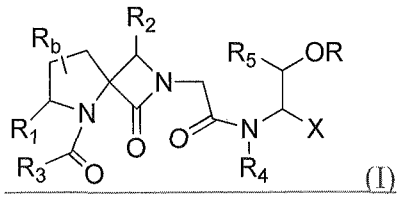
S, wherein the heteroaryl ring may be optionally substituted with one, two, or three substituents independently selected from the group consisting of halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl and phenyl; and

$R^c$ and $R^d$ are each independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, or phenyl, or $R^c$ and $R^d$ together with the nitrogen to which they are attached, form heterocyclyl including from 4 to 6 ring atoms; wherein the heterocyclyl includes not more than two ring heteroatoms (including the nitrogen atom attached to $R^c$ and $R^d$), and the second ring heteroatom, when present, is independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S; and wherein the heterocyclyl is optionally substituted with from 1-3 substituents independently selected from the group consisting of halogen, cyano, oxo, and $C_1$-$C_6$ alkyl.

In one aspect of the present disclosure, there is provided a compound represented by formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein

$R_b$ is selected from the group consisting of H, halogen, hydroxyl, cyano and $C_1$-$C_6$alkyl;

R is H, $C_1$-$C_6$ alkyl or –C(O)-$C_1$-$C_6$alkyl;

$R_1$ is H or $C_1$-$C_6$ alkyl;

$R_2$ is H or $C_1$-$C_6$ alkyl;

$R_3$ is $C_1$-$C_6$ alkyl; $C_1$-$C_6$ alkoxy; -O-$C_1$-$C_6$ alkylene-phenyl; $C_2$-$C_6$ alkenyl; $C_2$-$C_6$ alkynyl; $C_3$-$C_6$ cycloalkyl; phenyl; or heteroaryl including from 5 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S;, wherein $R_3$ is optionally substituted with one, two, or three substituents independently selected from the group consisting of amino, protected amino, halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl, phenyl (optionally substituted by one, two, or three substituents each independently selected from $R^a$), benzyl (optionally substituted by one, two, or three substituents each independently selected from $R^a$), and -$C_1$-$C_6$ alkylene-$C_3$-$C_6$ cycloalkyl

(optionally substituted by one, two or three substituents independent selected from halogen and $C_1$-$C_6$ alkyl);

$R^a$ is selected from the group consisting of halogen, $C_1$-$C_6$alkyl (optionally substituted by one, two or three halogens), $C_3$-$C_6$ cycloalkyl (optionally substituted by one, two or three halogens), and $C_1$-$C_6$ alkoxy (optionally substituted by one, two or three halogens);

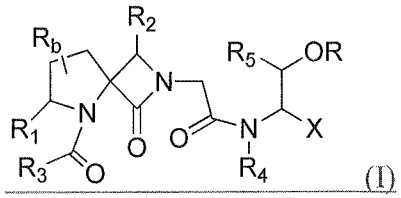
$R_4$ is H or $C_1$-$C_6$ alkyl;

$R_5$ is H or $C_1$-$C_6$ alkyl;

X is selected from the group consisting of: H; $C_1$-$C_6$ alkyl; -OH; $C_1$-$C_6$ alkoxy; $-CO_2H$; $-C(O)NR^cR^d$; and heteroaryl including from 5 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S, wherein the heteroaryl ring may be optionally substituted with one, two, or three substituents independently selected from the group consisting of halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl and phenyl; and

$R^c$ and $R^d$ are each independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, or phenyl, or $R^c$ and $R^d$ together with the nitrogen to which they are attached, form heterocyclyl including from 4 to 6 ring atoms; wherein the heterocyclyl includes not more than two ring heteroatoms (including the nitrogen atom attached to $R^c$ and $R^d$), and the second ring heteroatom, when present, is independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S; and wherein the heterocyclyl is optionally substituted with from 1-3 substituents independently selected from the group consisting of halogen, cyano, oxo, and $C_1$-$C_6$ alkyl.

