CLAIMS:

1. ~~A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering~~ Use of dexmedetomidine or a pharmaceutically acceptable salt thereof in the manutfature of a medicament for the treatment of agitation in a human subject with schizophrenia or bilpolar disorder, wherein the medicament is to be administered at a dose resulting in a mean total exposure of dexmedetomidine, as measured by plasma $AUC_{0\text{-}inf}$, from ~~T_0~~ 600 ng*h/L to ~~T∞, of~~ about ~~3800~~ 12600 ng*h/L.

~~2. A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose resulting in a total exposure of dexmedetomidine, as measured by plasma AUC from T_0 to T∞, from about 600 ng*h/L to about 12600 ng*h/L.~~

~~3.~~2. ~~A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose resulting in a mean total exposure of dexmedetomidine, as measured by plasma AUC from T_0 to T∞, of about 1800 ng*h/L.~~The use of claim 1, wherein the dose is about 120 µg to about 240 µg.

~~4.~~3. ~~A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose resulting in a total exposure of dexmedetomidine, as measured by plasma AUC from T_0 to T∞, from about 590 ng*h/L to about 8750 ng*h/L.~~The use of claim 1 or 2, wherein the human subject has schizophrenia.

~~5.~~4. The ~~method~~ use of claims 1 ~~to 4~~or 2, wherein ~~said agitation or signs of agitation is associated with schizophrenia~~the human subject has bipolar disorder.

~~6.~~5. The ~~method~~ use of any one of claims 1 to ~~5~~4, wherein the $AUC_{0\text{-}inf}$ is about 2300 ng*h/L to about 3600 ng*h/L; and wherein C_{max} is about 300 ng/L to about 500 ng/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually, buccally, orally, intranasally or parenterally~~.

~~7.~~6. The ~~method~~ use of claim ~~6~~5, wherein the C_{max} is within the range of about 80% to about 125% of about 400 ng/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a tablet, film, spray, gel or drops~~.

~~8.~~7. The ~~method~~ use of claim ~~7~~5, wherein the $AUC_{0\text{-}inf}$ is within the range of about 80% to about 125% of about 2900 ng*h/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a film~~.

~~9.~~8. The ~~method~~ use of ~~claim~~ any one of claims ~~6~~1-4, wherein the $AUC_{0\text{-}inf}$ is about 1100 ng*h/L to about 1800 ng*h/L; and wherein C_{max} is about 150 ng/L to about 300 ng/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered buccally in the form of a film, patch or tablet~~.

~~10.~~9. The ~~method~~ use of claim ~~6~~8, wherein the C_{max} is within the range of about 80% to about 125% of about 220 ng/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered parenterally in the form of an intramuscular injection~~.

~~11.~~10. The ~~method~~ use of claim ~~6~~8, wherein the $AUC_{0\text{-}inf}$ is within the range of about 80% to about 125% of about 1410 ng*h/L~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered orally~~.

~~12.~~11. The ~~method~~ use of ~~claims 1 to 4~~claim 8, wherein the plasma T_{max} is about 1 hour to about 8 hours~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered as a single dose~~.

~~13.~~12. The ~~method~~ use of ~~claims 1 to 4~~claim 8, wherein the plasma T_{max} is about 5 minutes to about 4 hours~~dexmedetomidine or a pharmaceutically acceptable salt thereof is administered as a single dose containing about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof~~.

~~14.~~13. The ~~method~~ use of any of claims ~~1 to 4~~1-12, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is to be administered oromucosally, orally, intranasally or parenterally~~as a single dose containing about 120 µg dexmedetomidine or a pharmaceutically acceptable salt thereof~~.

~~15.~~14. The ~~method~~ use of claim 13, wherein the dexmedetomidine or a pharmaceutically acceptable salt is to be administered oromucosally~~resulting in a total exposure of dexmedetomidine, as measured by plasma AUC from T_0 to $T\infty$, from about 600 ng*h/L to about 9500 ng*h/L~~.

~~16.~~15. The ~~method~~ use of claim ~~10~~14, wherein the dexmedetomidine or a pharmaceutically acceptable salt is to be administered sublingually~~thereof is administered at a dose of about 140 µg to about 190 µg~~.

~~17.~~16. The ~~method~~ use of claim ~~11~~14, wherein dexmedetomidine or a pharmaceutically acceptable salt is to be administered buccally~~thereof is administered at a dose of about 900 µg to about 1200 µg~~.

~~18.~~17. The ~~method~~ use of any one of claims ~~1 to 4~~1-16, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is to be administered in the form of a tablet, film, spray, gel or drops~~agitation or signs of agitation is treated without also inducing clinically significant cardiovascular effects~~.

~~19.~~18. The ~~method~~ use of ~~claims 1 to 4~~claim 17, wherein the dexmedetomidine or a pharmaceutically acceptable salt thereof is to be administered sublingually in the form of a film~~agitation or signs of agitation are significantly reduced within 60 minutes of administering dexmedetomidine or a pharmaceutically acceptable salt thereof, as measured by a significant relative change in PEC score just prior to and 60 minutes after administering dexmedetomidine or a pharmaceutically acceptable salt thereof~~.

~~20.~~19. The ~~method~~ use of claim ~~19~~17, wherein the dexmedetomidine or a pharmaceutically acceptable salt thereof is to be administered buccally in the form of a film, patch or tablet~~the said relative PEC scores are different by at least six or eight points~~.

~~21. The method of claim 20, wherein the difference in relative PEC scores is maintained for at least six hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~22. The method of claim 21, wherein the said relative PEC scores are different by at least eight points, and wherein this difference of at least eight points is maintained for up to at least about 6 to 24 hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~23. The method of claim 1, wherein the mean plasma Cmax is about 400 ng/L.~~

~~24. The method of claim 1, wherein the median plasma Tmax is about 2 hours.~~

~~25. The method of claim 1, wherein the mean plasma Cmax is about 400 ng/L and the median plasma Tmax is about 2 hours.~~

~~26. The method of claim 2, wherein the plasma Cmax is about 100 ng/L to about 1100 ng/L.~~

~~27. The method of claim 2, wherein the plasma Cmax is about 200 ng/L to about 800 ng/L.~~

~~28. The method of claim 2, wherein the plasma Cmax is about 3000 ng/L to about 5000 ng/L.~~

~~29. The method of claim 2, wherein the plasma Tmax is about 1 hour to about 8 hours.~~

~~30. The method of claim 2, wherein the plasma Tmax is about 5 minutes to about 4 hours.~~

~~31. The method of claim 2, wherein the plasma tmax is about 5 minutes to about 15 minutes.~~

~~32. The method of claim 3, wherein the mean plasma Cmax is about 200 ng/L.~~

~~33. The method of claim 3, wherein the median plasma Tmax is about 2.0 hours.~~

~~34. The method of claim 3, wherein the mean plasma Cmax is about 200 ng/L and the median plasma Tmax is about 2 hours.~~

~~35. The method of claim 4, wherein the plasma Cmax is about 100 ng/L to about 500 ng/L.~~

~~36. The method of claim 4, wherein the plasma Cmax is about 150 ng/L to about 700 ng/L.~~

~~37. The method of claim 4, wherein the plasma Cmax is about 1400 ng/L to about 4500 ng/L~~

~~38. The method of claim 4, wherein the plasma Tmax is about 1 hour to about 4 hours.~~

