

CLAIMS

1. A melatonin/5-HT1A receptor agonist for use in the treatment of a human subject afflicted with a neurological disorder or disease, wherein
 - a) the human subject has been diagnosed with schizophrenia or an autism spectrum disorder and has a SNP in the 2:107,510,000-107,540,000 locus, or
 - b) the human subject has been diagnosed with symptomatic Alzheimer's disease and does not have a SNP in the 2:107,510,000-107,540,000 locus;wherein the SNP is selected from 2:107516926 and/or 2:107521253 and/or 2:107522069 and/or 2:107523546 and/or 2:107525598 and/or 2:107535946, and/or a SNP in linkage disequilibrium with any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37 (GRCh37), and wherein the human subject having the SNP has:
 - at least one C allele at rs12328439 (T>C); and/or
 - at least one A allele at rs62155556 (T>A) ;and/or
 - at least one T allele at rs62155557 (G>T); and/or
 - at least one A allele at rs62155558 (G>A); and/or
 - at least one G allele at rs17033479 (A>G); and/or
 - at least one A allele at rs9789618 (T>A).
2. The melatonin/5-HT1A receptor agonist for use of claim 1, wherein the melatonin/5-HT1A receptor agonist for use comprises a pharmaceutical composition comprising piromelatine and a pharmaceutically acceptable carrier.
3. The melatonin/5-HT1A receptor agonist for use of claim 2, wherein the pharmaceutical composition comprises 1 to 100 mg piromelatine.
4. The melatonin/5-HT1A receptor agonist for use of claim 3, wherein the treatment comprises 1 to 100 mg piromelatine daily.
5. The melatonin/5-HT1A receptor agonist for use of claim 4, wherein the treatment comprises 5 mg piromelatine daily.
6. The melatonin/5-HT1A receptor agonist for use of claim 3, wherein the treatment comprises 20 mg piromelatine daily.
7. The melatonin/5-HT1A receptor agonist for use of claim 3, wherein the treatment comprises 50 mg piromelatine daily.

8. The melatonin/5-HT1A receptor agonist for use of claim , wherein the treatment further comprises a combination therapy with an additional Alzheimer's disease therapeutic agent if the human subject has been diagnosed with symptomatic Alzheimer's disease, or with an additional therapeutic agent for schizophrenia if the human subject has been diagnosed with schizophrenia, or with an additional therapeutic agent for autism spectrum disorder if the human subject has been diagnosed with an autism spectrum disorder.

9. An Alzheimer's disease therapeutic agent that is not a melatonin/5-HT1A receptor agonist for use in the treatment of a patient diagnosed with symptomatic Alzheimer's disease and carrying a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618.

10. Piromelatine for use in the treatment of a patient diagnosed with schizophrenia and having a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618.

11. A method of predicting the response of a subject to a therapy comprising a melatonin/5-HT1A receptor agonist, the method comprising:

determining if the subject has a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618, wherein

- (i) if the patient has been diagnosed with symptomatic Alzheimer's disease, and has a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618 predicts that the subject will respond negatively to a therapy comprising the melatonin/5-HT1A receptor agonist, and
- (ii) if the patient has been diagnosed with schizophrenia or an autism spectrum disorder, and has a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618 predicts that the subject will respond positively to a therapy comprising the melatonin/5-HT1A receptor agonist.

12. A method of assessing risks of deterioration of cognition in an symptomatic Alzheimer's disease patient being treated with a melatonin/5-HT1A receptor agonist therapy, comprising determining if the patient has a SNP in at least one of rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618, and if the patient has the SNP, then determining that the subject is at risk of deterioration of cognition due to the administration of the melatonin/5-HT1A receptor agonist therapy.

13. A melatonin/5-HT1A receptor agonist for use in the treatment for improving attention and focus in a subject with an attention disorder associated with schizophrenia, an attention deficit disorder, or an autism spectrum disorder, wherein the subject has a SNP in at least one of rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618.

