

different somatic symptoms, such as sleep disturbances, fatigue, stiffness, balance problems, hypersensitivity to physical and psychological environmental stimuli, depression and anxiety (*CNS Drugs*, **2012**, 26, 2, 135-53).

Schizoaffective disorders: includes psychotic and affective symptoms, this disorder falls on a spectrum between bipolar disorders (with depressive and manic episodes, alcohol and drug addiction, substance abuse) and schizophrenia. *J. Clin. Psychiatry*, **2010**, 71, S2, 14-9, *Pediatr. Drugs* **2011**, 13, 5, 291-302

Major depression: *BMC Psychiatry* **2011**, 11, 86

Treatment resistant depression: *Journal of Psychopharmacology*, 0(0) 1- 16

Anxiety: *European Neuropsychopharmacology*, **2011**, 21, 429-449

Bipolar disorders: *Encephale*, *International J. of Neuropsychopharmacology*, **2011**, 14, 1029-104, *International J. of Neuropsychopharmacology*, **2012**, 1-12; *J. of Neuropsychopharmacology*, **2011**, 0, 0, 1- 15

Mood disorders: *J. Psychopharmacol.* **2012**, Jan 11, *CNS Drugs*, **2010**, 2, 131-61

Autism: *Current opinion in pediatrics*, **2011**, 23, 621 – 627; *J. Clin. Psychiatry*, **2011**, 72, 9, 1270-1276

Alzheimer's disease: *J. Clin. Psychiatry*, **2012**, 73, 1, 121-128

Parkinson's disease: *Movement Disorders*, **2011**, 26, 6

Chronic fatigue syndrome: *European Neuropsychopharmacology*, **2011**, 21, 282-286

Borderline Personality disorder: *J. Clin. Psychiatry*, **2011**, 72, 10, 1363-1365

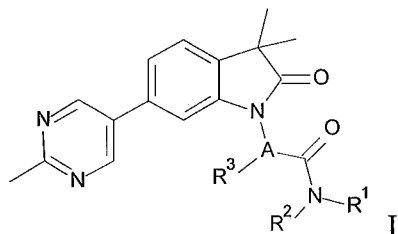
J. Clin. Psychiatry, **2011**, 72, 10, 1353-1362

Anti-inflammatory effects in arthritis: *European J. of Pharmacology*, **2012**, 678, 55-60

Objects of the embodiments disclosed herein are novel compounds of formula I and the use of compounds of formula I and their pharmaceutically acceptable salts for the treatment of CNS diseases related to positive (psychosis) and negative symptoms of schizophrenia, substance abuse, alcohol and drug addiction, obsessive-compulsive disorders, cognitive impairment, bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis, arthritis, autoimmune disease, viral and fungal infections,

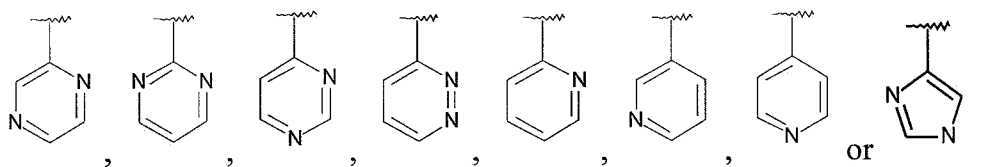
cardiovascular diseases, ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders with co-morbid epilepsy.

In one aspect, there is provided a compound of formula



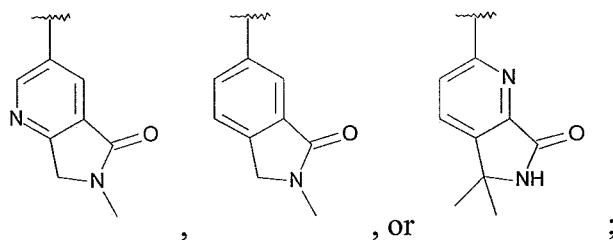
5 wherein

A is phenyl or a five or six membered heteroaryl group, containing one or two N atoms, selected from



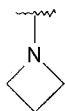
or the amide group $-C(O)-NR^1R^2$ may form together with two neighboring carbon atoms

10 from the group A an additional fused ring, selected from



R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-C_{1-7}$ -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;

15 or R^1 and R^2 may form together with the N atom to which they are attached the group

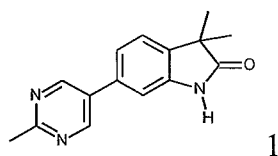


R^3 is hydrogen or C_{1-7} -alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

20 In another aspect, there is provided a combination of a compound of formula I as described herein together with a known marketed antipsychotic, antidepressant, anxiolytic or mood stabilizer.