In another aspect of the present disclosure, there is provided a compound represented by formula I:




(I)

and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

$R_b$ is selected from the group consisting of H, halogen, hydroxyl, cyano and $C_1$-$C_6$alkyl;

R is H, $C_1$-$C_6$ alkyl or –C(O)-$C_1$-$C_6$alkyl;

$R_1$ is H or $C_1$-$C_6$ alkyl;

$R_2$ is H or $C_1$-$C_6$ alkyl;

$R_3$ is $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_6$ cycloalkyl, phenyl, or a 4-6 membered heteroaryl with one, two or three heteroatoms each selected from O, S or N, wherein $R_3$ may be optionally substituted with one two or three substituents each selected from the group consisting of amino, halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl, phenyl (optionally substituted by one, two or three substituents each independently selected from $R^a$) or benzyl (optionally substituted by one two or three substituents each independently selected from $R^a$);

$R^a$ is selected from the group consisting of halogen, $C_1$-$C_6$alkyl (optionally substituted by one, two or three halogens), $C_3$-$C_6$ cycloalkyl (optionally substituted by one, two or three halogens), or $C_1$-$C_6$ alkoxy (optionally substituted by one, two or three halogens);

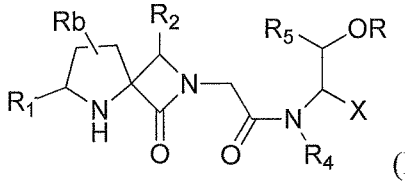
$R_4$ is H or $C_1$-$C_6$ alkyl;

$R_5$ is H or $C_1$-$C_6$ alkyl;

X is selected from the group consisting of: H, $C_1$-$C_6$ alkyl, -OH, $C_1$-$C_6$ alkoxy, $-CO_2H$, $-C(O)NR^cR^d$, and a 4- to 6-membered heteroaryl ring with one, two or three heteroatoms each selected from O, S or N, wherein the heteroaryl ring may be optionally substituted with one two or three substituents each selected from the group consisting of halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl and phenyl; and

$R^c$ and $R^d$ are each independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, or phenyl, or together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring, which may have an additional heteroatom selected from O, S, or N; wherein the 4-6 membered heterocyclic ring may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, and $C_1$-$C_6$ alkyl.

Also provided herein, at least in part, are compounds that are NMDA modulators, for example, partial agonists of NMDA. For example, disclosed herein are compounds represented by the formula:




(II)

and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

$R_b$ is selected from the group consisting of H, halogen, hydroxyl, cyano and $C_1$-$C_6$alkyl;

R is H, $C_1$-$C_6$ alkyl or –C(O)-$C_1$-$C_6$alkyl;

$R_1$ is H or $C_1$-$C_6$ alkyl;

$R_2$ is H or $C_1$-$C_6$ alkyl;

$R_4$ is H or $C_1$-$C_6$ alkyl;

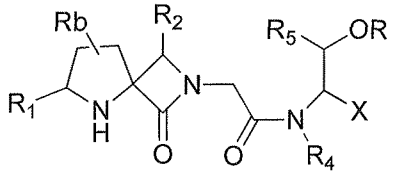
$R_5$ is H or $C_1$-$C_6$ alkyl;

X is selected from the group consisting of: H; $C_1$-$C_6$ alkyl; -OH; $C_1$-$C_6$ alkoxy; -$CO_2$H; -C(O)$NR^cR^d$; and heteroaryl including from 5 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S, wherein the heteroaryl ring may be optionally substituted with one, two, or three substituents

independently selected from the group consisting of halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl and phenyl; and

$R^c$ and $R^d$ are each independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, or phenyl, or $R^c$ and $R^d$ together with the nitrogen to which they are attached, form heterocyclyl including from 4 to 6 ring atoms; wherein the heterocyclyl includes not more than two ring heteroatoms (including the nitrogen atom attached to $R^c$ and $R^d$), and the second ring heteroatom, when present, is independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S; and wherein wherein the heterocyclyl is optionally substituted with from 1-3 substituents independently selected from the group consisting of halogen, cyano, oxo, and $C_1$-$C_6$ alkyl.