14. A method of identifying a prognostic genotype of a subject's response to a drug for treating mental disorders and/or intellectual ability in a human subject, the method comprising determining the genotype of the subject of at least 1 position of single nucleotide polymorphism (SNP) selected from 2:107516926 and/or 2:107521253 and/or 2:107522069 and/or 2:107523546 and/or 2:107525598 and/or 2:107535946, and/or a SNP in linkage disequilibrium with any one of said SNPs, wherein said SNPs are as disclosed in the GRCh37, and wherein the presence of:

at least one C allele at rs12328439 (T>C); and/or

at least one A allele at rs62155556 (T>A); and/or

at least one T allele at rs62155557 (G>T); and/or

at least one A allele at rs62155558 (G>A); and/or

at least one G allele at rs17033479 (A>G); and/or

at least one A allele at rs9789618 (T>A) is indicative of a subject having a positive response to a melatonin/5HT1A receptor agonist when the subject has been diagnosed with schizophrenia, an attention disorder, or an autism spectrum disorder, or negative response to the melatonin/5HT1A receptor agonist when the subject has been diagnosed with symptomatic Alzheimer's disease.

15. A melatonin/5-HT1A receptor agonist for use in the treatment of a patient with

(i) symptomatic Alzheimer disease, wherein the patient does not carry a SNP in any of rs12328439, rs62155556, rs62155557, rs62155558, rs17033479, and rs9789618; or

(ii) schizophrenia, an attention disorder, or an autism spectrum disorder, wherein the patient carries a SNP in at least one of rs12328439, rs62155556, rs62155557, rs62155558, rs17033479, and rs9789618.

16. A melatonin/5-HT1A receptor agonist for use in the treatment of dementia in a human subject, wherein a human subject that has been diagnosed with symptomatic Alzheimer Disease, and has at least one SNP in the 2:107,510,000-107,540,000 locus is excluded from the treatment, and wherein a human subject included for the treatment has been diagnosed with symptomatic Alzheimer Disease, but does not have a SNP in the 2:107,510,000-107,540,000 locus, wherein the SNP is selected from 2:107516926 and/or 2:107521253 and/or 2:107522069 and/or 2:107523546 and/or 2:107525598 and/or 2:107535946, and/or a SNP in linkage disequilibrium with any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37 (GRCh37), and wherein the human subject having the SNP has:

at least one C allele at rs12328439 (T>C); and/or
at least one A allele at rs62155556 (T>A) ;and/or
at least one T allele at rs62155557 (G>T); and/or
at least one A allele at rs62155558 (G>A); and/or
at least one G allele at rs17033479 (A>G); and/or
at least one A allele at rs9789618 (T>A).

17. A melatonin/5-HT1A receptor agonist for use in the treatment of schizophrenia, an autism spectrum disorder, or an attention disorder in a human subject,
wherein a human subject included for treatment has a SNP in the 2:107,510,000-107,540,000 locus
and has been diagnosed with schizophrenia, an autism spectrum disorder, or an attention disorder, ,
and

wherein a human subject is excluded from the treatment if the human subject has been diagnosed
with schizophrenia, an autism spectrum disorder, or an attention disorder, but does not have a SNP
in the 2:107,510,000-107,540,000 locus, ,

wherein the SNP is selected from 2:107516926 and/or 2:107521253 and/or 2:107522069 and/or
2:107523546 and/or 2:107525598 and/or 2:107535946, and/or a SNP in linkage disequilibrium with
any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37
(GRCh37), and wherein the human subject having the SNP has:

at least one C allele at rs12328439 (T>C); and/or
at least one A allele at rs62155556 (T>A) ;and/or
at least one T allele at rs62155557 (G>T); and/or
at least one A allele at rs62155558 (G>A); and/or
at least one G allele at rs17033479 (A>G); and/or
at least one A allele at rs9789618 (T>A).