~~39. The method of claim 4, wherein the plasma Tmax is about 5 minutes to about 15 minutes.~~

~~40. A method of treating a condition (e.g. agitation) in a human subject, comprising administering to said subject about 180 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof sublingually or buccally to said subject, resulting in mean plasma absorption levels of dexmedetomidine from about 80% to about 125% of the following values: Cmax of about 400 ng/L and AUC from T_0 to T∞ of about 2900 ng*h/L.~~

~~41. A method of treating a condition (e.g. agitation) in a human subject, comprising administering to said subject about 180 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof sublingually or buccally to said subject, resulting in plasma absorption levels of dexmedetomidine from about 80% to about 125% of the following values: Cmax from about 100 ng/L to about 800 ng/L and AUC from T_0 to T∞ of about 600 hr*ng/L to about 9500 hr*ng/L.~~

~~42. A method of treating a condition (e.g. agitation) in a human subject, comprising administering to said subject about 120 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof sublingually or buccally to said subject, resulting in mean plasma absorption levels of dexmedetomidine from about 80% to about 125% of the following values: Cmax of about 200 ng/L and AUC from T_0 to T∞ of about 1420 ng*h/L.~~

~~43. A method of treating a condition (e.g. agitation) in a human subject, comprising administering to said subject about 120 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof sublingually or buccally to said subject, resulting in plasma absorption levels of dexmedetomidine from about 80% to about 125% of the following values: Cmax from about 110 ng/L to about 400 ng/L and AUC from T_0 to T∞ of about 5900 hr*ng/L to about 4400 hr*ng/L.~~

~~44. The method of claims 40 to 43, wherein the condition is agitation or signs of agitation.~~

~~45. The method of claim 44, wherein said agitation or signs of agitation is associated with schizophrenia or bipolar disorder.~~

~~46. The method of claims 40 to 43, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a tablet, film, spray, gel or drops.~~

~~47. The method of claim 46, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a film.~~

~~48. The method of claims 40 to 43, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered buccally in the form of a film, patch or tablet.~~

~~49. The method of claim 48, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered buccally in the form of a film.~~

~~50. The method of claims 40 to 43, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered as a single dose.~~

~~51. The method of claims 40 to 43, wherein the subject is treated without also inducing significant sedation.~~

~~52. The method of claims 40 to 43, wherein the subject is treated without also inducing clinically significant cardiovascular effects.~~

~~53. The method of claim 45, wherein agitation or signs of agitation are significantly reduced within 60 minutes of administering dexmedetomidine or a pharmaceutically acceptable salt thereof, as measured by a significant relative change in PEC scores just prior to and 60 minutes after administering dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~54. The method of claim 53, wherein the said relative PEC scores are different by at least six or eight points.~~

~~55. The method of claim 54, wherein the difference in relative PEC scores is maintained for at least six hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~56. The method of claim 54, wherein the said relative PEC scores are different by at least eight points, and wherein this difference of at least eight points is maintained for up to at least about 24 hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~57. The method of claims 40 to 43, wherein the median plasma Tmax is about 2 hours.~~

58. The method of claims 40 to 43, wherein the plasma Tmax is about 1 hour to about 8 hours.

59. A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof as a single dose.

60. A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering about 120 µg dexmedetomidine or a pharmaceutically acceptable salt thereof as a single dose.

61. A method of mitigation or preventing the occurrence of a further agitation event in a human subject with schizophrenia or bipolar disorder within about 24 hours of an earlier agitation event, comprising administering about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof as a single dose immediately following said earlier agitation event.

62. A method of mitigation or preventing the occurrence of a further agitation event in a human subject with schizophrenia or bipolar disorder within about 24 hours of an earlier agitation event, comprising administering about 120 µg dexmedetomidine or a pharmaceutically acceptable salt thereof as a single dose immediately following said earlier agitation event.

63. The method of claims 59 or 60, wherein said agitation or signs of agitation is associated with schizophrenia.

64. A method of reducing a period of opioid withdrawal by administering to a human subject of at least 18 years in need thereof dexmedetomidine twice daily for the period of withdrawal, wherein the period of withdrawal is up to 14 days.

65. The method of claim 64, wherein the dexmedetomidine is administered at a dose range between 30 µg and 200 µg.

66. The method of claim 64, wherein the dexmedetomidine is administered at a unit dose of about 30 µg, 60 µg, 90 µg, 120 µg and 180 µg.

67. The method of claim 64, wherein the period of withdrawal is up to: 13 days, 12 days, 11 days, 10 days, 9 days, 8 days, 7 days, 6 days, 5 days, 4 days, or 3 days.

68. The method of claim 64, wherein the opioid is selected from the group comprising of fentanyl, morphine, codeine, heroin, oxycodone, hydrocodone, alfentanil carfentanil, tramadol, hydromorphone, buprenorphine, naloxone, naltrexone, remifentanil

butorphanol, meperidine, methadone, dextropropoxyphene (propoxyphene) thebaine, sufentanil or pentazocine.

69. The method of claim 64, wherein the opioid had been administered for amount of time longer than neonate treatment prior to withdrawal.

70. The method of claims 59 to 64, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually, buccally, orally, intranasally or parenterally.

71. The method of claims 59 to 64, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a tablet, film, spray, gel or drops..

72. The method of claims 59 to 64, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually in the form of a film.

73. The method of claims 59 to 64, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered buccally in the form of a film, patch or tablet..

74. The method of claim 59 to 64, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered buccally in the form of a film.

75. The method of claims 59 to 62, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered parenterally in the form of an intravenous or intramuscular injection or an intravenous infusion.

76. The method of claim 59 to 62, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered by intramuscular injection.

77. The method of claim 59 to 62, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered once a day.

78. The method of claim 59 to 64, wherein agitation or signs of agitation is treated without also inducing clinically significant cardiovascular effects.

79. The method of claim 59 or claim 61, wherein a single dose of about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof is effective for up to at least about 24 hours.

80. A method of treating agitation or signs of agitation in a human subject with schizophrenia or bipolar disorder, without also inducing significant sedation, comprising administering an oromucosal film comprising about 120 µg or about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof as a single dose.

81. The method of claims 80, wherein the subject has been previously administered a liquid formulation of dexmedetomidine or a pharmaceutically acceptable salt thereof via a

~~parenteral route (intravenous, intramuscular, subcutaneous injection or intravenous infusion).~~

~~82. The method of any of claims 80 and 81, wherein the oromucosal administration is followed within 3 to 5 hours of previous administration of liquid formulation of dexmedetomidine via a parenteral route.~~

~~83. The method of any of claims 80, wherein the parenteral administration is followed within 3 to 5 hours of previous administration of oromucosal film.~~

~~84. The method of claim 80, wherein the liquid formulation is pre-filled in disposable syringes for self-administration by patients with an auto-injector.~~

~~85. The method of claims 59 to 63, wherein the subject is currently is co-treated with an anti-psychotic.~~

~~86. The method of claims 59 to 63, wherein the anti-psychotic is .~~

~~is selected from but are not limited to aripiprazole, benperidol. flupentixol, amisulpride, chlorpromazine, asenapine , risperidone, ziprasidone, lurasidone, clozapine, cariprazine, olanzapine and quetiapine. In a preferred embodiment, the anti-psychotic is aripiprazole.~~

~~87. The method of claims 59 to 63, wherein agitation or signs of agitation are significantly reduced within 60 minutes of administering dexmedetomidine or a pharmaceutically acceptable salt thereof, as measured by a significant relative change in PEC scores just prior to and 60 minutes after administering dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~88. The method of claim 87, wherein the said relative PEC scores are different by at least six points or eight points.~~

~~89. The method of claims 87 or claim 88, wherein the difference in relative PEC scores is maintained for at least six hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~90. The method of claim 87, wherein the said relative PEC scores are different by at least eight points, and wherein this difference of at least eight points is maintained for up to at least about 24 hours following administration of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~91. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:~~

~~(i) about 180 micrograms of dexmedetomidine or a pharmaceutically acceptable salt thereof;~~

(ii) one or more water-soluble polymers; and, optionally,

one or more pharmaceutically acceptable carriers.

92. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:

about 120 micrograms of dexmedetomidine or a pharmaceutically acceptable salt thereof;

(ii) one or more water-soluble polymers; and, optionally,

(iii) one or more pharmaceutically acceptable carriers.

93. The method of claim 91 or claim 92, wherein (ii) comprises a low molecular weight, water-soluble polymer and two high molecular weight, water-soluble polymers.

94. The method of claims 93, wherein the low molecular weight, water-soluble polymer has a molecular weight from about 5,000 daltons to about 49,000 daltons, and each high molecular weight, water-soluble polymer has a molecular weight of greater than about 60,000 daltons.

95. The method of claim 93, wherein the low molecular weight, water-soluble polymer has a molecular weight of about 40,000 daltons, one of the two high molecular weight, water-soluble polymers has a molecular weight of about 140,000 daltons, and the other high molecular weight, water-soluble polymer has a molecular weight of about 370,000 daltons.

96. The method of claim 91 or claim 92, wherein each water-soluble polymer is hydroxypropyl cellulose.

97. The method of claim 91 or claim 92, wherein the film also comprises a polyethylene oxide.

98. The method of claim 97, wherein the polyethylene oxide has a molecular weight of about 600,000 daltons.

99. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:

(i) about 180 micrograms of dexmedetomidine or a pharmaceutically acceptable salt thereof;

(ii) a low molecular weight, water-soluble polymer having a molecular weight of about 40,000 daltons;

(iii) a high molecular weight, water-soluble polymer having a molecular weight from about 140,000 daltons;

~~(iv) a high molecular weight, water-soluble polymer having a molecular weight from about 370,000 daltons; and~~

~~(v) a water-soluble polyethylene oxide having a molecular weight of about 600,000 daltons.~~

~~100. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:~~

~~(i) about 120 micrograms of dexmedetomidine or a pharmaceutically acceptable salt thereof;~~

~~(ii) a low molecular weight, water-soluble polymer having a molecular weight of about 40,000 daltons;~~

~~(iii) a high molecular weight, water-soluble polymer having a molecular weight from about 140,000 daltons;~~

~~(iv) a high molecular weight, water-soluble polymer having a molecular weight from about 370,000 daltons; and~~

~~(v) a water-soluble polyethylene oxide having a molecular weight of about 600,000 daltons.~~

~~101. The method of claim 99 or claim 100, wherein the film components excluding dexmedetomidine or a pharmaceutically acceptable salt thereof form a single layer film substrate, and dexmedetomidine or a pharmaceutically acceptable salt thereof is present on the surface of the film substrate.~~

~~102. The method of claim 99 or claim 100, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is present on the surface of the film substrate within a composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof, a low molecular weight, water-soluble polymer having a molecular weight of about 40,000 daltons, and a high molecular weight, water-soluble polymer having a molecular weight of about 140,000 daltons.~~

~~103. The method of claim 99 or claim 100, wherein each water-soluble polymer is hydroxypropyl cellulose.~~

~~104. The method of claim 99 or claim 100, wherein the dexmedetomidine or a pharmaceutically acceptable salt thereof is dexmedetomidine hydrochloride.~~

~~105.~~20. The ~~method of claim 72~~use of any one of claims 1-19, wherein said film is a self-supporting, dissolvable, film, comprising:

~~(a) a composition comprising:~~

(i) dexmedetomidine or a pharmaceutically acceptable salt thereof~~about 180 micrograms of dexmedetomidine hydrochloride~~;

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii) hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate comprising:~~

(i) hydroxypropyl cellulose (40,000MW);

(ii) hydroxypropyl cellulose (140,000MW);

(iii) hydroxypropyl cellulose (370,000MW); and

(iv) polyethylene oxide (600,000MW)~~;~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b)~~.

~~106. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:~~

~~(a) a composition consisting essentially of:~~

~~(i) about 180 micrograms of dexmedetomidine hydrochloride;~~

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii) hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate consisting essentially of:~~

~~(i) hydroxypropyl cellulose (40,000MW);~~

~~(ii) hydroxypropyl cellulose (140,000MW);~~

~~(iii) hydroxypropyl cellulose (370,000MW); and~~

~~(iv) polyethylene oxide (600,000MW);~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b).~~

~~107. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:~~

~~(a) a composition comprising:~~

~~(i) about 180 micrograms of dexmedetomidine hydrochloride;~~

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii) hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate comprising:~~

~~(i) hydroxypropyl cellulose (40,000MW);~~

~~(ii) hydroxypropyl cellulose (140,000MW);~~

~~(iii) hydroxypropyl cellulose (370,000MW); and~~

~~(iv) polyethylene oxide (600,000MW);~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b).~~

~~108. The method of claim 72, wherein said film is a self-supporting, dissolvable, film, comprising:~~

~~(a) a composition consisting essentially of:~~

~~(i) about 180 micrograms of dexmedetomidine hydrochloride;~~

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii) hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate consisting essentially of:~~

~~(i) hydroxypropyl cellulose (40,000MW);~~

~~(ii) hydroxypropyl cellulose (140,000MW);~~

~~(iii) hydroxypropyl cellulose (370,000MW); and~~

~~(iv) polyethylene oxide (600,000MW);~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b).~~

~~109.~~21. The ~~method~~ use of ~~claims 105 to~~ claim ~~108~~20, wherein ~~dexmedetomidine hydrochloride is present at about 0.1% to about 0.2% w/w of the total film weight,~~ hydroxypropyl cellulose (40,000MW) is present at about ~~4~~3% to about ~~6~~15% w/w of the total film weight, hydroxypropyl cellulose (140,000MW) is present at about ~~4~~3% to about ~~6~~8% w/w of the total film weight, hydroxypropyl cellulose (370,000MW) is present at about ~~27~~10% to about ~~30~~50% w/w of the total film weight, and polyethylene oxide (600,000MW) is present at about ~~55~~40% to about ~~60~~70% w/w of the total film weight.