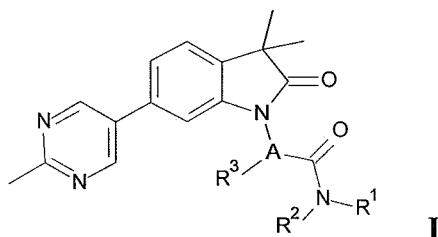
In another aspect, there is provided a process for preparation of a compound of formula I as described herein reacting a compound of formula



with a compound of formula



to a compound of formula

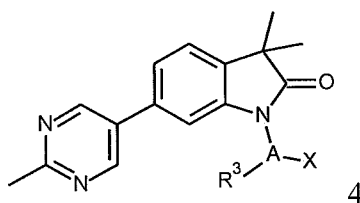


wherein Y is Cl, Br or I and the other groups have the meaning as described above and,

if desired, converting the compounds obtained into pharmaceutically acceptable acid

10 addition salts; or

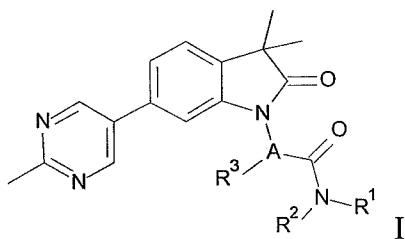
a) reacting a compound of formula



with HNR^1R^2

by aminocarbonylation in the presence of a ferrocene-palladium catalyst, with a source of carbon

15 monoxide, preferentially Molybden-hexacarbonyl or with CO gaz (50 bar) to a compound of formula

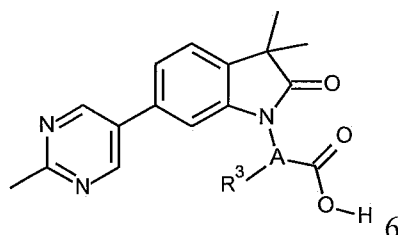


wherein X is Cl or Br and the other groups have the meaning as described above, and,

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition

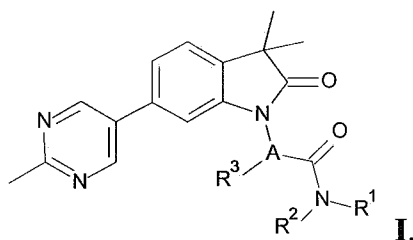
20 salts; or

b) amidation of a compound of formula



with HNR^1R^2

using an activating agent, preferred is HATU or TBTU, to give the compounds of formula I

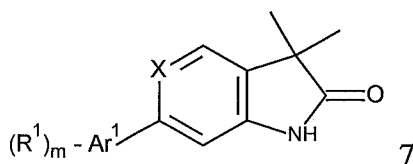


5

wherein the groups have the meaning as described above, and,

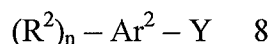
if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts;

reacting a compound of formula 7

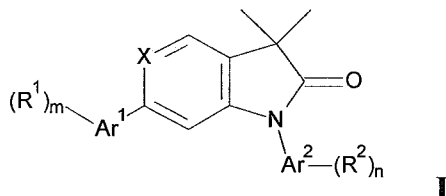


10

with a compound of formula



to a compound of formula



15 wherein Y is Cl, Br or I and the other groups have the meaning as described above and,

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

In another aspect, there is provided a compound as described herein for use as therapeutically active substance.

In another aspect, there is provided a pharmaceutical composition comprising a compound as described herein and a therapeutically active carrier for the treatment of CNS diseases related to positive (psychosis) and negative symptoms of schizophrenia, substance abuse, alcohol and drug addiction, obsessive-compulsive disorders, cognitive impairment, 5 bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis, effects in arthritis, autoimmune disease, viral and fungal infections, cardiovascular diseases, 10 ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders with co-morbid epilepsy.