18. A method of identifying a genotype of a population of human subjects diagnosed with
symptomatic Alzheimer's disease and then selecting a suitable treatment for the human subjects, the
method comprising:

(i) identifying the human subjects in the population having at least one single nucleotide
polymorphism (SNP) in the 2:107,510,000-107,540,000 and excluding those human subjects from
treatment with a melatonin/5-HT1A receptor agonist; and

(ii) identifying the human subjects in the population that do not have at least one SNP in
2:107,510,000-107,540,000 locus,

wherein the human subjects in (i) have

at least one C allele at rs12328439 (T>C); and/or
at least one A allele at rs62155556 (T>A) ;and/or

at least one T allele at rs62155557 (G>T); and/or
at least one A allele at rs62155558 (G>A); and/or
at least one G allele at rs17033479 (A>G); and/or
at least one A allele at rs9789618 (T>A);
and wherein the human subjects in (ii) lack a SNP at 2:107516926, 2:107521253, 2:107522069, 2:107523546, 2:107525598, 2:107535946, and a SNP in linkage disequilibrium with any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37 (GRCh37).

19. A method of identifying a genotype of a population of human subjects diagnosed with schizophrenia, an autism spectrum disorder, or an attention disorder, and then selecting a suitable treatment for the human subjects, the method comprising:

(i) identifying the human subjects in the population having at least one single nucleotide polymorphism (SNP) in a 2:107,510,000-107,540,000 locus; and

(ii) identifying the human subjects in the population that do not have at least one SNP in 2:107,510,000-107,540,000 locus and excluding those human subjects from treatment with a melatonin/5-HT_{1A} receptor agonist,

wherein the human subjects in (i) have

at least one C allele at rs12328439 (T>C); and/or

at least one A allele at rs62155556 (T>A); and/or

at least one T allele at rs62155557 (G>T); and/or

at least one A allele at rs62155558 (G>A); and/or

at least one G allele at rs17033479 (A>G); and/or

at least one A allele at rs9789618 (T>A); and

wherein the human subjects in (ii) lack a SNP at 2:107516926, 2:107521253, 2:107522069, 2:107523546, 2:107525598, 2:107535946, and a SNP in linkage disequilibrium with any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37 (GRCh37).

20. A method of identifying a genotype of a human subject afflicted with a neurological disorder or disease and then selecting a suitable treatment, the method comprising:

(i) identifying a human subject having a single nucleotide polymorphism (SNP) in a 2:107,510,000-107,540,000 locus; and

(ii) selecting a treatment with 3 mg to 10 mg of a melatonin/5-HT_{1A} receptor agonist for the human subject,

wherein the SNP is selected from 2:107516926 and/or 2:107521253 and/or 2:107522069 and/or 2:107523546 and/or 2:107525598 and/or 2:107535946, and/or a SNP in linkage disequilibrium with any one of said SNPs as disclosed in the Genome Reference Consortium Human genome build 37 (GRCh37), and wherein the human subject having the SNP has:

at least one C allele at rs12328439 (T>C); and/or
at least one A allele at rs62155556 (T>A) ;and/or
at least one T allele at rs62155557 (G>T); and/or
at least one A allele at rs62155558 (G>A); and/or
at least one G allele at rs17033479 (A>G); and/or
at least one A allele at rs9789618 (T>A).

21. The method of any one of claims 11, 12, 14, 18, 19, or 20, or the melatonin/5-HT1A receptor agonist for use according to any one of claims 1, 13, 15, 16, or 17, wherein the melatonin/5-HT1A receptor agonist is piromelatine.

22. The method of any one of claims 11, 12, 14, 18, 19, or 20, comprising amplifying DNA from a sample obtained from the subject; and contacting the DNA with an array comprising a plurality of probes for determining the identity of at least one allele at a position of SNP as follows:

at least one C allele at rs12328439 (T>C); and/or
at least one A allele at rs62155556 (T>A); and/or
at least one T allele at rs62155557 (G>T); and/or
at least one A allele at rs62155558 (G>A); and/or
at least one G allele at rs17033479 (A>G); and/or
at least one A allele at rs9789618 (T>A).

23. A melatonin/5-HT1A receptor agonist for use in the treatment a patient diagnosed with symptomatic Alzheimer's disease and carrying a SNP selected from rs12328439 and/or rs62155556 and/or rs62155557 and/or rs62155558 and/or rs17033479 and/or rs9789618, wherein the dose of the melatonin/5-HT1A receptor agonist is between 3 mg and 10 mg per day.