In an example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, the sole active ingredient for injection, the active pharmaceutical ingredient, or the active pharmaceutical ingredient for injection.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide as the sole active ingredient.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide as the active pharmaceutical ingredient.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide as the active pharmaceutical ingredient for injection.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the sole active ingredient.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the sole active ingredient for injection.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the active pharmaceutical ingredient.

In another example, the disclosure provides a pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the active pharmaceutical ingredient for injection.

In an aspect, there is provided an injectable composition or preparation comprising:

a) glycerol dioleate (GDO);

b) phosphatidylcholine:

c) an alcohol;

d) setmelanotide as the sole active pharmaceutical ingredient; and

e) optionally, a polar solvent.

In an example, component a) of the composition comprises a neutral diacyl lipid. In example, the neutral diacyl lipid comprises diacyl glycerol. In an example, the neutral diacyl lipid comprises glycerol dioleate (GDO).

In an example, component b) of the composition comprises phosphatidylcholine. In another example, the phospholipid comprises soybean phosphatidylcholine.

In an example, component c) of the composition comprises ethanol. In an example, the ethanol is provided in an amount that is sufficiently great that it provides a solubility of setmelanotide of at least 10 mg/g, 20 mg/g or 30 mg/g.

In an example, component d) of the composition comprises a polar solvent, *e.g.*, a buffer, e.g., a citrate buffer, optionally wherein the pH of the buffer is 6.4. In an example, the polar solvent, *e.g.*, buffer, comprises citrate acid monohydrate. In another example, the polar solvent, *e.g.*, buffer, comprises an additional component, *e.g.*, an antioxidant or a chemical or physical stabilizing agent. In an example, the antioxidant is EDTA. In an example, the polar solvent, *e.g.*, buffer, comprises citric acid monohydrate, disodium EDTA, and water.

In an example, component e) of the composition comprises setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11). In an example, component e) of the composition comprises setmelanotide.

In an example, component e) provides setmelanotide as the sole active ingredient.

In an example, component e) provides setmelanotide as the active pharmaceutical ingredient.

In an example, component e) provides setmelanotide as the active pharmaceutical ingredient for injection.

In an example, component e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient.

In an example component, e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as as the sole active ingredient for injection.

In an example component, e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient.

In an example component, e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C,

001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient for injection.

In an example, the composition comprises a neutral diacyl lipid comprising glycerol dioleate; a phospholipid comprising phosphatidylcholine; an alcohol comprising ethanol; a polar solvent, *e.g.*, a buffer comprising a citrate buffer, *e.g.*, at pH 6.4 comprising EDTA; and setmelanotide.

In an example, the composition comprises, per one milliliter of composition, 419.8 mg glycerol dioleate (GDO); 419.8 mg soybean phosphatidylcholine; 105 mg ethanol; 20 mg citrate buffer; and 30 mg setmelanotide.

In another example, the disclosure provides an injectable pharmaceutical product comprising: a) a neutral diacyl lipid and/or a tocopherol; b) a phospholipid; c) an alcohol; d) optionally, a polar solvent, *e.g.*, a buffer, optionally comprising an antioxidant; and e) setmelanotide or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11).

In an example component, e) provides setmelanotide as the sole active ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient for injection.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as as the sole active ingredient for injection.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient.

In an example component, e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient for injection.

In an example, component a) of the composition comprises a neutral diacyl lipid. In example, the neutral diacyl lipid comprises diacyl glycerol. In an example, the neutral diacyl lipid comprises glycerol dioleate (GDO).

In an example, component b) of the composition comprises phosphatidylcholine. In an example, the phospholipid comprises soybean phosphatidylcholine.

In an example, component c) of the composition comprises ethanol. In an example, the ethanol is provided in an amount that is sufficiently great that it provides a solubility of setmelanotide of at least 10 mg/g, 20 mg/g or 30 mg/g.