~~110. A self-supporting, dissolvable, film, comprising:~~

~~(a) a composition consisting essentially of:~~

~~(i) about 180 micrograms of dexmedetomidine hydrochloride;~~

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii)hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate consisting essentially of:~~

~~(i) hydroxypropyl cellulose (40,000MW);~~

~~(ii) hydroxypropyl cellulose (140,000MW);~~

~~(iii)hydroxypropyl cellulose (370,000MW); and~~

~~(iv)polyethylene oxide (600,000MW);~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b).~~

~~111. A self-supporting, dissolvable, film, comprising:~~

~~(a) a composition consisting essentially of:~~

~~(i) about 120 micrograms of dexmedetomidine hydrochloride;~~

~~(ii) hydroxypropyl cellulose (40,000MW); and~~

~~(iii)hydroxypropyl cellulose (140,000MW); and~~

~~(b) a film substrate consisting essentially of:~~

~~(i) hydroxypropyl cellulose (40,000MW);~~

~~(ii) hydroxypropyl cellulose (140,000MW);~~

~~(iii)hydroxypropyl cellulose (370,000MW); and~~

~~(iv)polyethylene oxide (600,000MW);~~

~~wherein the composition of part (a) is present on the surface of the film substrate (b).~~

~~112. The film of claim 110 or claim 111, wherein dexmedetomidine hydrochloride is present at about 0.1% to about 0.2% w/w of the total film weight, hydroxypropyl cellulose (40,000MW) is present at about 4% to about 6% w/w of the total film weight, hydroxypropyl cellulose (140,000MW) is present at about 4% to about 6% w/w of the total film weight, hydroxypropyl cellulose (370,000MW) is present at about 27% to about 30% w/w of the total film weight, and polyethylene oxide (600,000MW) is present at about 55% to about 60% w/w of the total film weight.~~

~~113~~22. ~~A method of treating agitation associated with schizophrenia or bipolar disorder, comprising administering a unit dose composition comprising about 120 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient~~The use of any one of claims 1-7 or 10-21, wherein the dose of dexmedetomidine or a pharmaceutically acceptable salt thereof is about 180 µg.

~~114~~23. The use of any one of claims 1-4 or 8-21, wherein the dose of dexmedetomidine or a pharmaceutically acceptable salt thereof is about 120 µg~~method of claim 113, wherein the patient has schizophrenia~~.

~~115~~24. The use of any one of claims 1-23, wherein the dexmedetomidine or a pharmaceutically acceptable salt thereof is dexmedetomidine hydrochloride~~method of claim 113 or claim 114, wherein the patient has bipolar I disorder~~.

~~116~~25. The use of any one of claims 1-24, further comprising a second dose to be administered after a period of time ranging from about 30 minutes to about 12

hoursmethod of any one of claims 113-115, wherein the composition comprises dexmedetomidine hydrochloride.

11726. The use of claim 25, wherein the second dose is about 60µg or about 90µgmethod of any one of claims 113-116, wherein the composition is administered sublingually or buccally.

11827. The use of any one of claims 1-26, wherein the agitation is reduced, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline of at least -4 pointsmethod of claim 117, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.

11928. The use of any one of claims 1-26, wherein the agitation is reduced, as measured by the Agitation-Calmness Evaluation Scale (ACES), wherein the ACES score is a 3 (mild agitation) or 4 (normal behavior)method of claim 117, wherein the composition is administered buccally in the form of a film, patch or tablet.

12029. The use of claims 27 or 28, wherein the reduction in agitation is maintained for about 2 hours to about 6 hoursmethod of any one of claims 113-119, further comprising administering a second dose after a period of time ranging from about 30 minutes to about 12 hours.

12130. The use of claim 27 or 28, wherein the agitation is reduced within about 20 minutes to about 1 hourmethod of claim 120, wherein the additional dose is about 60µg or 90µg.

122. The method of claim 120 or claim 121, wherein the second dose is administered after a period of about 2 hours.

123. The method of any one of claims 113-122, wherein the patient is in a fed state.

124. The method of any one of claims 113-122, wherein the patient is in a fasted state.

~~125. The method of any one of claims 113-124, wherein agitation is significantly reduced within about 2 hours of administering the composition, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~126. The method of claim 125, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~127. The method of claim 125 or claim 126, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~128. The method of claim 127, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

~~129. The method of any one of claims 125-128, wherein the PEC score is ≥30% lower than placebo.~~

~~130. The method of claim 129, wherein the PEC score is ≥60% lower than placebo.~~

~~131. The method of any one of claims 125-130, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering the composition.~~

~~132. The method of claim 131, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.~~

~~133. The method of claim 131, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.~~

~~134. The method of any one of claims 125-133, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.~~

135. The method of any one of claims 125-134, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 6 hours following administration of the composition.

136. The method of any one of claims 113-135, wherein the subject is treated without experiencing significant sedation.

137.. The method of any one of claims 113-136, wherein the subject is treated without experiencing clinically significant cardiovascular effects.

138. The method of any one of claims 113-137, wherein administration of a single dose provides a mean C_{max} within the range of about 80% to about 125% of about 110 ng/L to about 400 ng/L.

139. The method of claim 138, wherein the mean C_{max} is within the range of about 80% to about 125% of about 238 ng/L.

140. The method of claim 138, wherein the mean C_{max} is about 238 ng/L

141. The method of any one of claims 113-140, wherein administration of a single dose provides a mean AUC_{0-inf} within the range of about 80% to about 125% of about 590 hr*ng/L to about 4400 hr*ng/L.

142. The method of claim 141, the mean AUC_{0-inf} is within the range of about 80% to about 125% of about 1810 ng*h/L.

143. The method of claim 141, wherein the mean AUC_{0-inf} is about 1810 ng*h/L..

144. The method of any one of claims 113-143 wherein administration of a single dose provides a mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 4 hours.

145. The method of claim 144, wherein the mean T_{max} is within the range of about 80% to about 125% of about 2 hours.

~~146. The method of claim 144, wherein the mean T_{max} is about 2 hours.~~

~~147. The method of any one of claims 113-146, wherein administration of a single dose provides a geometric mean C_{max} within the range of about 80% to about 125% of about 110 ng/L to about 400 ng/L.~~

~~148. The method of claim 147, wherein the geometric mean C_{max} is within the range of about 80% to about 125% of about 220 ng/L.~~

~~149. The method of claim 147, wherein the geometric mean C_{max} is about 220 ng/L~~

~~150. The method of any one of claims 113-149, wherein administration of a single dose provides a geometric mean AUC_{0-inf} within the range of about 80% to about 125% of about 590 hr*ng/L to about 4400 hr*ng/L.~~

~~151. The method of claim 150, the geometric mean AUC_{0-inf} is within the range of about 80% to about 125% of about 1410 ng*h/L.~~

~~152. The method of claim 150, wherein the geometric mean AUC_{0-inf} is about 1410 ng*h/L.~~

~~153. The method of any one of claims 113-152 wherein administration of a single dose provides a geometric mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 4 hours.~~

~~154. The method of claim 153, wherein the geometric mean T_{max} is within the range of about 80% to about 125% of about 2 hours.~~

~~155. The method of claim 153, wherein the geometric mean T_{max} is about 2 hours.~~

~~156. The method of any one of claims 113-155, wherein administration of a single dose provides a median C_{max} within the range of about 80% to about 125% of about 110 ng/L to about 400 ng/L.~~

157. The method of claim 156, wherein the median C_{max} is within the range of about 80% to about 125% of about 230 ng/L.

158. The method of claim 156, wherein the median C_{max} is about 230 ng/L.

159. The method of any one of claims 113-158, wherein administration of a single dose provides a median AUC_{0-inf} within the range of about 80% to about 125% of about 590 hr*ng/L to about 4400 hr*ng/L.

160. The method of claim 159, the median AUC_{0-inf} is within the range of about 80% to about 125% of about 1180 ng*h/L.

161. The method of claim 141, wherein the median AUC_{0-inf} is about 1810 ng*h/L.

162. The method of any one of claims 113-161 wherein administration of a single dose provides a median T_{max} within the range of about 80% to about 125% of about 1 hour to about 4 hours.