In another aspect, there is provided use of a compound of formula I as described herein for the manufacture of a medicament for the treatment of CNS diseases related to positive (psychosis) and negative symptoms of schizophrenia, substance abuse, alcohol and drug 15 addiction, obsessive-compulsive disorders, cognitive impairment, bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis, effects in arthritis, 20 autoimmune disease, viral and fungal infections, cardiovascular diseases, ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders with co-morbid epilepsy.

In another aspect, there is provided a compound as described herein for use in the treatment of CNS diseases related to positive (psychosis) and negative symptoms of 25 schizophrenia, substance abuse, alcohol and drug addiction, obsessive-compulsive disorders, cognitive impairment, bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic 30 lateral sclerosis, effects in arthritis, autoimmune disease, viral and fungal infections, cardiovascular diseases, ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders with co-morbid epilepsy.

Further objects of the embodiments disclosed herein are medicaments containing such novel compounds as well as methods for preparation of compounds of formula I, a combination of compounds of formula I with marketed antipsychotics, antidepressants, anxiolytics or mood stabilizers, and methods for the treatment of CNS disorders as mentioned above.

5 Encompassed by the present disclosure are corresponding prodrugs of compounds of formula I.

 A common antipsychotic drug for the treatment of schizophrenia is olanzapine. Olanzapine (Zyprexa) belongs to a drug class known as atypical antipsychotics. Other members of this class include for example clozapine (Clozaril), risperidone (Risperdal), aripiprazole
10 (Abilify) and ziprasidone (Geodon).

 Olanzapine is approved for the treatment of psychotic disorders, long term treatment of bipolar disorders and in combination with fluoxetine for the treatment of depressive episodes associated with bipolar disorders and for the treatment of resistant depression.

 The compounds of the present disclosure may be combined with antipsychotic drugs like
15 olanzapine (Zyprexa), clozapine (Clozaril), risperidone (Risperdal), aripiprazole (Abilify), amisulpride (Solian), asenapine (Saphris), blonanserin (Lonasen), clotiapine (Entumine), iloperidone (Fanapt), lurasidone (Latuda), mosapramine (Cremin), paliperidone (Invega), perospirone (Lullan), quetiapine (Seroquel), remoxipride (Roxiam), sertindole (Serdolect), sulpiride (Sulpirid, Eglonyl), ziprasidone (Geodon, Zeldox), zotepine (Nipolept), haloperidol
20 (Haldol, Serenace), droperidol (Droleptan), chlorpromazine (Thorazine, Largactil), fluphenazine (Prolixin), perphenazine (Trilafon), prochlorperazine (Compazine), thioridazine (Mellaril, Melleril), trifluoperazine (Stelazine), triflupromazine (Vesprin), levomepromazine (Nozinan), promethazine (Phenergan), pimozide (Orap) and cyamemazine (Tercian).

 One preferred embodiment of the disclosure is a combination, wherein the marketed
25 antipsychotic drug is olanzapine (Zyprexa), clozapine (Clozaril), risperidone (Risperdal), aripiprazole (Abilify) or ziprasidone.

 Furthermore, the compounds of the present disclosure can be combined with antidepressants such as selective serotonin reuptake inhibitors [Citalopram (Celexa), Escitalopram (Lexapro, Ciprallex), Paroxetine (Paxil, Seroxat), Fluoxetine (Prozac), Fluvoxamine
30 (Luvox), Sertraline (Zoloft, Lustral)], serotonin-norepinephrine reuptake inhibitors [Duloxetine (Cymbalta), Milnacipran (Ixel, Savella), Venlafaxine (Effexor), Desvenlafaxine (Pristiq),