In an example, component d) of the composition comprises a polar solvent, *e.g.*, a buffer, e.g., a citrate buffer, optionally wherein the pH of the buffer is 6.4. In an example, the polar solvent, *e.g.*, buffer, comprises citrate acid monohydrate. In an example, the polar solvent, *e.g.*, buffer, comprises an additional component, *e.g.*, an antioxidant or a chemical or physical stabilizing agent. In an example, the antioxidant is EDTA. In an example, the polar solvent, *e.g.*, buffer, comprises citric acid monohydrate, disodium EDTA, and water.

In an example, component e) is setmelanotide. In an example, component e) is an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11).

In an example component, e) provides setmelanotide as the sole active ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient for injection.

In an example component, e) provides an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as as the sole active ingredient for injection.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient for injection.

In another aspect, there is provided a unit dosage form comprising the composition as defined above, wherein:

(i) the unit dosage form comprises at least 2, 1.8, 1.6, 1.4, 1.2, 1, 0.8, 0.6, 0.4, or 0.2 mL of the composition; and/or

(ii) the unit dosage form is disposed in a liquid tight enclosure, optionally, a vial or a cartridge; and/or;

(iii) the unit dosage form is disposed in an injection device, optionally a manual syringe, or an auto-injector; and/or

(iv) the unit dosage form comprises 10-70; 20-60, 25-50; 25-40; or 25-35 mg of setmelanotide.

In an example, the injectable pharmaceutical product comprises setmelanotide as the active pharmaceutical ingredient. In an example, the injectable pharmaceutical product comprises a neutral diacyl lipid comprising glycerol dioleate; a phospholipid comprising phosphatidylcholine; an alcohol comprising ethanol; a polar solvent, *e.g.*, a buffer comprising a citrate buffer, *e.g.*, at pH 6.4 comprising EDTA; and setmelanotide.

In an example, the injectable pharmaceutical product comprises, per one milliliter of composition, 419.8 mg glycerol dioleate (GDO); 419.8 mg soybean phosphatidylcholine; 105 mg ethanol; 20 mg citrate buffer; and 30 mg setmelanotide.

In another aspect, there is provided a method of making a preparation or composition formulated for injection, comprising setmelanotide as sole active pharmaceutical ingredient , comprising:

i) providing a mixture of setmelanotide, a first amount of EtOH, and one or more of components:

a) a neutral diacyl lipid and/or a tocopherol;

b) a phospholipid;

c) an alcohol;

d) a polar solvent, and

ii) adding a second amount of EtOH,

thereby making a preparation or composition, formulated for injection, comprising setmelanotide as sole active pharmaceutical ingredient.

In another example, the disclosure provides a method of making a preparation or composition, *e.g.*, a pharmaceutical composition, comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, *e.g.*, a preparation or composition having a controlled level of EtOH, comprising:

i) providing a mixture of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), a first amount of EtOH and one or more of components:

a) a neutral diacyl lipid and/or a tocopherol;

b) a phospholipid;

c) an alcohol; and

d) a polar solvent, *e.g.*, a buffer; and

ii) adding a second amount of EtOH,

thereby making a preparation or composition, *e.g.*, a pharmaceutical composition, comprising a setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11).

In an example, the pharmaceutical product comprises setmelanotide.

In an example, the method further comprises making a mixture comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection; as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; EtOH, a neutral diacyl lipid and/or a tocopherol and a phospholipid,

wherein one or both of the neutral diacyl lipid and/or a tocopherol and phospholipid are added after setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C,

001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; and the EtOH are combined,

thereby making a setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection composition or preparation, *e.g.*, a pharmaceutical product.

In another example, a method of making a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a, component b, component d, and a predetermined amount of alcohol, comprises:

combining (in any order) setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a, component b, component d and alcohol, to provide a mixture, and

comparing a value for alcohol content in the mixture with a reference value for alcohol content,

thereby making a formulation of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection., component a, component b, component d, and a predetermined amount of alcohol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, the method further comprises, responsive to the value or comparison, increasing or decreasing the amount of alcohol in the mixture to provide a formulation having a predetermined amount of alcohol. In an example, the method comprises adding an addition amount of alcohol to the mixture.

