WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the add-on treatment of schizophrenia in a subject in need thereof, wherein the subject is also being administered at least one co-therapeutic agent for the treatment of schizophrenia.

2. The use of claim 1, wherein the subject has at least one sign or symptom of schizophrenia.

3. The use of claim 1 or 2, wherein the subject has at least one positive, negative, and/or cognitive sign or symptom of schizophrenia.

4. The use of claim 2 or 3, wherein the at least one sign or symptom is delusions, hallucinations, disorganized speech, disorganized behavior or attention, anhedonia, catatonic behavior, affective flattening, alogia, avolition, conceptual disorganization, or any combination thereof.

5. Use of a therapeutically effective amount of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the add-on treatment of schizophrenia in a subject in need thereof, wherein the subject has at least one symptom chosen from the following symptoms in Positive and Negative Symptom Scale (PANSS): P1 (delusions), P3 (hallucinations), P6 (suspiciousness), and G9 (unusual thought content), and further wherein the subject is also being administered at least one co-therapeutic agent for the treatment of schizophrenia.

6. The use of claim 5, wherein the subject has a total PANSS score ≥70.

7. The use of claim 5 or 6, wherein the subject has Clinical Global Impression of Severity (CGI-S) score ≥ 4.

8. The use of any one of claims 5-7, wherein the subject has a stable background antipsychotic medication dose.

9. The use of any one of claims 5-8, wherein the subject has a stable PANSS total score.

10. The use of any one of claims 1-9, wherein the subject is residually symptomatic or has at least one residual sign or symptom after first- or second-line treatment of schizophrenia.

11. The use of any one of claims 1-10, wherein the subject is residually symptomatic or has at least one residual sign or symptom after mono- or combination therapy for schizophrenia.

12. The use of claim 11, wherein the mono- or combination therapy is initial therapy.

13. The use of any one of claims 1-12, wherein the at least one co-therapeutic agent is least one antipsychotic agent.

14. The use of claim 13, wherein the antipsychotic agent is a typical antipsychotic agent.

15. The use of claim 14, wherein the typical antipsychotic agent is benperidol, chlorpromazine, droperidol, flupentixol, fluphenazine, haloperidol, levomepromazine, loxapine, molindone, pericyazine, perphenazine, pimozide, prochlorperazine, promazine, sulpiride, thiothixene, trifluoperazine, thioridazine, zuclopenthixol, or any combination thereof.

16. The use of claim 13, wherein the antipsychotic agent is an atypical antipsychotic agent.

17. The use of claim 16, wherein the atypical antipsychotic agent is clozapine, olanzapine, risperidone, sertindole, quetiapine, paliperidone, asenapine, ziprasidone, surmontil, iloperidone, aripiprazole, or any combination thereof.

18. The use of any one of claims 13-17, wherein the subject is receiving concomitant treatment with a subtherapeutic dose of a second antipsychotic agent.

19. The use of claim 18, wherein the concomitant treatment with a subtherapeutic dose of a second antipsychotic is used to treat insomnia or anxiety.

20. The use of claim 19, wherein the concomitant treatment with a subtherapeutic dose of a second antipsychotic is used to treat symptoms other than refractory positive psychosis symptoms.

21. The use of any one of claims 13-20, wherein the subject has an inadequate response to the at least one antipsychotic agent.

22. The use of any one of claims 13-21, wherein the subject is on at least a second clinical use of the at least one antipsychotic agent.

23. The use of any one of claims 1-22, wherein the subject is also being administered risperidone and/or a risperidone equivalent.

24. The use of claim 23, wherein the subject is also being administered a total daily dose of from about 4 mg to about 8 mg of risperidone and/or risperidone equivalents.

25. The use of any one of claims 1-24, wherein the subject is receiving background antipsychotic therapy at a total daily dose of from about 4 mg to about 8 mg of risperidone equivalents according to Table 2.

26. The use of claim 25, wherein the subject has a stable antipsychotic agent dose.

27. The use of claim 26, wherein the stable antipsychotic agent dose is defined as ≤25% change in risperidone equivalent total daily dose.