163. The method of claim 162, wherein the median T_{max} is within the range of about 80% to about 125% of about 2 hours.

164. The method of claim 162, wherein the median T_{max} is about 2 hours.

165. The method of any one of claims 138-164, wherein the pharmacokinetic parameters are non-steady state.

166. A method of treating agitation associated with schizophrenia or bipolar disorder, comprising administering a unit dose composition comprising about 180 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient.

167. The method of claim 166, wherein the patient has schizophrenia.

~~168. The method of claim 166 or claim 167, wherein the patient has bipolar I disorder.~~

~~169. The method of any one of claims 166-168, wherein the composition comprises dexmedetomidine hydrochloride.~~

~~170. The method of any one of claims 166-169, wherein the composition is administered sublingually or buccally.~~

~~171. The method of claim 170, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.~~

~~172. The method of claim 170, wherein the composition is administered buccally in the form of a film, patch or tablet.~~

~~173. The method of any one of claims 166-172, further comprising administering a second dose after a period of time ranging from about 30 minutes to about 12 hours.~~

~~174. The method of claim 173, wherein the additional dose is about 60µg or 90µg.~~

~~175. The method of claim 8 or claim 174, wherein the second dose is administered after a period of about 2 hours.~~

~~176. The method of any one of claims 166-175, wherein the patient is in a fed state.~~

~~177. The method of any one of claims 166-175, wherein the patient is in a fasted state.~~

~~178. The method of any one of claims 166-177, wherein agitation is significantly reduced within about 2 hours of administering the composition, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~179. The method of claim 178, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~180. The method of claim 178 or claim 179, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~181. The method of claim 180, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

~~182. The method of any one of claims 178-181, wherein the PEC score is ≥30% lower than placebo.~~

~~183. The method of claim 182, wherein the PEC score is ≥60% lower than placebo.~~

~~184. The method of any one of claims 178-183, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering the composition.~~

~~185. The method of claim 184, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.~~

~~186. The method of claim 184, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.~~

~~187. The method of any one of claims 178-186, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.~~

~~188. The method of any one of claims 178-187, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 24 hours following administration of the composition.~~

~~189. The method of any one of claims 166-188, wherein the subject is treated without experiencing significant sedation.~~

~~190.. The method of any one of claims 166-189, wherein the subject is treated without experiencing clinically significant cardiovascular effects.~~

~~191. The method of any one of claims 166-190, wherein administration of a single dose provides a mean C_{max} within the range of about 80% to about 125% of about 100 ng/L to about 800 ng/L.~~

~~192. The method of claim 191, wherein the mean C_{max} is within the range of about 80% to about 125% of about 440 ng/L~~

~~193. The method of claim 191, wherein the mean C_{max} is about 440 ng/L~~

~~194. The method of any one of claims 166-193, wherein administration of a single dose provides a mean AUC_{0-inf} within the range of about 80% to about 125% of about 600 hr*ng/L to about 9500 hr*ng/L.~~

~~195. The method of claim 194, the mean AUC_{0-inf} is within the range of about 80% to about 125% of about 3800 ng*h/L.~~

~~196. The method of claim 194, the mean AUC_{0-inf} is about 3800 ng*h/L.~~

~~197. The method of any one of claims 166-196, herein administration of a single dose provides a mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 8 hours.~~

~~198. The method of claim 197, wherein the mean T_{max} is within the range of about 80% to about 125% of about 2 hours.~~

~~199. The method of claim 197, wherein the mean T_{max} is about 2 hours.~~

~~200. The method of any one of claims 166-199, wherein administration of a single dose provides a geometric mean C_{max} within the range of about 80% to about 125% of about 100 ng/L to about 800 ng/L.~~

~~201. The method of claim 200, wherein the geometric mean C_{max} is within the range of about 80% to about 125% of about 380 ng/L.~~

202. The method of claim 200, wherein the geometric mean C_{max} is about 380 ng/L

203. The method of any one of claims 166-202, wherein administration of a single dose provides a geometric mean AUC_{0-inf} within the range of about 80% to about 125% of about 600 hr*ng/L to about 9500 hr*ng/L.

204. The method of claim 203, the geometric mean AUC_{0-inf} is within the range of about 80% to about 125% of about 2880 ng*h/L.

205. The method of claim 203, wherein the geometric mean AUC_{0-inf} is about 2880 ng*h/L..

206. The method of any one of claims 166-205 wherein administration of a single dose provides a geometric mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 8 hours.

207. The method of claim 206, wherein the geometric mean T_{max} is within the range of about 80% to about 125% of about 2 hours.

208. The method of claim 206, wherein the geometric mean T_{max} is about 2 hours.

209. The method of any one of claims 166-208, wherein administration of a single dose provides a median C_{max} within the range of about 80% to about 125% of about 110 ng/L to about 800 ng/L.

210. The method of claim 209, wherein the median C_{max} is within the range of about 80% to about 125% of about 485 ng/L.

211. The method of claim 209, wherein the median C_{max} is about 485 ng/L.

212. The method of any one of claims 166-211, wherein administration of a single dose provides a median AUC_{0-inf} within the range of about 80% to about 125% of about 600 hr*ng/L to about 9500 hr*ng/L.

213. The method of claim 212, the median AUC_{0-inf} is within the range of about 80% to about 125% of about 2900 ng*h/L.

214. The method of claim 194, wherein the median AUC_{0-inf} is about 2900 ng*h/L.

215. The method of any one of claims 166-214 wherein administration of a single dose provides a median T_{max} within the range of about 80% to about 125% of about 1 hour to about 8 hours.

216. The method of claim 215, wherein the median T_{max} is within the range of about 80% to about 125% of about 2 hours.

217. The method of claim 215, wherein the median T_{max} is about 2 hours.

218. The method of any one of claims 191-217, wherein the pharmacokinetic parameters are non-steady state.

219. A method of treating agitation associated with schizophrenia or bipolar disorder, comprising administering a unit dose composition comprising about 120 µg to about 180 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient.

220. The method of claim 219, wherein the patient has schizophrenia.

221. The method of claim 219 or claim 220, wherein the patient has bipolar I disorder.

222. The method of any one of claims 219-221, wherein the composition comprises dexmedetomidine hydrochloride.

223. The method of any one of claims 219-222, wherein the unit dose of dexmedetomidine is about 120 µg.

~~224. The method of any one of claims 219-222, wherein the unit dose of dexmedetomidine is about 180 µg.~~

~~225. The method of any one of claims 219-224, wherein the composition is administered sublingually or buccally.~~

~~226. The method of claim 225, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.~~

~~227. The method of claim 225, wherein the composition is administered buccally in the form of a film, patch or tablet.~~

~~228. The method of any one of claims 219-227, further comprising administering a second dose after a period of time ranging from about 30 minutes to about 12 hours.~~

~~229. The method of claim 228, wherein the additional dose is about 60µg or 90µg.~~

~~230. The method of claim 228 or claim 229, wherein the second dose is administered after a period of about 2 hours.~~

~~231. The method of any one of claims 219-230, wherein agitation is significantly reduced within about 2 hours of administering the composition, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~232. The method of claim 231, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~233. The method of claim 231 or claim 232, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~234. The method of claim 233, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

~~235. The method of any one of claims 231-234, wherein the PEC score is ≥30% lower than placebo.~~

~~236. The method of claim 235, wherein the PEC score is ≥60% lower than placebo.~~

~~237. The method of any one of claims 231-236, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering dexmedetomidine.~~

~~238. The method of claim 237, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.~~

~~239. The method of claim 237, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.~~

~~240. The method of any one of claims 231-239, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.~~

~~241. The method of any one of claims 231-240, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 24 hours following administration of the composition.~~

~~242. The method of any one of claims 219-241, wherein the subject is treated without experiencing significant sedation.~~

~~243.. The method of any one of claims 219-242, wherein the subject is treated without experiencing clinically significant cardiovascular effects.~~

~~244. The method of any one of claims 219-243, wherein administration of a single dose provides a mean peak plasma concentration (C_{max}) within the range of about 80% to about 125% of about 100 ng/L to about 800 ng/L.~~

~~245. The method of claim 244, wherein the mean C_{max} is within the range of about 80% to about 125% of about 200 ng/L to about 500 ng/L.~~

246. The method of claim 244, wherein the mean C_{max} is within the range of about 80% to about 125% of 230 ng/L to about 440 ng/L.