Tramadol (Tramal, Ultram), Sibutramine (Meridia, Reductil)], serotonin antagonist and reuptake inhibitors [Etoperidone (Axiomin, Etonin), Lubazodone (YM-992, YM-35,995), Nefazodone (Serzone, Nefadar), Trazodone (Desyrel)], norepinephrine reuptake inhibitors [Reboxetine (Edronax), Viloxazine (Vivalan), Atomoxetine (Strattera)], norepinephrine-dopamine reuptake inhibitors [Bupropion (Wellbutrin, Zyban), Dexamethylphenidate (Focalin), Methylphenidate (Ritalin, Concerta)], norepinephrine-dopamine releasing agents [Amphetamine (Adderall), Dextroamphetamine (Dexedrine), Dextromethamphetamine (Desoxyn), Lisdexamfetamine (Vyvanse)], tricyclic antidepressants [Amitriptyline (Elavil, Endep), Clomipramine (Anafranil), Desipramine (Norpramin, Pertofrane), Dosulepin [Dothiepin] (Prothiaden), Doxepin (Adapin, Sinequan), Imipramine (Tofranil), Lofepramine (Feprapax, Gamanil, Lomont), Nortriptyline (Pamelor), Protriptyline (Vivactil), Trimipramine (Surmontil)], tetracyclic antidepressants [Amoxapine (Asendin), Maprotiline (Ludiomil), Mianserin (Bolvidon, Norval, Tolvon), Mirtazapine (Remeron)], monoamine oxidase inhibitors [Isocarboxazid (Marplan), Moclobemide (Aurorix, Manerix), Phenelzine (Nardil), Selegiline [L-Deprenyl] (Eldepryl, Zelapar, Emsam), Tranylcypromine (Parnate), Pirlindole (Pirazidol)], 5-HT_{1A} Receptor Agonists [Buspirone (Buspar), Tandospirone (Sediel), Vilazodone (Viibryd)], 5-HT₂ Receptor Antagonists [Agomelatine (Valdoxan), Nefazodone (Nefadar, Serzone), selective Serotonin Reuptake Enhancers [Tianeptine].

A preferred embodiment of this disclosure is a combination, wherein the marketed anti-depressive drug is citalopram (Celexa), escitalopram (Lexapro, Cipralext), paroxetine (Paxil, Seroxat), fluoxetine (Prozac), sertraline (Zoloft, Lustral) duloxetine (Cymbalta), milnacipran (Ixel, Savella), venlafaxine (Effexor), or mirtazapine (Remeron).

Compounds can also be combined with anxiolytics such as Alprazolam (Helex, Xanax, Xanor, Onax, Alprox, Restyl, Tafil, Paxal), Bretazenil, Bromazepam (Lectopam, Lexotanil, Lexotan, Bromam), Brotizolam (Lendormin, Dormex, Sintonal, Noctilan), Chlordiazepoxide (Librium, Risolid, Elenium), Cinolazepam (Gerodorm), Clonazepam (Rivotril, Klonopin, Iktorivil, Paxam), Clorazepate (Tranxene, Tranxilium), Clotiazepam (Veratran, Clozan, Rize), Cloxazolam (Sepazon, Olcadil), Delorazepam (Dadumir), Diazepam (Antenex, Apaurin, Apzepam, Apozepam, Hexalid, Pax, Stesolid, Stedon, Valium, Vival, Valaxona), Estazolam (ProSom), Etizolam (Etilaam, Pasaden, Depas), Flunitrazepam (Rohypnol, Fluscand, Flunipam, Ronal, Rohydorm), Flurazepam (Dalmadorm, Dalmane), Flutoprazepam (Restas), Halazepam (Paxipam), Ketazolam (Anxon), Loprazolam (Dormonox), Lorazepam (Ativan, Temesta, Tavor, Lorabenz), Lormetazepam (Loramet, Noctamid, Pronoxan), Medazepam

(Nobrium), Midazolam (Dormicum, Versed, Hypnovel, Dormonid), Nimetazepam (Erimin), Nitrazepam (Mogadon, Alodorm, Pacisyn, Dumolid, Nitrazadon), Nordazepam (Madar, Stilny), Oxazepam (Seresta, Serax, Serenid, Serepax, Sobril, Oxabenz, Oxapax), Phenazepam (Phenazepam), Pinazepam (Domar), Prazepam (Lysanxia, Centrax), Premazepam, Quazepam (Doral), Temazepam (Restoril, Normison, Euhypnos, Temaze, Tenox), Tetrazepam (Mylostan), Triazolam (Halcion, Rilamir), Clobazam (Frisium, Urbanol), Eszopiclone (Lunesta), Zaleplon (Sonata, Starnoc), Zolpidem (Ambien, Nytamel, Stilnoct, Stilnox, Zoldem, Zolnod), Zopiclone (Imovane, Rhovane, Ximovan; Zileze; Zimoclone; Zimovane; Zopitan; Zorclone), Pregabalin (Lyrica) and Gabapentin (Fanatrex, Gabarone, Gralise, Neurontin, Nupentin).