28. The use of any one of claims 13-27, wherein the subject is also being administered up to two antipsychotic agents.

29. The use of claim 28, wherein the total combined antipsychotic dose is from about 4 mg to about 8 mg daily dose of risperidone equivalents according to Table 2.

30. The use of any one of claims 13-29, wherein the antipsychotic agent is other than clozapine.

31. The use of any one of claims 13-30, wherein the subject is treated with a stable regimen of antipsychotic agent(s) with no clinically meaningful change in the prescribed dose.

32. The use of claim 31, wherein the no clinically meaningful change in the prescribed dose is no increase in dose or ≤25% decrease in dose for tolerability.

33. The use of claim 32, wherein no dose adjustment is anticipated.

34. The use of any one of claims 13-33, wherein the subject is also being administered a long-acting injectable antipsychotic.

35. The use of claim 34, wherein there is no dose change in the long-acting injectable antipsychotic.

36. The use of any one of claims 21-35, wherein the inadequate response comprises at least one baseline criterion selected from:

Positive and Negative Symptom Scale (PANSS) total score of ≥70;

PANSS score of ≥4 on at least one symptom selected from P1 (delusions), P3 (hallucinations), P6 (suspiciousness), and G9 (unusual thought content);

Clinical Global Impression of Severity (CGI-S) score of ≥4;

stable background antipsychotic medication dose of ≤25% change in risperidone equivalent total daily dose according to Table 2; and

a stable PANSS total score of ≤15% change.

37. The use of any one of claims 1-36, wherein the subject has a confirmed diagnosis of schizophrenia as defined by the MINI Version 7.0.2 for Psychotic Disorders for the Psychotic Disorders for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) for a subject ≥18 years of age or K-SADS-PL for a subject 13 to 17 years of age.

38. The use of any one of claims 1-37, wherein the subject has a confirmed initial diagnosis of schizophrenia for at least one year.

39. The use of any one of claims 1-38, wherein the subject is at least 13 years of age with a body weight of at least 50 kg.

40. The use of any one of claims 1-39, wherein the subject is an outpatient with stable symptomatology.

41. The use of any one of claims 1-40, wherein the subject does not have comorbid Parkinsonism and/or does not or exhibit more than a minimal level of extrapyramidal signs or symptoms as defined by a score on the modified Simpson Angus Scale (SAS; excluding #10, akathisia) >6.

42. The use of any one of claims 1-41, wherein the subject does not have treatment-resistant schizophrenia, as defined by at least one of the following criteria:

a history of clozapine treatment for treatment-resistant psychosis; and/or

a history of multiple adequate and failed antipsychotic medication trials, wherein the subject demonstrated minimal or no improvement.

43. The use of any one of claims 1-42, wherein the subject does not have a diagnosis of schizoaffective disorder; a lifetime diagnosis of bipolar disorder; a lifetime diagnosis of obsessive-compulsive disorder; a recent occurrence of panic disorder, a depressive episode, and/or other comorbid psychiatric condition(s) requiring clinical attention based on the MINI Version 7.0.2.

44. The use of any one of claims 1-43, wherein the subject does not have evidence of depression as measured by a Calgary Depression Scale for Schizophrenia (CDSS) score >8.

45. The use of any one of claims 1-44, wherein the subject has not attempted suicide and/or does not have positive answers on item numbers 4 or 5 on the Columbia-Suicide Severity Rating Scale (C-SSRS).

46. The use of any one of claims 1-45, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-

a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be administered via a titration scheme that comprises the up-titration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2, 1-a]isoquinolin-2-yl ester over a period of no more than about six weeks until an optimized dose is to be administered.

47. The use of claim 46, wherein the titration scheme comprises the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof to be administered at an initial dose equivalent to about 40 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily for about two weeks, provided that the patient tolerates the initial dose and that the patient has not had an adequate response, increasing the dose, wherein the increased dose is to be administered to the subject.

48. The use of claim 47, wherein the increased dose is equivalent to about 60 mg of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.

49. The use of claim 47, wherein the increased dose is equivalent to about 80 mg of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.

50. The use of any one of claims 46-49, wherein the titration scheme further comprises the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof to be administered at the increased dose for about two weeks.