In another example, a method of making a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, comprises:

combining (in any order) setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or

MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4) and alcohol, to provide a mixture, and

comparing a value for alcohol content in the mixture with a reference value for alcohol content,

thereby making a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, the method further comprises adding an addition amount of alcohol to the mixture. In an example, the addition amount of alcohol is greater than the predetermined amount of alcohol.

In an example, a method of making a pharmaceutical product comprising component e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprises:

(i) providing a mixture comprising component e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as

the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11)), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, and alcohol (a component e)-alcohol mixture), *e.g.*, setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; in contact with, *e.g.*, dissolved or dispersed in an alcohol, *e.g.*, ethanol; and

(ii) combining the component e) -alcohol mixture with an amount of component a, *e.g.*, GDO, component b, *e.g.*, soybean PC, and component d, *e.g.*, citrate buffer at pH 6.4, or all of components a, b, and d.

In an example, the method further comprises performing step (i), (ii), or (i) and (ii) in a closed vessel.

In an example, the disclosure provides a method of making a preparation of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, or evaluating a candidate preparation, *e.g.*, for a quality control or release specification, comprising:

providing a value for the amount of EtOH in a candidate preparation of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as

the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection,; and

comparing the value with a reference value for amount of EtOH;

thereby making a preparation of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection,.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, provided herein is a method of making a setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, composition or preparation, *e.g.*, a pharmaceutical product, comprising:

making a mixture comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active

pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; EtOH, a neutral diacyl lipid and/or a tocopherol and a phospholipid,

wherein one or both of the neutral diacyl lipid and/or a tocopherol and phospholipid are added after setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, and the EtOH are combined,

thereby making a setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection composition or preparation, *e.g.*, a pharmaceutical product.

In an example, one or both of the neutral diacyl lipid and/or a tocopherol and a phospholipid are added after at least 10%, 25%, 50%, 75%, or all of the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, is allowed to go into solution.

In an example, the order of formation of the mixture is:

i) setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$

(*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; is contacted with EtOH (and optionally water or buffer);

ii) phospholipid is added to the mixture resulting from i); and

iii) neutral diacyl lipid and/or a tocopherol is added to the mixture resulting from ii).

In an example, the pharmaceutical product comprises setmelanotide.

In another example, a method of making a pharmaceutical product of component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprises the following steps in order:

(i) providing a mixture comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection and alcohol (a component (e)-alcohol mixture), *e.g.*, setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C,

001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol; and

(ii) combining the component (e)-alcohol mixture with an amount of component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), and component d (*e.g.*, citrate buffer at pH 6.4), or an amount of all of components a, b, and d;

thereby making a a pharmaceutical product of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, *e.g.*, a pharmaceutical product setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprising a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, a method of making a pharmaceutical product of component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C,

001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, *e.g.*, a pharmaceutical product of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection; for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprising a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In yet another example, a method of making a pharmaceutical product comprising setmelanotide; component a, component b, component d, and a predetermined amount of alcohol, comprises

combining, in a specified order, setmelanotide, component a, component b, component d and an addition amount of alcohol, wherein the addition amount of alcohol results in a predetermined amount of alcohol in the pharmaceutical product, and wherein the specified order comprises the following steps in order:

(i) providing a mixture comprising setmelanotide and an addition amount of alcohol (a setmelanotide -alcohol mixture), *e.g.*, setmelanotide in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol; and

(ii) combining the setmelanotide-alcohol mixture with an amount of components a, b, and d or all of components a, b, and d;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising setmelanotide, component a, component b, component d, and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In another example, a method of making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated

active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol; and

(ii) combining the component (e)-alcohol mixture with an amount of component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), and component d (*e.g.*, citrate buffer at pH 6.4), or all of components a, b, and d;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In another example, a method of making a pharmaceutical product comprising setmelanotide, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, comprises

combining, in a specified order, setmelanotide; component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and an addition amount of alcohol, wherein the addition amount of alcohol results in a predetermined amount of alcohol in the pharmaceutical product, wherein the specified order

comprises the following steps in order:

(i) providing a mixture comprising setmelanotide and an addition amount of alcohol (a setmelanotide moiety-alcohol mixture), *e.g.*, setmelanotide in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol; and

(ii) combining the setmelanotide-alcohol mixture with an amount of component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), and component d (*e.g.*, citrate buffer at pH 6.4), or all of components a, b, and d;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising setmelanotide, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In another example, a method of making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, component a, component b, component d, and a predetermined amount of alcohol, comprises

combining, in a specified order, component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a, component b, component d and an addition amount of alcohol, wherein the addition amount of alcohol results in a predetermined amount of alcohol in the pharmaceutical product, wherein the specified order comprises the following steps in order:

(i) providing a mixture comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; an addition amount of alcohol and component d, *e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4 (a component (e)-buffer mixture), *e.g.*, setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol and a citrate buffer at pH 6.4; and

(ii) combining the component (e)-alcohol-buffer mixture with an amount of components a and b or all of components a and b;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a, component b, component d, and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example component, e) provides setmelanotide as the sole active ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient.

In an example component, e) provides setmelanotide as the active pharmaceutical ingredient for injection.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as as the sole active ingredient for injection.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient.

In an example component, e) provides an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the active pharmaceutical ingredient for injection.

In an example, a method of making a pharmaceutical product comprising setmelanotide, component a, *e.g.*, GDO, component b, *e.g.*, soybean PC, component d, *e.g.*, citrate buffer at pH 6.4, and a predetermined amount of alcohol, comprises:

combining, in a specified order, the setmelanotide, component a, component b, component d and an addition amount of alcohol, wherein the addition amount of alcohol results in a predetermined amount of alcohol in the pharmaceutical product, wherein the specified order comprises the following steps in order:

(i) providing a mixture comprising a setmelanotide, an addition amount of alcohol and component d, *e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4 (a setmelanotide-alcohol-buffer mixture), *e.g.*, setmelanotide in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol and a citrate buffer at pH 6.4; and

(ii) combining setmelanotide-alcohol-buffer mixture with an amount of components a and b or all of components a and b;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising setmelanotide, component a, component b, component d, and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In another example, a method of making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injectionl; component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, comprises

combining, in a specified order, component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a, component b, component d and an addition amount of alcohol, wherein the addition amount of alcohol results in a predetermined amount of alcohol in the pharmaceutical product, wherein the specified order comprises the following steps in order:

(i) providing a mixture comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active

pharmaceutical ingredient for injection; an addition amount of alcohol and component d, *e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4 (a component (e)-alcohol-buffer mixture), *e.g.*, component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol and a citrate buffer at pH 6.4; and

(ii) combining the component (e)-alcohol-buffer mixture with an amount of component a (*e.g.*, GDO), and component b (*e.g.*, soybean PC) or all of components a and b;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising component (e) comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, a method of making a pharmaceutical product comprising setmelanotide, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, comprises:

combining, in a specified order, the setmelanotide, component a, component b, component d and an addition amount of alcohol, wherein the addition amount of alcohol results

in a predetermined amount of alcohol in the pharmaceutical product, wherein the specified order comprises the following steps in order:

(i) providing a mixture comprising the setmelanotide, an addition amount of alcohol and component d, *e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4 (a setmelanotide-alcohol-buffer mixture), *e.g.*, setmelanotide in contact with, *e.g.*, dissolved or dispersed in, an alcohol, *e.g.*, ethanol and a citrate buffer at pH 6.4; and