In a further aspect of the present disclosure, there is provided a compound represented by formula II:




(II)

or a pharmaceutically acceptable salt thereof, wherein

$R_b$ is selected from the group consisting of H, halogen, hydroxyl, cyano and $C_1$-$C_6$alkyl;

R is H, $C_1$-$C_6$ alkyl or –C(O)-$C_1$-$C_6$alkyl;

$R_1$ is H or $C_1$-$C_6$ alkyl;

$R_2$ is H or $C_1$-$C_6$ alkyl;

$R_4$ is H or $C_1$-$C_6$ alkyl;

$R_5$ is H or $C_1$-$C_6$ alkyl;

X is selected from the group consisting of: H; $C_1$-$C_6$ alkyl; -OH; $C_1$-$C_6$ alkoxy; -$CO_2$H; -C(O)N$R^cR^d$; and heteroaryl including from 5 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S, wherein the heteroaryl ring may be optionally substituted with one, two, or three substituents independently selected from the group consisting of halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl and phenyl; and

$R^c$ and $R^d$ are each independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, or phenyl, or $R^c$ and $R^d$ together with the nitrogen to which they are attached, form heterocyclyl

including from 4 to 6 ring atoms; wherein the heterocyclyl includes not more than two ring heteroatoms (including the nitrogen atom attached to $R^c$ and $R^d$), and the second ring heteroatom, when present, is independently selected from the group consisting of N, NH, N(C1-C3 alkyl), O, and S; and wherein wherein the heterocyclyl is optionally substituted with from 1-3 substituents independently selected from the group consisting of halogen, cyano, oxo, and $C_1$-$C_6$ alkyl.

**[0009]** In another aspect of the present disclosure, there is provided ~~Also provided herein are~~ a pharmaceutically acceptable compositions comprising a disclosed compound, and a pharmaceutically acceptable excipient. For example, such compositions may be suitable for oral or intravenous administration to a patient.

**[0009a]** In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein in the manufacture of a medicament for treating depression, Alzheimer's disease, attention deficit disorder, schizophrenia, or anxiety, in a patient in need thereof.

**[0010]** The present disclosure also relates to ~~In another aspect,~~ a method of treating a condition selected from the group consisting of autism, anxiety, depression, bipolar disorder, attention deficit disorder, attention deficit hyperactivity disorder (ADHD), schizophrenia, a psychotic disorder, a psychotic symptom, social withdrawal, obsessive-compulsive disorder, phobia, post-traumatic stress syndrome, a behavior disorder, an impulse control disorder, a substance abuse disorder, a sleep disorder, a memory disorder, a learning disorder, urinary incontinence, multiple system atrophy, progressive supra-nuclear palsy, Friedrich's ataxia, Down's syndrome, fragile X syndrome, tuberous sclerosis, olivio-ponto-cerebellar atrophy, cerebral palsy, drug-induced optic neuritis, ischemic retinopathy, diabetic retinopathy, glaucoma, dementia, AIDS dementia, Alzheimer's disease, Huntington's chorea, spasticity, myoclonus, muscle spasm, Tourette's syndrome, epilepsy, cerebral ischemia, stroke, a brain tumor, traumatic brain injury, cardiac arrest, myelopathy, spinal cord injury, peripheral neuropathy, acute neuropathic pain, and chronic neuropathic, in a patient in need thereof is provided. Such methods may comprise administering to the patient a pharmaceutically effective amount of a disclosed compound or pharmaceutically acceptable salts, stereoisomers, N-oxides, and hydrates thereof.

**[0011]** In some embodiments, a contemplated method includes treating depression. For example, depression may include one or more of major depressive disorder, dysthymic disorder, psychotic depression, postpartum depression, seasonal affective disorder, bipolar

38. The compound of any one of claims 26-37, wherein $R_b$ is H.

39. The compound of claim 1 or 26, wherein the compound is selected from the compounds delineated in Table 1.

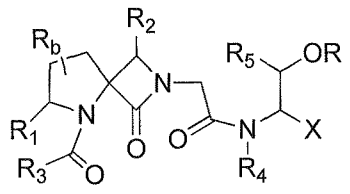
40. A pharmaceutical composition comprising a compound of any one of claims 1-39, and a pharmaceutically acceptable excipient.

