Suitably, the dementia is selected from frontotemporal dementia (including MND related frontotemporal dementia), vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease,

[0050] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of Parkinson's Disease

[0051] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of multiple sclerosis.

[0052] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of epilepsy.

[0053] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a disease related to the inactivation of the X-chromosome. Suitably, the disease related to the inactivation of the X-chromosome is selected from Adrenal hypoplasia; siderius X-linked mental retardation syndrome; Agammaglobulinaemia, Bruton type; Choroidoretinal degeneration; Choroidaemia; Albinism, ocular; Dent's disease 2; fragile X syndrome; Rett/ Epileptic encephalopathy, early infantile, 2 (CDKL5 deficiency disorder); Albinism-deafness syndrome; paroxysmal nocturnal hemoglobinuria; Aldrich syndrome; Alport syndrome; Anaemia, hereditary hypochromic; Anemia, sideroblastic, with ataxia; Fabry disease; Spinal muscular atrophy 2; Cataract, congenital; Charcot-Marie-Tooth, peroneal; Spastic paraplegia; Colour blindness; Diabetes insipidus, nephrogenic; DDX3X syndrome; Dyskeratosis congenita; Ectodermal dysplasia, anhidrotic; Faciogenital dysplasia (Aarskog syndrome); Glucose-6-phosphate dehydrogenase deficiency; Glycogen storage disease type VIII; Gonadal dysgenesis (XY female type); Granul omatous disease (chronic); Haemophilia

A; Haemophilia B; Hydrocephalus (aqueduct stenosis); Hypophosphataemic rickets; Lesch-Nyhan syndrome (hypoxanthine-guanine-phosphoribosyl transferase deficiency); Incontinentia pigmenti; Kallmann syndrome; Keratosis follicularis spinulosa; Lowe (oculocerebrorenal) syndrome; Menkes syndrome; Renpenning Syndrome; Mental retardation, with or without fragile site (numerous specific types); Coffin-Lowry syndrome; Microphthalmia with multiple anomalies (Lenz syndrome); Muscular dystrophy (Becker, Duchenne and Emery-Dreifuss types); Myotubular myopathy; Night blindness, congenital stationary; Norrie's disease (pseudoglioma); Nystagmus, oculomotor or 'jerky'; Orofaciodigital syndrome (type I); Omithine transcarbamylase deficiency (type I hyperammonaemia); Phosphoglycerate kinase deficiency; Phosphoribosylpyrophosphate synthetase deficiency; Retinitis pigmentosa; Retinoschisis; Rett syndrome; Muscular atrophy; Dihydrotestosterone receptor deficiency; Spinal muscular atrophy; Spondyloepiphyseal dysplasia tarda; Thrombocytopenia, hereditary; Thyroxine-binding globulin, absence; or McLeod syndrome. More suitably, the disease related to the inactivation of the X-chromosome is RETT syndrome.

[0054] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in reactivating expression of a silenced X-chromosome.

[0055] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of RETT syndrome.

[0056] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in promoting an immune response (e.g. anti-viral or anti-tumour immune response).

[0057] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in increasing an innate immune response in a subject.

[0058] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in increasing or enhancing an anti-tumour immune response during immune-oncology therapy.

[0059] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an autoimmune disease.

[0060] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a neurological disease.

[0061] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an infectious disease.

[0062] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a viral infection. Suitably, the viral infection is a RNA viral infection. Suitably, the viral infection is human papillomavirus (HPV) or hepatitis.

[0063] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an inflammatory disease.

[0064] In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, in the manufacture of a medicament for the treatment of a proliferative condition. In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a proliferative condition.

[0065] In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, in the manufacture of a medicament for the treatment of cancer. In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of cancer. In a particular example, the medicament is for use in the treatment of human cancers. The cancer may be any of the cancers described herein.

[0066] In a particular example, the medicament is for use in the treatment of a cancer of the CNS. Cancers of the CNS include but are not limited to Glioma, Glioblastoma Multiforme (GBM), Astrocytomas, Oligodendrogliomas, Ependyomas, Meningiomas, other brain neoplasms or secondary tumours that have metastasized to the brain.

[0067] In a particular example, the medicament is for use in the treatment of a cancer of the CNS. leukaemia, (e.g. acute myeloid leukaemia (AML), acute lymphocytic leukaemia (ALL), chronic myeloid leukaemia, chronic lymphocytic leukaemia (CLL))

[0068] In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, in the manufacture of a medicament for the inhibition of METTL3 activity. In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the inhibition of METTL3 activity.

