**WHAT IS CLAIMED IS:**

~~1. A crystalline solid form of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid or a crystalline hydrochloride salt of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid.~~

~~2. The crystalline solid form of Claim 1, wherein the crystalline solid form is crystalline (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid.~~

~~3~~1. ~~The~~ A crystalline solid form of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid~~Claim 2, wherein the crystalline solid form is~~ in Form I which is characterized by an x-ray powder diffraction pattern having diffraction peaks at 2θ values of 6.92±0.20 and 15.34±0.20, and having two or more diffraction peaks at 2θ values selected from 10.24±0.20, 11.48±0.20, 12.32±0.20, 13.46±0.20, 14.04±0.20, 17.30±0.20, 18.06±0.20, 20.30±0.20, 21.42±0.20, 23.48±0.20, 25.54±0.20, 26.96±0.20, 29.30±0.20, and 30.72±0.20.

~~4~~2. The crystalline solid form of ~~Claim 3~~Claim 1, wherein the x-ray powder diffraction pattern comprises three or more diffraction peaks at 2θ values selected from 6.92±0.20, 10.24±0.20, 13.46±0.20, 15.34±0.20, 18.06±0.20, and 21.42±0.20.

~~5~~3. The crystalline solid form of ~~Claim 2~~Claim 1, wherein the crystalline solid form is characterized by a differential scanning calorimetry trace recorded at a heating rate of 10 °C per minute which shows a maximum in endothermic heat flow at a temperature between-162 °C and 170 °C.

~~64~~. A crystalline solid form of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid in Form II~~The crystalline solid form of Claim 2, wherein the crystalline solid form~~ which is characterized by an x-ray powder diffraction pattern having diffraction peaks at 2θ values of 9.05±0.20 and 16.52±0.20, and having two or more diffraction peaks at 2θ values selected from 9.80±0.20, 12.44±0.20, 12.92±0.20, 14.21±0.20, 15.62±0.20, 17.27±0.20, 19.04±0.20, 19.85±0.20, 21.29±0.20, 22.43±0.20, 23.48±0.20, 23.99±0.20, and 26.09±0.20.

~~75~~. The crystalline solid form of ~~Claim 6~~Claim 4, wherein the x-ray powder diffraction pattern comprises two or more diffraction peaks at 2θ values selected from 9.05±0.20, 9.80±0.20, 12.44±0.20, 12.92±0.20, 16.52±0.20, 23.99±0.20, and 26.09±0.20.

~~86~~. ~~The crystalline solid form of Claim 1, wherein the crystalline solid form is the~~ A crystalline hydrochloride salt of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid.

~~9. The crystalline solid form of Claim 8, wherein the crystalline solid form~~ which is characterized by an x-ray powder diffraction pattern having two or more diffraction peaks at 2θ values selected from 6.80±0.20, 9.80±0.20, 12.71±0.20, 13.31±0.20, 15.14±0.20, 19.97±0.20, 21.44±0.20, 22.64±0.20, 23.27±0.20, 24.44±0.20, and 25.37±0.20.

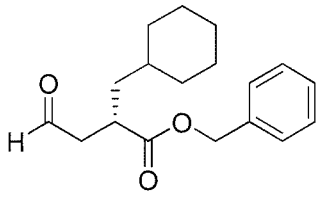
~~107~~. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the crystalline solid form of any one of ~~Claims 1 to 9~~Claims 1 to 6.

~~118~~. A process for preparing crystalline (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid (compound **1**), the process comprising deprotecting (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric

acid benzyl ester by catalytic hydrogenolysis in the presence of a polar diluent comprising between 10 % and 20 % water to form crystalline compound **1.**

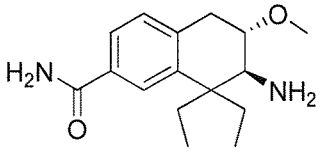
~~12~~9. A process for preparing crystalline (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid (compound **1**), the process comprising:

(a) reacting (*S*)-2-cyclohexylmethyl-4-oxo-butyric acid benzyl ester (**4**)



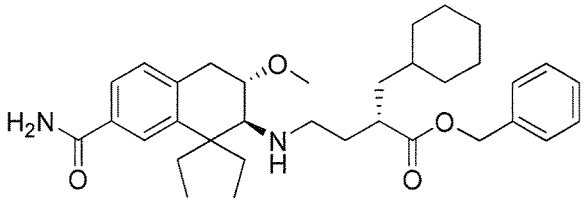
**4**

with (6*S*,7*S*)-7-amino-8,8-diethyl-6-methoxy-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid amide (**3**)



**3**

to provide (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid benzyl ester (**2**)