10 One preferred embodiment of the disclosure is a combination, wherein the marketed anxiolytic drug is alprazolam (Helex, Xanax, Xanor, Onax, Alprox, Restyl, Tafil, Paxal), chlordiazepoxide (Librium, Risolid, Elenium), clonazepam (Rivotril, Klonopin, Iktorivil, Paxam), diazepam (Antenex, Apaurin, Apzepam, Apozepam, Hexalid, Pax, Stesolid, Stedon, Valium, Vival, Valaxona), Estazolam (ProSom), eszopiclone (Lunesta), zaleplon (Sonata, 15 Starnoc), zolpidem (Ambien, Nytamel, Stilnoct, Stilnox, Zoldem, Zolnod), pregabalin (Lyrica) or gabapentin (Fanatrex, Gabarone, Gralise, Neurontin, Nupentin).

A further object of the disclosure is a combination with mood stabilizers such as Carbamazepine (Tegretol), Lamotrigine (Lamictal), Lithium (Eskalith, Lithane, Lithobid), and Valproic Acid (Depakote).

20 Compounds can also be combined with procognitive compounds such as donepezil (Aricept), galantamine (Razadyne), rivastigmine (Exelon) and memantine (Namenda).

The preferred indications using the compounds of the present disclosure are psychotic diseases like schizophrenia.

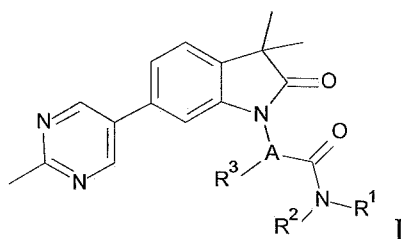
As used herein, the term "lower alkyl" denotes a saturated straight- or branched-chain 25 group containing from 1 to 7 carbon atoms, for example, methyl, ethyl, propyl, isopropyl, n-butyl, i-butyl, 2-butyl, t-butyl and the like. Preferred alkyl groups are groups with 1 - 4 carbon atoms.

As used herein, the term "lower alkoxy" denotes an alkyl group as defined above, wherein the alkyl residue is attached via an oxygen atom.

30 As used herein, the term "lower alkyl substituted by hydroxy" denotes a group wherein the alkyl residue is as defined above, wherein at least one hydrogen atom is replaced by a hydroxy group.

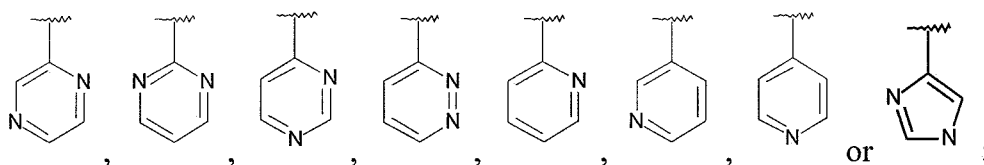
Claims

1. A compound of formula

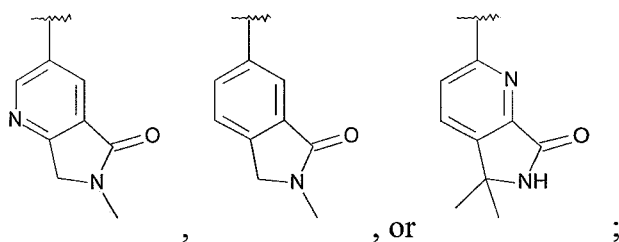


wherein

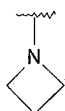
5 A is phenyl or a five or six membered heteroaryl group, containing one or two N atoms, selected from



or the amide group $-C(O)-NR^1R^2$ may form together with two neighboring carbon atoms from the group A an additional fused ring, selected from