(ii) combining the setmelanotide-alcohol-buffer mixture with an amount of component a (*e.g.*, GDO), and component b (*e.g.*, soybean PC) or all of components a and b;

wherein (i), (ii) or (i) and (ii) are performed in a closed vessel, thereby making a pharmaceutical product comprising setmelanotide, component a (*e.g.*, GDO), component b (*e.g.*, soybean PC), component d (*e.g.*, a polar solvent, *e.g.*, a buffer, *e.g.*, a citrate buffer at pH 6.4), and a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In another example, a method of making a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprises the following steps in order:

i) combining an amount of one or more of (*e.g.*, all of) components a, b, c and d;

ii) providing to this mixture setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection; and

iii) mixing the mixture of (i) and (ii) for a specified amount of time to dissolve or disperse setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for

injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection,

thereby making a pharmaceutical product setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), *e.g.*, a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) , as the sole active ingredient, as the sole active ingredient for injection; for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprising a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide. In an example, the mixing is performed for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 hours. In an example, the mixing is performed for 1-30 hours. In another example, the mixing is performed for no more than 30, 40, or 50 hours.

In an example, a method of making a pharmaceutical product comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C,

22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, comprising a predetermined amount of alcohol, *e.g.*, 10 wt. % alcohol, *e.g.*, ethanol.

In an example, the pharmaceutical product comprises setmelanotide.

In an example, the mixing is performed for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 hours. In an example, the mixing is performed for 1-30 hours. In another example, the mixing is performed for no more than 30, 40, or 50 hours.

In another example, disclosed herein is a method of providing setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, to a subject, comprising administering to the subject, and effective amount of a pharmaceutical product described herein, or a pharmaceutical product made by one or more of the methods described herein.

In an example, the subject has, or is at risk of having a disorder responsive to modulation of melanocortin-4 receptor (MC4R). In an example, the disorder is chosen from: type 1 diabetes, type 2 diabetes, obesity, insulin resistance, metabolic syndrome, male erectile dysfunction, female sexual disorder, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, disorders of substance abuse, including alcoholism, feeding disorders, cachexia, inflammation or anxiety**.** In an example, the disorder is obesity. In an example, the disorder is type 1 diabetes. In an example, the disorder is type 2 diabetes. In an example, the disorder is Prader-Willi Syndrome. In an example, the disorder is Bardet-Biedl syndrome. In an embodimdnet, the disorder is Alström syndrome.

In an example, the subject is between 1-80 years of age. In an example, the

subject is between 1-10 years old, between 10-20 years old, between 20-30 years old, between 30-40 years old, between 40-50 years old, between 50-60 years old, between 60-70 years old or between 70-80 years old. In an example, the subject is more than 80 years old.

In a related example, the disclosure provides a method of treating a subject comprising administering to a subject in need thereof, an effective amount of a composition comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection.

In an example, the subject has, or is at risk of having a disorder responsive to modulation of melanocortin-4 receptor (MC4R). In an example, the disorder is chosen from: type 1 diabetes, type 2 diabetes, obesity, insulin resistance, metabolic syndrome, male erectile dysfunction, female sexual disorder, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, disorders of substance abuse, including alcoholism, feeding disorders, cachexia, inflammation or anxiety. In an example, the disorder is obesity. In an example, the disorder is type 1 diabetes. In an example, the disorder is type 2 diabetes. In an example, the disorder is Prader-Willi Syndrome. In an example, the disorder is Bardet-Biedl syndrome. In an embodimdnet, the disorder is Alström syndrome.

In an example, the subject is between 1-80 years of age. In an example, the subject is between 1-10 years old, between 10-20 years old, between 20-30 years old, between 30-40 years old, between 40-50 years old, between 50-60 years old, between 60-70 years old or between 70-80 years old. In an example, the subject is more than 80 years old.

In an example, provided herein is a composition comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-

22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, for use in treating a subject in need thereof, comprising administering to the subject an effective amount of the composition.

