

What is claimed is:

1. A pharmaceutical composition comprising:
an amount between about 85 mg and about 600 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and
an amount between about 15 mg and about 100 mg (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base;
in the enantiomeric ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride between about 65:35 and about 88:12 by weight of free base.
2. The pharmaceutical composition of claim 1 wherein the ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride is between about 75:25 to about 88:12 by weight of free base.
3. The pharmaceutical composition of claim 1 wherein the ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride is between about 80:20 to about 88:12 by weight of free base.
4. The pharmaceutical composition of claim 1 wherein the ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride is between about 85:15 by weight of free base.
5. The pharmaceutical composition of claim 1 comprising:
an amount between about 170 mg and about 340 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and
an amount between about 30 mg and about 60 mg (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base.
6. The pharmaceutical composition of claim 1 comprising:
an amount about 170 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and
an amount about 30 mg of (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base.
7. The pharmaceutical composition of claim 1 comprising:

an amount about 340 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and

an amount about 60 mg of (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base.

8. The pharmaceutical composition of claim 1, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is about 100mg, 200mg, 300mg, 400mg, 500mg, 600mg or 700mg by weight of free base.

9. The pharmaceutical composition of claim 1, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is between about 200 mg and about 600 mg by weight of free base.

10. The pharmaceutical composition of claim 1, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is between about 200 mg and about 400 mg by weight of free base.

11. The pharmaceutical composition of claim 1, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is about 200 mg by weight of free base.

12. The pharmaceutical composition of claim 1, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is about 400 mg by weight of free base.

13. The pharmaceutical composition of claim 1, wherein the (R)-(+)-amisulpride is crystalline (R)-(+)-amisulpride of crystal Form A; and the (S)-(-)-amisulpride is crystalline (S)-(-)-amisulpride of crystal Form A'.

14. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration an occupancy of dopamine D2 receptors between about 20% and about 60%.
15. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration an occupancy of dopamine D2 receptors between about 30% and about 50%.
16. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a decrease in REM sleep by an amount greater than about 10 minutes.
17. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a decrease in REM sleep by an amount between about 15 minutes and about 45 minutes.
18. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a decrease in REM sleep by an amount between about 15 minutes and about 30 minutes.
19. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a latency to REM sleep by an amount greater than about 20 minutes.

20. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a latency to REM sleep by an amount greater than about 30 minutes.

21. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a decrease in total REM sleep time relative to total sleep time by an amount greater than about 5 %.

22. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration a suppression of the time in rapid eye movement (REM) sleep as characterized by a decrease in total REM sleep time relative to total sleep time by an amount greater than about 6.5 %.

23. The pharmaceutical composition of claim 1 comprising a combined amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, effective to provide in the subject after administration:

an occupancy of dopamine D2 receptors between about 30% and about 50%; and
a suppression of the time in rapid eye movement (REM) sleep by an amount between about 15 minutes and about 45 minutes.

24. A pharmaceutical composition comprising an unequal mixture of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, wherein the amount of (R)-(+)-amisulpride is greater than the amount of (S)-(-)-amisulpride, and wherein the amount of (R)-(+)-amisulpride and (S)-(-)-amisulpride in the composition is effective to provide in a subject after administration:

an occupancy of dopamine D2 receptors between about 20% and about 60%;
and

a suppression of time in rapid eye movement (REM) sleep as characterized by one or more of:

- a decrease in REM sleep by an amount greater than about 10 minutes,
- a latency to REM sleep by an amount greater than about 20 minutes, or
- a decrease in total REM sleep time relative to total sleep time by an amount greater than about 5 %.

25. The pharmaceutical composition of claim 24, wherein the occupancy of dopamine D2 receptors is between about 30% and about 50%.
26. The pharmaceutical composition of claim 24, wherein the decrease in REM sleep is between about 15 minutes and about 45 minutes.
27. The pharmaceutical composition of claim 24, wherein the latency to REM sleep is by an amount greater than about 30 minutes.
28. The pharmaceutical composition of claim 24, wherein the decrease in total REM sleep time relative to total sleep time is by an amount greater than about 6.5 %.
29. The pharmaceutical composition of claim 24 wherein the ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride is between about 85:15 by weight of free base.
30. The pharmaceutical composition of claim 24, wherein the combined amount of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, is between about 100 mg and about 700 mg by weight of free base.
31. A pharmaceutical composition comprising an unequal mixture of (R)-(+)-amisulpride and (S)-(-)-amisulpride, or pharmaceutically acceptable salts thereof, wherein the amount of (R)-(+)-amisulpride is greater than the amount of (S)-(-)-amisulpride, in amounts effective to provide in a subject after administration:

inhibition of dopamine D2 activity and serotonin 5-HT7 activity in said subject such that the ratio of the serotonin 5-HT7 receptor inhibitory constant to the dopamine D2 receptor inhibitory constant is in the range between about 2 to about 6.

32. The pharmaceutical composition of claim 31, wherein the ratio of the serotonin 5-HT7 receptor inhibitory constant to the dopamine D2 receptor inhibitory constant is in the range between about 3 to about 5.
33. The pharmaceutical composition of claim 31, wherein the ratio of the serotonin 5-HT7 receptor inhibitory constant to the dopamine D2 receptor inhibitory constant is about 4.
34. The pharmaceutical composition of claim 31, wherein the dopamine D2 receptor inhibitory constant is in the range between about 11 nM to about 20 nM and the serotonin 5-HT7 receptor inhibitory constant is in the range between about 40 nM to about 85 nM.
35. The pharmaceutical composition of claim 31, wherein the dopamine D2 receptor inhibitory constant is about 17 nM and the serotonin 5-HT7 receptor inhibitory constant is about 66 nM.
36. The pharmaceutical composition of claim 31, wherein the composition is provided in a solid oral dosage form comprising one or more pharmaceutically acceptable excipients.
37. The pharmaceutical composition of claim 36, wherein
the total combined amount of (R)-amisulpride and (S)-amisulpride comprises between about 20% to about 40% of the total weight of the pharmaceutical composition; and
the one or more pharmaceutically acceptable excipients comprise:
a filler comprising between about 30% and about 55% of the total weight of the pharmaceutical composition; and
a disintegrant comprising between about 15% and about 30% of the total weight of the pharmaceutical composition.
38. A liquid pharmaceutical composition comprising:
one or more pharmaceutically acceptable excipients; and

an aqueous solution comprising an unequal mixture of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, with a combined amount between about 5 mg/mL and about 200 mg/mL, wherein the ratio of (R)-(+)-amisulpride to (S)-(-)-amisulpride is in the range between about 65:35 to about 88:12 by weight of free base.

39. A method of treating a psychiatric disorder in a subject comprising administering a pharmaceutical composition of any one of claims 1-38.
40. The method of claim 39 wherein the psychiatric disorder is a depressive disorder.
41. The method of claim 39 wherein the psychiatric disorder is major depressive disorder (MDD).
42. The method of claim 39 wherein the psychiatric disorder is major depressive disorder with mixed features (MDD-MF).
43. The method of claim 39 wherein the psychiatric disorder is treatment resistant depression (TRD).
44. The method of claim 39 wherein the psychiatric disorder is one or more of schizophrenia and negative symptoms of schizophrenia.
45. The method of claim 39 wherein the psychiatric disorder is schizoaffective disorder.
46. The method of claim 39 wherein the psychiatric disorder is bipolar disorder.
47. The method of claim 39 wherein the psychiatric disorder is bipolar depression.
48. The method of claim 39 wherein method of treatment treats two or more of schizophrenia, negative symptoms of schizophrenia, treatment resistant depression, bipolar disorder and depression.

49. The method of claim 39 wherein the composition is administered once daily.
50. A method of treating bipolar depression comprising administering once daily to a subject in need thereof an effective amount of a composition comprising:
an amount about 170 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and
an amount about 30 mg of (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base.
51. A method of treating bipolar depression comprising administering once daily to a subject in need thereof an effective amount of a composition comprising:
an amount about 340 mg of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base; and
an amount about 60 mg of (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof, by weight of free base.
52. A method of inhibiting dopamine D2 activity and serotonin 5-HT7 activity in a subject, comprising administering to a subject an effective amount of an unequal mixture of (R)-(+)-amisulpride, or a pharmaceutically acceptable salt thereof, and (S)-(-)-amisulpride, or a pharmaceutically acceptable salt thereof.