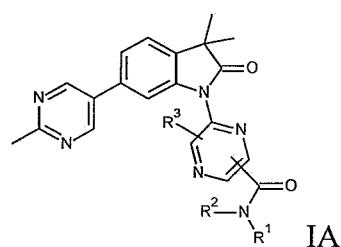
10 R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-$ C_{1-7} -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen; or R^1 and R^2 may form together with the N atom to which they are attached the group



15 R^3 is hydrogen or C_{1-7} -alkyl;

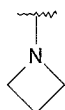
as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

20 2. A compound of formula IA according to claim 1,



wherein

R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-$ C_{1-7} -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
 or R^1 and R^2 may form together with the N atom to which they are attach the group



R^3 is hydrogen or C_{1-7} -alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

3. A compound of formula IA according to claim 2, which compounds are
 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylpyrazine-2-carboxamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpyrazine-2-carboxamide

1-(6-(azetidine-1-carbonyl)pyrazin-2-yl)-3,3-dimethyl-6-(2-methylpyrimidin-5-yl)indolin-2-one

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)pyrazine-2-carboxamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2-methoxyethyl)-N-methylpyrazine-2-carboxamide

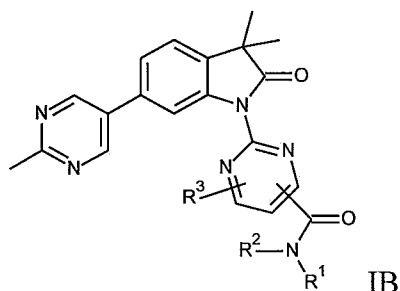
6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2-hydroxyethyl)pyrazine-2-carboxamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2-methoxyethyl)pyrazine-2-carboxamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2,2,2-trifluoroethyl)pyrazine-2-carboxamide

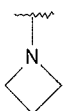
- 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-isopropylpyrazine-2-carboxamide
- 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-carboxamide
- 5-[3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindol-1-yl]-dimethylpyrazine-2-carboxamide
- 5 N-(tert-butyl)-5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpyrazine-2-carboxamide
- 1-(5-(azetidine-1-carbonyl)pyrazin-2-yl)-3,3-dimethyl-6-(2-methylpyrimidin-5-yl)indolin-2-one
- 5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2-methoxyethyl)-N-methylpyrazine-2-carboxamide
- 10 5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-carboxamide
- N-cyclopropyl-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-carboxamide
- N-(3,3-difluorocyclobutyl)-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-carboxamide
- 15 N-cyclobutyl-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-carboxamide
- 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(oxetan-3-yl)pyrazine-2-carboxamide or
- N-(tert-butyl)-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)pyrazine-2-
- 20 carboxamide.

4. A compound of formula IB according to claim 1,



wherein

- 25 R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-$ C_{1-7} -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
- or R^1 and R^2 may form together with the N atom to which they are attach the group

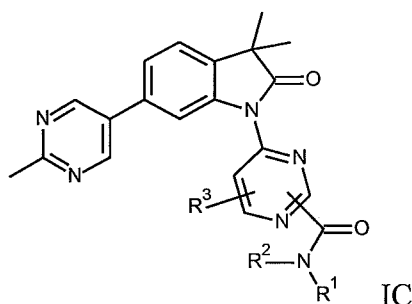


R^3 is hydrogen or C_{1-7} alkyl;
as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

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5. A compound of formula IB according to claim 4, which compounds are
2-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpyrimidine-4-
carboxamide
2-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylpyrimidine-4-
carboxamide or
2-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,5-dimethylpyrimidine-4-
carboxamide.