247. The method of any one of claims 219-246, wherein administration of a single dose provides a mean area under the curve $(AUC)_{0-inf}$ within the range of about 80% to about 125% of about 590 hr*ng/L to about 9500 hr*ng/L.

248. The method of claim 247, wherein the mean AUC_{0-inf} is within the range of about 80% to about 125% of 1400 ng*h/L to about 4000 hr*ng/L.

249. The method of claim 247, wherein the mean AUC_{0-inf} is within the range of about 80% to about 125% of 1800 ng*h/L to about 3800 ng*h/L.

250. The method of any one of claims 219-249 wherein administration of a single dose provides a mean time to peak plasma concentration (T_{max}) within the range of about 80% to about 125% of about 1 hour to about 8 hours.

251. The method of claim 250, wherein the mean T_{max} is within the range of about 80% to about 125% of about hours.

252. The method of claim 250, wherein the mean T_{max} is about 2 hours.

253. The method of any one of claims 244-252, wherein the pharmacokinetic parameters are non-steady state.

254. The method of any one of claims 219-253, wherein the patient is in a fed state.

255. The method of any one of claims 219-253, wherein the patient is in a fasted state.

256. A method of treating or ameliorating opioid withdrawal symptoms, comprising administering a composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient in need thereof, wherein the patient is at least 18 years and wherein the period of withdrawal is up to 14 days.

~~257. The method of claim 256, wherein the treatment comprises reducing the period of opioid withdrawal.~~

~~258. The method of claim 256 or claim 257, wherein the treating or ameliorating is measured by the Clinical Opiate Withdrawal Scale (COWS) and/or Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) score.~~

~~259. The method of any one of claims 256-258, wherein the composition is administered twice daily.~~

~~260. The method of any one of claims 256-259, wherein the composition comprises a dose range of dexmedetomidine or a pharmaceutically acceptable salt thereof of between about 30 µg and about 200 µg.~~

~~261. The method of any one of claims 256-260, wherein the composition comprises a unit dose of about 30 µg, about 60 µg, about 90 µg, about 120 µg, or 180 µg of dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~262. The method of any one of claims 256-261, wherein the period of withdrawal is up to 13 days, 12 days, 11 days, 10 days, 9 days, 8 days, 7 days, 6 days, 5 days, 4 days, or 3 days.~~

~~263. The method of any one of claims 256-262, wherein the opioid is selected from the group comprising of fentanyl, morphine, codeine, heroin, oxycodone, hydrocodone, alfentanil carfentanil, tramadol, hydromorphone, buprenorphine, naloxone, naltrexone, remifentanil butorphanol, meperidine, methadone, dextropropoxyphene (propoxyphene) thebaine, sufentanil and pentazocine.~~

~~264. The method of claim 263, wherein the opioid is selected from the group comprising of fentanyl.~~

~~265. The method of any one of claims 256-262, wherein the opioid had been administered for amount of time longer than neonate treatment prior to withdrawal.~~

~~266. The method of any one of claims 256-265, wherein the composition is administered sublingually, buccally, orally, intranasally or parenterally.~~

~~267. The method of claims any one of claims 256-266, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.~~

~~268. The method of claim 267, wherein the composition is administered sublingually in the form of a film.~~

~~269. The method of any one of claims 256-266, wherein the compositon is administered buccally in the form of a film, patch or tablet..~~

~~270. The method of claim 269, wherein the composition is administered buccally in the form of a film.~~

~~271. The method of any one of claims 256-270, wherein the patient is treated without also inducing clinically significant cardiovascular effects.~~

~~272. The method of any one of claims 256-271 wherein a single dose of a composition comprising about 180 µg dexmedetomidine or a pharmaceutically acceptable salt thereof is effective for up to at least about 24 hours.~~

~~273. The method of any one of claims 256-272, wherein the composition comprises dexmedetomidine hydrochloride.~~

~~274. The method of any one of claims 256-273, wherein the opioid withdrawal symptom is agitation.~~

~~275. The method of any one of claims 256-274, wherein the composition is administered twice daily for 7 days.~~

~~276. A pharmaceutical composition comprising from about 20 µg to about 240 µg dexmedetomidine or a pharmaceutically acceptable salt thereof.~~

~~277. The composition of claim 276, wherein dexmedetomidine is present as dexmedetomidine hydrochloride.~~

~~278. The composition of claim 276 or claim 277, wherein the dose of dexmedetomidine is about 120 µg.~~

~~279. The composition of any one of claims 276-278, wherein the dose of dexmedetomidine is about 180 µg.~~

~~280. The composition of any one of claims 276-279, wherein the composition is formulated for sublingual or buccal administration.~~

~~281. The composition of claim 280, wherein the composition is formulated for sublingual administration in the form of a tablet, film, spray, gel or drops.~~

~~282. The composition of claim 280, wherein the composition is formulated for buccal administration in the form of a film, patch or tablet.~~

~~283. The composition of any one of claims 276-282, wherein if administered to a patient having agitation associated with schizophrenia or bipolar disorder, the agitation is significantly reduced within about 2 hours of administering the composition as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~284. The composition of claim 283, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~285. The composition of claim 283 or claim 284, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~286. The composition of claim 285, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

287. The composition of any one of claims 283-286, wherein the PEC score is ≥30% lower than placebo.

288. The composition of claim 287, wherein the PEC score is ≥60% lower than placebo.

289. The composition of any one of claims 283-288, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering the composition.

290. The composition of claim 289, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.

291. The composition of claim 289, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.

292. The composition of any one of claims 283-291, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.

293. The composition of any one of claims 283-292, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 24 hours following administration of the composition.

294. The composition of any one of claims 283-293, wherein the subject is treated without experiencing significant sedation.

295.. The composition of any one of claims 283-294, wherein the subject is treated without experiencing clinically significant cardiovascular effects.

296. The composition of any one of claims 276-295, wherein if administered to a patient having schizophrenia or bipolar disorder, a single dose provides a mean Cmax within the range of about 80% to about 125% of about 100 ng/L to about 800 ng/L.

297. The composition of claim 296, wherein the geometric mean C_{max} is from about 200 ng/L to about 400 ng/L.

298. The composition of claim 296, wherein the mean C_{max} is within the range of about 80% to about 125% of 230 ng/L to about 440 ng/L.

299. The composition of any one of claims 276-298, wherein if administered to a patient having schizophrenia or bipolar disorder, a single dose provides a mean $aAUC_{0-inf}$ within the range of about 80% to about 125% of about 590 hr*ng/L to about 9500 hr*ng/L.