41. The pharmaceutical composition of claim 40, suitable for oral administration.

42. The pharmaceutical composition of claim 40, suitable or intravenous administration.

43. Use of a compound of any one of claims 1-39 in the manufacture of a medicament for~~A method of treating of~~ treating depression, Alzheimer's disease, attention deficit disorder, schizophrenia, or anxiety, in a patient in need thereof~~, comprising administering to said patient: a pharmaceutically effective amount of a compound of any one of claims 1-39~~.

44. A compound represented by formula I:



(I)

and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

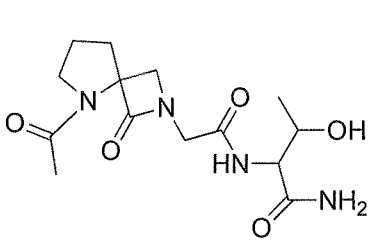
$R_b$ is selected from the group consisting of H, halogen, hydroxyl, cyano and $C_1$-$C_6$alkyl;

R is H, $C_1$-$C_6$ alkyl or –C(O)-$C_1$-$C_6$alkyl;

$R_1$ is H or $C_1$-$C_6$ alkyl;

$R_2$ is H or $C_1$-$C_6$ alkyl;

$R_3$ is $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_6$ cycloalkyl, phenyl, or a 4-6 membered heteroaryl with one, two or three heteroatoms each selected from O, S or N, wherein $R_3$ may be optionally substituted with one two or three substituents each selected from the group consisting of amino, halogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, hydroxyl, phenyl (optionally substituted by one, two or three substituents each independently selected from $R^a$) or benzyl (optionally substituted by one two or three substituents each independently selected from $R^a$);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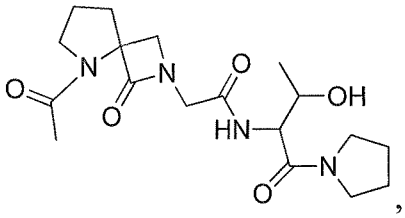
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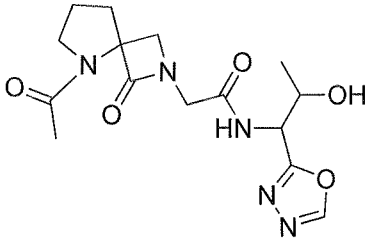
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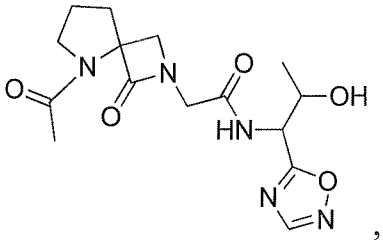
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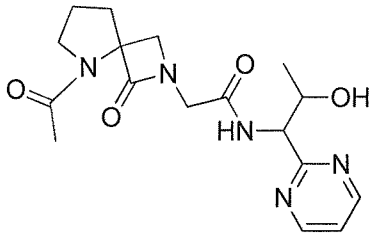
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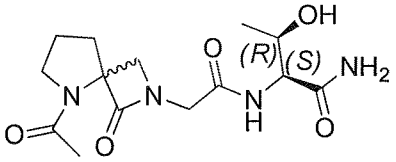
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56. A pharmaceutical composition comprising a compound of any one of claims 44-55, and a pharmaceutically acceptable excipient.

57. The pharmaceutical composition of claim 56, suitable for oral administration.

58. The pharmaceutical composition of claim 56, suitable or intravenous administration.

59. Use of a compound of any one of claims 44-55 in the manufacture of a medicament for~~A method of treating of~~ treating depression, Alzheimer's disease, attention deficit disorder, schizophrenia, or anxiety, in a patient in need thereof~~, comprising administering to said patient: a pharmaceutically effective amount of a compound of any one of claims 44-55~~.