**2** and

(b) deprotecting the compound of formula **2** by catalytic hydrogenolysis in the presence of a polar diluent comprising between 10 % and 20 % water to provide crystalline compound **1.**

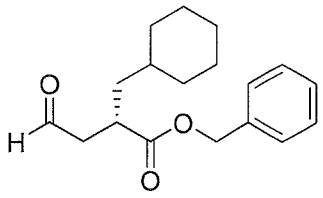
~~13~~10. A process for preparing crystalline (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid, the process comprising:

(a) dispersing (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid in a polar diluent comprising between 3 % and 20 % water to form a mixture;

(b) holding the mixture for at least 12 hours; and

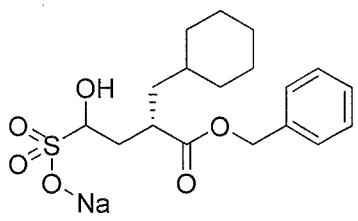
(c) isolating the crystalline (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid from the mixture.

~~14~~11. A compound of formula **4**



**4**

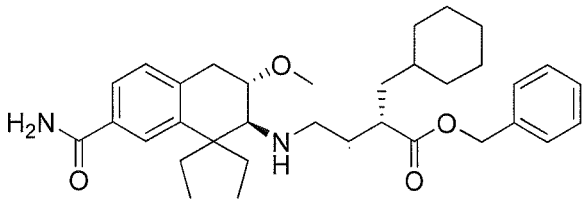
denoted by the chemical name (*S*)-2-cyclohexylmethyl-4-oxo-butyric acid benzyl ester; or a bisulfite adduct thereof of formula **5**



**5**

denoted by the chemical name sodium (*S*)-3-benzyloxycarbonyl-4-cyclohexyl-1-hydroxy-butane-1-sulfonate.

~~15~~12. A compound of formula **2**



**2**

denoted by the chemical name (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid benzyl ester or a hydrochloride salt thereof.

~~16~~13. A crystalline hydrochloride salt of (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid benzyl ester.

~~17~~14. A process for preparing (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid, the process comprising:

(a) reacting (*S*)-2-cyclohexylmethyl-4-oxo-butyric acid benzyl ester (**4**) with (6*S*,7*S*)-7-amino-8,8-diethyl-6-methoxy-5,6,7,8-tetrahydro-naphthalene-2-carboxylic acid amide (**3**) to provide (*S*)-4-((2*S*,3S)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid benzyl ester (**2**); and

(b) deprotecting compound **2** by catalytic hydrogenolysis to provide (*S*)-4-((2*S*,3*S*)-7-carbamoyl-1,1-diethyl-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamino)-2-cyclohexylmethyl-butyric acid.

~~18~~15. A crystalline solid form as claimed in any one of ~~Claims 1 to 9~~Claims 1 to 6 for use in the treatment of a disease or medical condition in a mammal ameliorated by treatment with a mu opioid receptor antagonist.

~~19~~16. The crystalline solid form of ~~Claim 18~~Claim 15 wherein the disease or condition is opioid-induced bowel dysfunction or post-operative ileus.

~~20~~17. The crystalline solid form of ~~Claim 18~~Claim 15 wherein the disease or condition is a disorder of reduced motility of the gastrointestinal tract.

~~21~~18. A crystalline solid form as claimed in any one of ~~Claims 1 to 9~~Claims 1 to 6 for use in reducing or preventing a side effect associated with use of an opioid agent in a mammal.

~~22~~19. Use of a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the crystalline solid form of any one of ~~Claims 1 to 9~~Claims 1 to 6 in the manufacture of a medicament for treating a mammal having a medical condition ameliorated by treatment with a mu opioid receptor antagonist.

~~23~~20. The use of ~~Claim 22~~Claim 19 wherein the medical condition is opioid-induced bowel dysfunction or post-operative ileus.

~~24~~21. Use of the crystalline solid form of any one of ~~Claims 1 to 9~~Claims 1 to 6 in the manufacture of a medicament for use in combination with an opioid agent for reducing a side effect associated with use of the opioid agent in a mammal.

~~25~~22. Use of a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the crystalline solid form of any one of ~~Claims 1 to 9~~Claims 1 to 6 in the manufacture of a medicament for enhancing motility of the gastrointestinal tract in a mammal.

~~26~~23. Use of a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the crystalline solid form of any one of ~~Claims 1 to 9~~Claims 1 to 6 in the manufacture of a medicament for antagonizing a mu opioid receptor in a mammal.

~~27~~24. The use of ~~Claim 24~~Claim 21, wherein the side effect is one or more of constipation, decreased gastric empyting, abdominal pain, bloating, nausea, gastroesophageal reflux, collectively termed opioid-induced bowel dysfunction.