300. The composition of claim 299, wherein the mean AUC_{0-inf} is within the range of about 80% to about 125% of 1400 ng*h/L to about 4000 hr*ng/L.

301. The composition of claim 299, wherein the mean AUC_{0-inf} is within the range of about 80% to about 125% of 1800 ng*h/L to about 3800 ng*h/L.

302. The composition of any one of claims 276-301, wherein if administered to a patient having schizophrenia or bipolar disorder, a single dose provides a mean time to peak plasma concentration (T_{max}) within the range of about 80% to about 125% of about 1 hour to about 8 hours.

303. The composition of claim 302, wherein the mean T_{max} is within the range of about 80% to about 125% of about hours.

304. The composition of claim 302, wherein the mean T_{max} is about 2 hours.

305. The composition of any one of claims 296-304, wherein the pharmacokinetic parameters are non-steady state.

306. The composition of any one of claims 283-305, wherein the patient is in a fed state.

307. The composition of any one of claims 283-305, wherein the patient is in a fasted state.

308. A method of treating agitation associated with schizophrenia or bipolar disorder, comprising administering a unit dose composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient, wherein the dose provides one or more of the following pharmacokinetic parameters:

(1) a mean C_{max} within the range of about 80% to about 125% of about 110 ng/L to about 400 ng/L; and/or

(2) a mean AUC_{0-inf} within the range of about 80% to about 125% of about 590 hr*ng/L to about 4400 hr*ng/L; and/or

(3) a mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 4 hours.

309. The method of claim 308, wherein the patient has schizophrenia.

310. The method of claim 308 or claim 309, wherein the patient has bipolar I disorder.

311. The method of any one of claims 308-310, wherein the composition comprises dexmedetomidine hydrochloride.

312. The method of any one of claims 308-311, wherein the composition is administered sublingually or buccally.

313. The method of claim 312, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.

314. The method of claim 312, wherein the composition is administered buccally in the form of a film, patch or tablet.

315. The method of any one of claims 308-314, further comprising administering a second dose after a period of time ranging from about 30 minutes to about 12 hours.

316. The method of claim 315, wherein the additional dose is about 60µg or 90µg.

317. The method of claim 315 or claim 316, wherein the second dose is administered after a period of about 2 hours.

~~318. The method of any one of claims 308-317, wherein the patient is in a fed state.~~

~~319. The method of any one of claims 308-317, wherein the patient is in a fasted state.~~

~~320. The method of any one of claims 308-319, wherein agitation is significantly reduced within about 2 hours of administering the composition, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~321. The method of claim 320, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~322. The method of claim 320 or claim 321, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~323. The method of claim 322, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

~~324. The method of any one of claims 320-323, wherein the PEC score is ≥30% lower than placebo.~~

~~325. The method of claim 324, wherein the PEC score is ≥60% lower than placebo.~~

~~326. The method of any one of claims 320-325, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering the composition.~~

~~327. The method of claim 326, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.~~

~~328. The method of claim 326, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.~~

329. The method of any one of claims 320-328, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.

330. The method of any one of claims 320-329, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 6 hours following administration of the composition.

331. The method of any one of claims 308-330, wherein the subject is treated without experiencing significant sedation.

332.. The method of any one of claims 308-331, wherein the subject is treated without experiencing clinically significant cardiovascular effects.

333. The method of any one of claims 308-332 wherein two or more of the pharmacokinetic parameters are present.

334. The method of any one of claims 308-333, wherein all three of the pharmacokinetic parameters are present.

335. The method of any one of claims 308-334, wherein the mean C_{max} is within the range of about 80% to about 125% of about 238 ng/L.

336. The method of claim 335, wherein the mean C_{max} is about 238 ng/L

337. The method of any one of claims 308-336, wherein administration of a single dose provides a mean AUC_{0-inf} within the range of about 80% to about 125% of about 1810 ng*h/L.

338. The method of claim 337, wherein the mean about 1810 ng*h/L.

339. The method of any one of claims 308-338 wherein administration of a single dose provides a mean T_{max} within the range of about 80% to about 125% of about 2 hours.

340. The method of claim 339, wherein the mean T_{max} is about 2 hours.

341. The method of any one of claims 308-340, wherein the pharmacokinetic parameters are non-steady state.

342. A method of treating agitation associated with schizophrenia or bipolar disorder, comprising administering a unit dose composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof to a human patient, wherein the dose provides one or more of the following pharmacokinetic parameters:

(1) a mean C_{max} within the range of about 80% to about 125% of about 100 ng/L to about 800 ng/L; and/or

(2) a mean AUC_{0-inf} within the range of about 80% to about 125% of about 600 hr*ng/L to about 9500 hr*ng/L; and/or

(3) a mean T_{max} within the range of about 80% to about 125% of about 1 hour to about 8 hours.

343. The method of claim 342, wherein the patient has schizophrenia.

344. The method of claim 342 or claim 343, wherein the patient has bipolar I disorder.

345. The method of any one of claims 342-344, wherein the composition comprises dexmedetomidine hydrochloride.

346. The method of any one of claims 342-345, wherein the composition is administered sublingually or buccally.

347. The method of claim 346, wherein the composition is administered sublingually in the form of a tablet, film, spray, gel or drops.

348. The method of claim 346, wherein the composition is administered buccally in the form of a film, patch or tablet.

349. The method of any one of claims 342-348, further comprising administering a second dose after a period of time ranging from about 30 minutes to about 12 hours.

~~350. The method of claim 349, wherein the additional dose is about 60µg or 90µg.~~

~~351. The method of claim 349 or claim 350, wherein the second dose is administered after a period of about 2 hours.~~

~~352. The method of any one of claims 342-351, wherein the patient is in a fed state.~~

~~353. The method of any one of claims 342-351, wherein the patient is in a fasted state.~~

~~354. The method of any one of claims 342-353, wherein agitation is significantly reduced within about 2 hours of administering the composition, as measured by a mean change in Positive and Negative Syndrome Scale Excited Component (PEC) scores relative to baseline.~~

~~355. The method of claim 354, wherein the agitation is significantly reduced within about 30 minutes to about 1 hour.~~

~~356. The method of claim 354 or claim 355, wherein the patient experiences ≥40% decrease from baseline in PEC score.~~

~~357. The method of claim 356, wherein the patient experiences ≥60% decrease from baseline in PEC score.~~

~~358. The method of any one of claims 354-357, wherein the PEC score is ≥30% lower than placebo.~~

~~359. The method of claim 358, wherein the PEC score is ≥60% lower than placebo.~~

~~360. The method of any one of claims 354-359, wherein the mean change in PEC score is greater than -4 (i.e. a decrease of 4 or more points) relative to baseline within 2 hours of administering the composition.~~

~~361. The method of claim 360, wherein mean change in PEC score is greater than -6 relative to baseline within 2 hours of administering the composition.~~

~~362. The method of claim 360, wherein mean change in PEC score is greater than -8 relative to baseline within 2 hours of administering the composition.~~

~~363. The method of any one of claims 354-362, wherein the decrease in PEC score is maintained for at least six hours following administration of the composition.~~

~~364. The method of any one of claims 354-363, wherein the mean change in PEC score is greater than or equal to -8 and is maintained from 2 hours post administration up to at least about 6 hours following administration of the composition.~~

~~365. The method of any one of claims 342-364, wherein the subject is treated without experiencing significant sedation.~~

~~366. The method of any one of claims 342-365, wherein the subject is treated without experiencing clinically significant cardiovascular effects.~~

~~367. The method of any one of claims 342-366 wherein two or more of the pharmacokinetic parameters are present.~~

~~368. The method of any one of claims 342-367, wherein all three of the pharmacokinetic parameters are present.~~

~~369. The method of any one of claims 342-368, wherein the mean C_{max} is within the range of about 80% to about 125% of about 440 ng/L.~~

~~370. The method of claim 369, wherein the mean C_{max} is about 440 ng/L~~

~~371. The method of any one of claims 342-370, wherein administration of a single dose provides a mean AUC_{0-inf} within the range of about 80% to about 125% of about 3800 ng*h/L.~~

~~372. The method of claim 371, wherein the mean about 3800 ng*h/L.~~

373. The method of any one of claims 342-372 wherein administration of a single dose provides a mean T_{max} within the range of about 80% to about 125% of about 2 hours.