51. The use of any one of claims 46-49, wherein if the subject does not tolerate the increased dose, the optimized dose is the initial dose.

52. The use of claim 50, wherein if the subject tolerates the increased dose and if the subject has had an adequate response, the optimized dose is the increased dose.

53. The use of claim 51 or 52, further comprising the optimized dose of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof to be administered to the subject.

54. The use of claim 50, wherein if the subject tolerates the increased dose and if the subject has not had an adequate response, the dose is to be further increased.

55. The use of claim 54, wherein the further increased dose is equivalent to about 80 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.

56. The use of claim 54 or 55, wherein if the subject does not tolerate the further increased dose, the optimized dose is the increased dose.

57. The use of claim 54 or 55, wherein if the subject tolerates the further increased dose and if the subject has had an adequate response, the optimized dose is the further increased dose.

58. The use of claim 56 or 57, further comprising the optimized dose of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof to be administered to the subject.

59. The use of any one of the preceding claims, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be administered in the afternoon or evening.

60. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject is treated with a stable regimen of antipsychotic agent(s) with ≤25% change in risperidone equivalent total daily dose.

61. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject is treated with a stable regimen of antipsychotic agent(s) with no clinically meaningful change in the prescribed dose.

62. The use of claim 51, wherein the no clinically meaningful change in the prescribed dose is no increase in dose or a ≤25% decrease in dose for tolerability in the prescribed dose for ≥3 weeks.

63. The use of claim 52, wherein no dose adjustment is anticipated.

64. The use of any one of the preceding claims, wherein the subject is also being administered a long-acting injectable antipsychotic with no dose change within 8 weeks prior

to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof.

65. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) diagnosis of schizophrenia.

66. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a confirmed diagnosis of schizophrenia as defined by the MINI Version 7.0.2 for Psychotic Disorders for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) for a subject ≥18 years of age or K-SADS-PL for a subject 13 to 17 years of age.

67. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a confirmed initial diagnosis of schizophrenia for at least one year.

68. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has at least one symptom chosen from the following symptoms in Positive and Negative Symptom Scale (PANSS): P1 (delusions), P3 (hallucinations), P6 (suspiciousness), and G9 (unusual thought content).

69. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a total PANSS score ≥70.

70. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant

thereof; or a pharmaceutically acceptable salt thereof, the subject has a stable PANSS total score with ≤15% change.

71. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a Clinical Global Impression of Severity (CGI-S) score ≥ 4.

72. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has a stable background antipsychotic medication dose with ≤25% change in risperidone equivalent total daily dose according to Table 2.

73. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject is an outpatient with stable symptomatology for ≥3 weeks.

74. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject does not have treatment-resistant schizophrenia, as defined by at least one of the following criteria:

a history of clozapine treatment for treatment-resistant psychosis; and/or

a history of multiple adequate and failed antipsychotic medication trials, wherein the subject demonstrated minimal or no improvement.

75. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject does not have a diagnosis of schizoaffective disorder; a lifetime diagnosis of bipolar disorder; a lifetime diagnosis of obsessive-compulsive disorder; a recent occurrence of panic disorder, a depressive episode, and/or other comorbid psychiatric condition requiring clinical attention based on the MINI Version 7.0.2.

76. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject does not have evidence of depression as measured by a Calgary Depression Scale for Schizophrenia (CDSS) score >8.

77. The use of any one of the preceding claims, wherein prior to administration of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof, the subject has not attempted suicide within one year and/or does not have positive answers on item numbers 4 or 5 on the Columbia-Suicide Severity Rating Scale (C-SSRS).

78. The use of any one of the preceding claims, wherein the add-on treatment results in a change in total PANSS score from Analysis Baseline to Week 10; a change in CGI-S of illness from Analysis Baseline to Week 10, a change in Personal and Social Performance (PSP) score from Analysis Baseline to Week 10, a change in VAS scores for the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L; subjects ≥18 years old) or EQ-5D Youth (EQ-5D-Y; subjects 13 to 17 years old) from baseline to Week 10; and/or a change in Sheehan Disability Score (SDS) from baseline to Week 10.