6. A compound of formula IC according to claim 1,

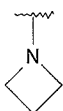


15

wherein

R^1/R^2 are independently from each other hydrogen, C_{1-7} alkyl, C_{1-7} alkyl substituted by halogen,
 C_{1-7} alkyl substituted by hydroxy, $-(CH_2)_2-$ C_{1-7} alkoxy, oxetanyl, cycloalkyl, CH_2 -
cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
or R^1 and R^2 may form together with the N atom to which they are attach the group

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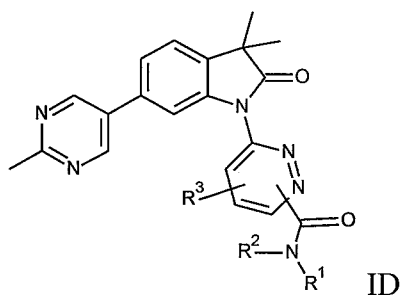
R^3 is hydrogen or C_{1-7} alkyl;
as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

25

7. A compound of formula IC according to claim 6, which compounds are 4-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylpyrimidine-2-carboxamide or

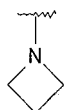
4-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpyrimidine-2-carboxamide.

8. A compound of formula ID according to claim 1,



wherein

R¹/R² are independently from each other hydrogen, C₁₋₇-alkyl, C₁₋₇-alkyl substituted by halogen, C₁₋₇-alkyl substituted by hydroxy, -(CH₂)₂- C₁₋₇-alkoxy, oxetanyl, cycloalkyl, CH₂-cycloalkyl, which cycloalkyl rings are optionally substituted by halogen; or R¹ and R² may form together with the N atom to which they are attach the group

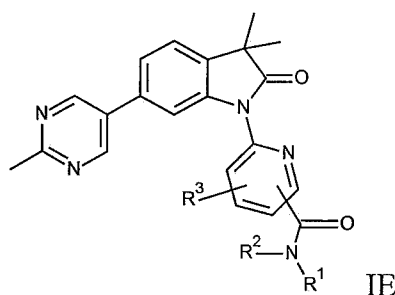


R³ is hydrogen or C₁₋₇-alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

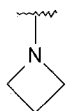
9. A compound of formula ID according to claim 8, which compound is 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylpyridazine-3-carboxamide.

10. A compound of formula IE according to claim 1



wherein

R¹/R² are independently from each other hydrogen, C₁₋₇-alkyl, C₁₋₇-alkyl substituted by halogen, C₁₋₇-alkyl substituted by hydroxy, -(CH₂)₂- C₁₋₇-alkoxy, oxetanyl, cycloalkyl, CH₂-cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
 5 or R¹ and R² may form together with the N atom to which they are attached the group



R³ is hydrogen or C₁₋₇-alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its
 10 corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

11. A compound of formula IE according to claim 10, which compounds are

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpicolinamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylpicolinamide

15 N-cyclopropyl-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)picolinamide

N-(cyclopropylmethyl)-6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)picolinamide

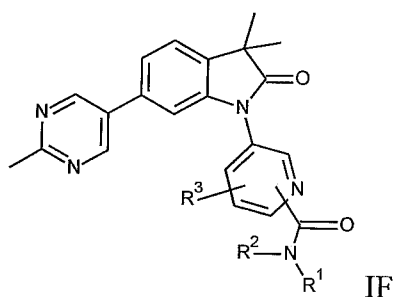
6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)picolinamide

6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,3-dimethylpicolinamide

20 6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N,3-trimethylpicolinamide or

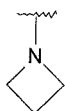
6-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylnicotinamide.

12. A compound of formula IF according to claim 1



wherein

R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-C_{1-7}$ -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
 or R^1 and R^2 may form together with the N atom to which they are attached the group



R^3 is hydrogen or C_{1-7} -alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

13. A compound of formula IF according to claim 12, which compounds are

5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,N-dimethylnicotinamide

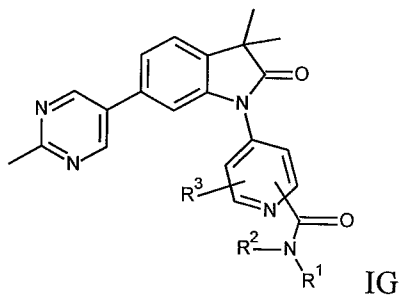
1-(5-(azetidine-1-carbonyl)pyridin-3-yl)-3,3-dimethyl-6-(2-methylpyrimidin-5-yl)indolin-2-one

5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-(2,2,2-trifluoroethyl)nicotinamide

5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylnicotinamide or

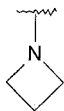
5-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,2-dimethylnicotinamide.