374. The method of claim 373, wherein the mean T_{max} is about 2 hours.

375. The method of any one of claims 342-374, wherein the pharmacokinetic parameters are non-steady state.

376. The method of any of the preceding claims, wherein agitation is reduced to a 1 (very much improved) or 2 (much improved) within 2 hours of administering the composition, as measured by the Clinical Global Impression – Improvement Scale.

377. The method of claim 376, wherein the agitation is reduced within about 30 minutes to about 1 hour.

378. The method of claim 377, wherein the agitation is reduced within about 30 minutes.

379. The method of any one of claims 376-378, wherein the reduction in agitation is reduced to a 1 (very much improved).

380. The method of claim any one of claims 376-379, wherein the reduction in agitation is maintained for greater than about 2 hours.

381. The method of any one of claims 376-380, wherein the reduction in agitation is maintained for greater than about 4 hours.

382. The method of any one of claims 376-381, wherein the reduction in agitation is maintained for greater than about 6 hours..

383. The method of any one of claims 376-382, wherein the reduction in agitation is maintained for greater than about 8 hours.

384. The method of any one of claims 376-383, wherein the composition comprises 120 µg of dexmedetomidine.

385. The method of any one of claims 376-383, wherein the composition comprises 180 µg of dexmedetomidine.

386. The method of any one of claims 376-385, wherein the patient has schizophrenia.

387. The method of any one of claims 376-386, wherein the patient has bipolar disorder.

388. The method of any of the preceding claims, wherein agitation is reduced to a 3 (mild agitation) or 4 (normal behavior) within 2 hours of administering the composition, as measured by the Agitation-Calmness Evaluation Scale (ACES).

389. The method of claim 388, wherein the agitation is reduced within about 30 minutes to about 1 hour.

390. The method of claim 388 or claim 389, wherein the reduction in agitation is reduced to a 4 (normal behavior).

391. The method of any one of claims 388-390, wherein the reduction in agitation is maintained for greater than about 2 hours.

392. The method of any one of claims 388-391, wherein the reduction in agitation is maintained for greater than about 4 hours.

393. The method of any one of claims 388-392, wherein the reduction in agitation is maintained for greater than about 6 hours.

394. The method of any one of claims 388-393, wherein the reduction in agitation is maintained for greater than about 8 hours.

395. The method of any one of claims 388-394, wherein the composition comprises 120 µg of dexmedetomidine.

~~396. The method of any one of claims 388-394, wherein the composition comprises 180 µg of dexmedetomidine.~~

~~397. The method of any one of claims 388-396, wherein the patient has schizophrenia.~~

~~398. The method of any one of claims 388-397, wherein the patient has bipolar disorder.~~

~~399. The method of any of the preceding claims, wherein the patient experiences a ≥40 reduction in agitation, as measured by the PEC Scale.~~

~~400. The method of claim 399, wherein the agitation is reduced within about 30 minutes to about 1 hour.~~

~~401. The method of claim 399 or claim 400, wherein the patient experiences a ≥60 reduction in agitation.~~

~~402. The method any one of claims 399-401, wherein the patient experiences a ≥80 reduction in agitation.~~

~~403. The method of any one of claims 399-402, wherein the reduction in agitation is maintained for greater than about 2 hours.~~

~~404. The method of any one of claims 399-403, wherein the reduction in agitation is maintained for greater than about 4 hours.~~

~~405. The method of any one of claims 399-404, wherein the reduction in agitation is maintained for greater than about 6 hours.~~

~~406. The method of any one of claims 399-405, wherein the reduction in agitation is maintained for greater than about 8 hours.~~

~~407. The method of any one of claims 399-406, wherein the composition comprises 120 µg of dexmedetomidine.~~

408. The method of any one of claims 399-406, wherein the composition comprises 180 µg of dexmedetomidine.

409. The method of any one of claims 399-408, wherein the patient has schizophrenia.

410. The method of any one of claims 399-409, wherein the patient has bipolar disorder.

411. A method of achieving a PEC score reduction in agitation for a sustained period of time in a subject with bipolar or schizophrenic subject comprising administering to the subject a pharmaceutical composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 120 mcg to about 180 mcg wherein the PEC score reduction is about -8 to about -10 and wherein the sustained period is about 2 hours to about 6 hours.

412. The method of claim 411, wherein the composition comprises dexmedetomidine hydrochloride.

413. The method of claim 411 or 412, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 120 mcg.

414. The method of claim 411 or 412, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 180 mcg.

415. The method according to any one of claims 411 to 414, wherein the sustained period is about 4 hours.

416. The method according to claim 415, wherein the sustained period is about 6 hours.

417. The method according to any one of claims 411-416, wherein the PEC score reduction is about -10.

418. A method of achieving an ACES score improvement for a sustained period of time in a subject with bipolar or schizophrenic subject comprising administering to the subject a pharmaceutical composition comprising dexmedetomidine or a

~~pharmaceutically acceptable salt thereof at a dose of about 120 mcg to about 180 mcg wherein the ACES score is improved to about 3 to about 4 and wherein the sustained period is about 2 hours to about 6 hours.~~

~~419. The method of claim 418, wherein the composition comprises dexmedetomidine hydrochloride.~~

~~420. The method of claim 418 or 419, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 120 mcg.~~

~~421. The method of claim 418 or 419, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 180 mcg.~~

~~422. The method according to any one of claims 418 to 421, wherein the sustained period is about 4 hours.~~

~~423. The method according to claim 422, wherein the sustained period is about 6 hours.~~

~~424. The method according to any one of claims 418-423, wherein the ACES score is about 4.~~

~~425. A method of achieving an CGI-I score improvement for a sustained period of time in a subject with bipolar or schizophrenic subject comprising administering to the subject a pharmaceutical composition comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 120 mcg to about 180 mcg wherein the CGI-I score is improved to about a 1 (very much improved) or about a 2 (much improved) and wherein the sustained period is about 2 hours to about 6 hours.~~

~~426. The method of claim 425, wherein the composition comprises dexmedetomidine hydrochloride.~~

~~427. The method of claim 425 or 426, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 120 mcg.~~

~~428. The method of claim 425 or 426, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a dose of about 180 mcg.~~

~~429. The method according to any one of claims 425 to 428, wherein the sustained period is about 4 hours.~~

~~430. The method according to claim 425, wherein the sustained period is about 6 hours.~~

~~431. The method according to any one of claims 425-430, wherein the CGI-I score is about 1.~~