[0069] In another aspect, the present disclosure provides use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, in the manufacture of a medicament for the treatment of:

i. a neurodegenerative disorder, a tauopathy, such as Alzheimer's disease, progressive supranuclear palsy, corticobasal syndrome, frontotemporal dementias, Pick's disease, globular glial tauopathy, argyrophilic grain disease, aging-related tau astrogliopathy, primary age-related tauopathy (PART), Progressive supranuclear palsy, and chronic traumatic encephalopathy; a motor neuron disease, a repeat expansion disease (such as Huntington's Disease), dementia (including frontotemporal dementia, vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease) or Parkinson's Disease;

ii. an autoimmune disease, a disorder of the CNS, a neurological disease, an inflammatory disease, an infectious disease, type 2 diabetes, a neuropsychiatric behavioural disorder, a depressive disorder or a disease related to the inactivation of the X-chromosome; or

iii. a disease related to the inactivation of the X-chromosome, e.g. Addison's disease with cerebral sclerosis; Adrenal hypoplasia; siderius X-linked mental retardation syndrome; Agammaglobulinaemia, Bruton type; Choroidoretinal degeneration; Choroidaemia; Albinism, ocular; Dent's disease 2; fragile X syndrome; Rett/ Epileptic encephalopathy, early infantile, 2 (CDKL5 deficiency disorder); Albinism-deafness syndrome; paroxysmal nocturnal hemoglobinuria; Aldrich syndrome; Alport syndrome; Anaemia, hereditary hypochromic; Anemia, sideroblastic, with ataxia; Fabry disease; Spinal muscular atrophy 2; Cataract, congenital; Charcot-Marie-Tooth, peroneal; Spastic paraplegia; Colour blindness; Diabetes insipidus, nephrogenic; DDX3X syndrome; Dyskeratosis congenita; Ectodermal dysplasia, anhidrotic; Faciogenital dysplasia (Aarskog syndrome); Glucose-6-phosphate dehydrogenase deficiency; Glycogen storage disease type VIII; Gonadal dysgenesis (XY female type); Granul omatous disease (chronic); Haemophilia A; Haemophilia B; Hydrocephalus (aqueduct stenosis); Hypophosphataemic rickets; Lesch-Nyhan syndrome (hypoxanthine-guanine-phosphoribosyl transferase deficiency); Incontinentia pigmenti; Kallmann syndrome; Keratosis follicularis spinulosa; Lowe (oculocerebrorenal) syndrome; Menkes syndrome; Renpenning Syndrome; Mental retardation, with or without fragile site (numerous specific types); Coffin-Lowry syndrome; Microphthalmia with multiple anomalies (Lenz syndrome); Muscular dystrophy (Becker, Duchenne and Emery-Dreifuss types); Myotubular myopathy; Night blindness, congenital stationary; Norrie's disease (pseudoglioma); Nystagmus, oculomotor or

'jerky'; Orofaciodigital syndrome (type I); Omithine transcarbamylase deficiency (type I hyperammonaemia); Phosphoglycerate kinase deficiency; Phosphoribosylpyrophosphate synthetase deficiency; Retinitis pigmentosa; Retinoschisis; Rett syndrome; Muscular atrophy; Dihydrotestosterone receptor deficiency; Spinal muscular atrophy; Spondyloepiphyseal dysplasia tarda; Thrombocytopenia, hereditary; Thyroxine-binding globulin, absence; or McLeod syndrome.

In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a neurodegenerative disorder, for example a tauopathy. The tauopathy may be selected from Alzheimer's disease, progressive supranuclear palsy, corticobasal

syndrome (also known as corticobasal degeneration), frontotemporal dementias, Pick's disease, globular glial tauopathy, argyrophilic grain disease, aging-related tau astrogliopathy, primary age-related tauopathy (PART), Progressive supranuclear palsy, and chronic traumatic encephalopathy.

[0070] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a motor neuron disease. Suitably, the motor neuron disease is selected from amyotrophic lateral sclerosis, progressive bulbar palsy, primary lateral sclerosis, progressive muscular atrophy, spinal muscular atrophy, Kennedy's disease, and post-polio syndrome. More suitably, the motor neuron disease is ALS.

[0071] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a repeat expansion disease (such as Huntington's Disease).

[0072] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of dementia (including frontotemporal dementia, vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease),

[0073] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of Alzheimer's Disease.

[0074] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of Parkinson's Disease.

[0075] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of multiple sclerosis.

[0076] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of epilepsy.

[0077] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a disease related to the inactivation of the X-chromosome.

[0078] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in reactivating expression of a silenced X-chromosome.

[0079] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of RETT syndrome.

[0080] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for promoting an immune response (e.g. anti-viral or anti-tumour immune response).

[0081] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for for use in increasing an innate immune response in a subject.

[0082] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing or enhancing an anti-tumour immune response during immune-oncology therapy.

[0083] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an autoimmune disease.

[0084] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a disorder of the central nervous system.

[0085] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a neurological disease.