14. A compound of formula IG according to claim 1



wherein

R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-C_{1-7}$ -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
or R^1 and R^2 may form together with the N atom to which they are attach the group



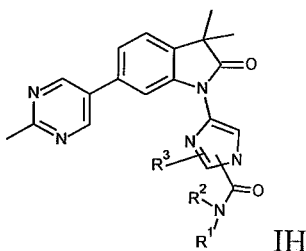
5

R^3 is hydrogen or C_{1-7} -alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

10 15. A compound of formula IG according to claim 1, which compounds are
4-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N,6-dimethylpicolinamide or
4-(3,3-dimethyl-6-(2-methylpyrimidin-5-yl)-2-oxoindolin-1-yl)-N-methylpicolinamide

16. A compound of formula IH according to claim 1

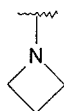


15

wherein

R^1/R^2 are independently from each other hydrogen, C_{1-7} -alkyl, C_{1-7} -alkyl substituted by halogen, C_{1-7} -alkyl substituted by hydroxy, $-(CH_2)_2-C_{1-7}$ -alkoxy, oxetanyl, cycloalkyl, CH_2 -cycloalkyl, which cycloalkyl rings are optionally substituted by halogen;
or R^1 and R^2 may form together with the N atom to which they are attach the group

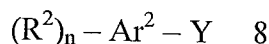
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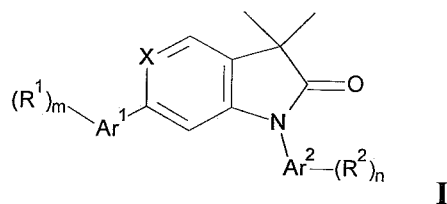
R^3 is hydrogen or C_{1-7} -alkyl;

as well as with a pharmaceutically acceptable salt thereof, with a racemic mixture, or with its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

25



to a compound of formula



wherein Y is Cl, Br or I and the other groups have the meaning as described above and,

5 if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

26. A compound according to any one of claims 1 – 19 for use as therapeutically active substance.

10

27. A pharmaceutical composition comprising a compound in accordance with any one of claims 1 –19 and a therapeutically active carrier for the treatment of CNS diseases related to positive (psychosis) and negative symptoms of schizophrenia, substance abuse, alcohol and drug addiction, obsessive-compulsive disorders, cognitive impairment, bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis, effects in arthritis, autoimmune disease, viral and fungal infections, cardiovascular diseases, ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders with co-morbid epilepsy.

15

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28. The use of a compound of formula I as claimed in any one of claims 1-19
for the manufacture of a medicament for the treatment of CNS diseases related to positive
(psychosis) and negative symptoms of schizophrenia, substance abuse, alcohol and drug
5 addiction, obsessive-compulsive disorders, cognitive impairment, bipolar disorders, mood
disorders, major depression, treatment resistant depression, anxiety disorders, Alzheimer's
disease, autism, Parkinson's disease, chronic pain, borderline personality disorder,
neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness, inflammatory
disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis, effects in arthritis,
10 autoimmune disease, viral and fungal infections, cardiovascular diseases, ophthalmology and
inflammatory retinal diseases and balance problems, epilepsy and neurodevelopmental disorders
with co-morbid epilepsy.

29. A compound according to any one of claims 1 –19 for use in the treatment of CNS
15 diseases related to positive (psychosis) and negative symptoms of schizophrenia, substance
abuse, alcohol and drug addiction, obsessive-compulsive disorders, cognitive impairment,
bipolar disorders, mood disorders, major depression, treatment resistant depression, anxiety
disorders, Alzheimer's disease, autism, Parkinson's disease, chronic pain, borderline personality
disorder, neurodegenerative disease, sleep disturbances, chronic fatigue syndrome, stiffness,
20 inflammatory disease, asthma, Huntington's disease, ADHD, amyotrophic lateral sclerosis,
effects in arthritis, autoimmune disease, viral and fungal infections, cardiovascular diseases,
ophthalmology and inflammatory retinal diseases and balance problems, epilepsy and
neurodevelopmental disorders with co-morbid epilepsy.