79. The use of any one of the preceding claims, wherein the treatment results in a reduction in the subject's CGI-S positive symptoms, relative to the subject's score at baseline.

80. The use of any one of the preceding claims, wherein the treatment results in a change in EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) scores from Analysis Baseline to Week 10 and/or a change in Sheehan Disability Score (SDS) from Analysis Baseline to Week 10.

81. The use of any one of claims 1-80, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is in a solid dosage form.

82. The use of any one of claims 1-81, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be orally administered.

83. The use of any one of claims 1-82, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is in the form of a capsule.

84. The use of any one of claims 1-83, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be administered daily.

85. The use of any one of claims 1-84, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be administered once daily or twice daily.

86. The use of any one of claims 1-85, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt thereof is to be administered once daily.

87. The use of any one of claims 1-86, wherein the therapeutically effective amount is an amount equivalent to from about 10 mg to about 90 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

88. The use of any one of claims 1-87, wherein the therapeutically effective amount is an amount equivalent to from about 20 mg to about 80 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

89. The use of any one of claims 1-88, wherein the therapeutically effective amount is an amount equivalent to about 20 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

90. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 40 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

91. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 60 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-

3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

92. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 80 mg of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base .

93. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 40 mg/day of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

94. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 60 mg/day of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

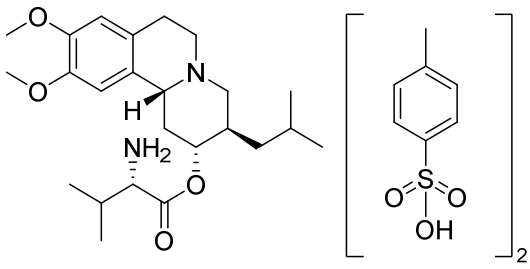
95. The use of any one of claims 1-89, wherein the therapeutically effective amount is an amount equivalent to about 80 mg/day of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base.

96. The use of any one of claims 1-95, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester is a free base.

97. The use of any one of claims 1-95, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester is a salt.

98. The use of any one of claims 1-97, wherein the salt is a tosylate salt.

99. The use of claim 98, wherein the tosylate salt is (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester tosylate salt of structural Formula (I):



(I).

100. The use of any one of claims 1-99, wherein the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt, is in crystalline form.

101. The use of claim 100, wherein the crystalline form of the (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester or an isotopic variant thereof; or a pharmaceutically acceptable salt, is Form I of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2, l-a]isoquinolin-2-yl ester tosylate salt having a differential scanning calorimetric (DSC) peak temperature within 2% of 243 °C.

102. The use of claim 100 or 101, wherein the DSC peak temperature of the crystalline form is within 1% of 243 °C.

103. The use of any one of claims 100-102, wherein the DSC peak temperature of the crystalline form is within 0.5% of 243 °C.

104. The use of any one of claims 100-103, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern comprising a peak at a two-theta angle of 6.3°±0.2°.

105. The use of any one of claims 100-104, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern comprising a peak at a two-theta angle of 17.9°±0.2°.

106. The use of any one of claims 100-105, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern comprising a peak at a two-theta angle of 19.7°±0.2°.

107. The use of any one of claims 100-106, wherein the crystalline form is stable upon exposure to about 25 °C and about 60% relative humidity.

108. The use of any one of claims 100-107, wherein the crystalline form has a D90 particle size of about 70 μM in length.

109. The use of any one of claims 100-107, wherein the crystalline form has a D10 particle size of about 10 μM in length.

110. The use of any one of claims 100-109, wherein the crystalline form has a purity of no less than 97% by weight of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2, l-a]isoquinolin-2-yl ester tosylate salt.

111. The use of any one of claims 100-110, wherein the crystalline form has a purity of no less than 98% by weight of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2, l-a]isoquinolin-2-yl ester tosylate salt.

112. The use of any one of claims 100-111, wherein the crystalline form has a purity of no less than 97% by weight of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2, l-a]isoquinolin-2-yl ester tosylate salt; and has an X-ray powder diffraction (XRPD) pattern comprising peaks at two-theta angles of 6.3°±0.2°, 17.9°±0.2°, and 19.7°±0.2°.