[0086] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an infectious disease.

[0087] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a viral infection. Suitably, the viral infection is a RNA viral infection. Suitably, the viral infection is human papillomavirus (HPV) or hepatitis.

[0088] In another example, the present disclosure provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an inflammatory disease.

[0089] In another example, the present disclosure provides a method of inhibiting METTL3 activity *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[0090] In another example, the present disclosure provides a method of inhibiting cell proliferation *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0091] In another example, the present disclosure provides a method of inhibiting metastasis *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0092] In another example, the present disclosure provides a method of promoting an immune response (e.g. anti-viral or anti-tumour immune response) in a subject in need thereof, said method comprising administering to the subject a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0093] In another example, the present disclosure provides a method of increasing an innate immune response in a subject in need thereof, said method comprising administering to the subject a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0094] In another example, the present disclosure provides a method of increasing or enhancing an anti-tumour immune response during immune-oncology therapy, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0095] In another example, the present disclosure provides a method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0096] In another example, the present disclosure provides a method of treating cancer, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein. The cancer may be a human cancer. The cancer may be a

cancer of the CNS. Cancers of the CNS include but are not limited to Glioma, Glioblastoma Multiforme (GBM), Astrocytomas, Oligodendrogliomas, Ependyomas, Meningiomas, other brain neoplasms or secondary tumours that have metastasized to the brain.

[0097] In another example, the present disclosure provides a method of treating an autoimmune disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0098] In another example, the present disclosure provides a method of treating a disorder of the central nervous system, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0099] In another example, the present disclosure provides a method of treating a neurological disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[00100] In another example, the present disclosure provides a method of treating an infectious disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[00101] In another example, the present disclosure provides a method of treating a viral infection, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein. Suitably, the viral infection is a RNA viral infection. Suitably, the viral infection is human papillomavirus (HPV) or hepatitis.

[00102] In another example, the present disclosure provides a method of treating an inflammatory disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[00103] In another example, the present disclosure provides a method of treating a neurodegenerative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[00104] The neurodegenerative disorder may be selected from a tauopathy, such as Alzheimer's disease, progressive supranuclear palsy, corticobasal syndrome, frontotemporal

dementias, Pick's disease, globular glial tauopathy, argyrophilic grain disease, aging-related tau astrogliopathy, primary age-related tauopathy (PART), Progressive supranuclear palsy, and chronic traumatic encephalopathy; a motor neuron disease (including ALS); a repeat expansion disease (such as Huntington's Disease), dementia (including frontotemporal dementia, vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease); multiple sclerosis; or Parkinson's Disease.

[00105] Suitably, the neurodegenerative disorder may be a tauopathy, for example Alzheimer's disease, progressive supranuclear palsy, corticobasal syndrome, frontotemporal dementias or chronic traumatic encephalopathy.

[00106] In another example, the present disclosure provides a method for treating a motor neuron disease (including ALS), said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein. Suitably, the motor neuron disease is selected from amyotrophic lateral sclerosis, progressive bulbar palsy, primary lateral sclerosis, progressive muscular atrophy, spinal muscular atrophy, Kennedy's disease, and post-polio syndrome. More suitably, the motor neuron disease is ALS.

In another example, the present disclosure provides a method for treating a repeat expansion disease (such as Huntington's Disease), said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00107] In another example, the present disclosure provides a method for treating dementia (including frontotemporal dementia, vascular dementia and dementia caused by a tauopathy, such as Alzheimer's Disease), said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00108] In another example, the present disclosure provides a method for treating Alzheimer's Disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00109] In another example, the present disclosure provides a method for treating Parkinson's Disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00110] In another example, the present disclosure provides a method for treating multiple sclerosis, said method comprising administering to a subject in need thereof a therapeutically

effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00111] In another example, the present disclosure provides a method for treating epilepsy said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00112] In another example, the present disclosure provides a method for treating a disease related to the inactivation of the X-chromosome, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00113] In another example, the present disclosure provides a method for reactivating expression of a silenced X-chromosome said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00114] In another example, the present disclosure provides a method of treating RETT syndrome, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00115] In one aspect, the present disclosure provides a combination comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, with one or more additional therapeutic agents.

[00116] The present disclosure further provides a method of synthesising a compound, or a pharmaceutically acceptable salt, as defined herein.

[00117] In another example, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt, obtainable by, or obtained by, or directly obtained by a method of synthesis as defined herein.

[00118] In another example, the present disclosure provides novel intermediates as defined herein which are suitable for use in any one of the synthetic methods as set out herein.

[00119] Preferred, suitable, and optional features of any one particular example of the present disclosure are also preferred, suitable, and optional features of any other example.

DETAILED DESCRIPTION OF THE INVENTION

Definitions