In an example, the subject has, or is at risk of having a disorder responsive to modulation of melanocortin-4 receptor (MC4R). In an example, the disorder is chosen from: type 1 diabetes, type 2 diabetes, obesity, insulin resistance, metabolic syndrome, male erectile dysfunction, female sexual disorder, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, disorders of substance abuse, including alcoholism, feeding disorders, cachexia, inflammation or anxiety. In an example, the disorder is obesity. In an example, the disorder is type 1 diabetes. In an example, the disorder is type 2 diabetes. In an example, the disorder is Prader-Willi Syndrome. In an example, the disorder is Bardet-Biedl syndrome. In an embodimdnet, the disorder is Alström syndrome.

In an example, the subject is between 1-80 years of age. In an example, the subject is between 1-10 years old, between 10-20 years old, between 20-30 years old, between 30-40 years old, between 40-50 years old, between 50-60 years old, between 60-70 years old or between 70-80 years old. In an example, the subject is more than 80 years old.

Optimized pharmaceutical products comprising setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$, *e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, and methods of making and using the same, are provided herein. Typically the pharmaceutical product comprises a neutral diacyl glycerol and/or a tocopherol, a phosphatidyl choline, an alcohol, a polar solvent (optionally comprising an antioxidant), and setmelanotide (or an $MC4RA_P$ disclosed herein). In an example, the pharmaceutical product has a low viscosity phase, such as an L_2 (reversed micellar) phase. Pharmaceutical products

disclosed herein provide a controlled release of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection.

In an example, the pharmaceutical product provides an optimized release profile, is relatively easy to manufacture, can be sterile-filtered, has low viscosity upon delivery (allowing easy and less painful administration through, *e.g.*, a narrow needle, *e.g.*, a 27 Gauge or smaller diameter needle), allows a high level of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, to be incorporated (thus in examples, allowing a smaller amount of composition and/or setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection to be used), allows shallow injection (*e.g.*, injection into the subcutaneous tissue layer) and/or forms a depot, *e.g.*, a non-lamellar depot, composition *in vivo*, *e.g.*, a depot having a "non-burst" release profile. In an example, the pharmaceutical product is formed from materials that are non-toxic, biotolerable and biodegradable, which can be administered by intra-muscular (i.m.), or subcutaneous (s.c.) administration, and are suitable for self-administration. In an example,

the pharmaceutical product minimizes or eliminates irritation on injection (including transient irritation).

While not wishing to be bound by theory, it is believed, that in an example, the pharmaceutical product generates a crystalline phase, *e.g.*, a non-lamellar liquid crystalline phase, after administration.

In an example, a pharmaceutical product provides low initial release ("non-burst profile") of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11, as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection). This may be defined such that the partial area under the drug concentration curve during the first hours (*e.g.*, first 6, 9, 12, 15, 18, 21, or 24 hours) after dosing, is less than 40% (*e.g.*, less than 35, 30, 25, 20, 15, 10% or lesser), relative to the area under the drug concentration time curve of a 7 day (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 14, 21, or 28 days) steady state dosing interval. In an example, the partial area under the drug concentration curve during the first 6 hours after dosing is less than 10% relative to the area under the drug concentration time curve of a 7 day (*e.g.*, 168 hour) steady state dosing interval. In an example, the partial area under the drug concentration curve during the first 12 hours after dosing is 10-20% (*e.g.*, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20%), relative to the area under the drug concentration time curve of a 7 day (*e.g.*, 168 hour) steady state dosing interval. In an example, the partial area under the drug concentration curve during the first 24 hours after dosing is 20-30% (*e.g.*, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30%), relative to the area under the drug concentration time curve of a 7 day (*e.g.*, 168 hour) steady state dosing interval.

In an example, the pharmaceutical product provides a mean maximum drug concentration (C_{max}) in plasma at steady state in the range of 5-15 ng/mL (*e.g.*, 11 ng/mL) following an injected dose in the range of 5-20mg (*e.g.*, an injected dose of 10mg) once weekly (*e.g.*, once every 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 days), which is no more than 3 times higher (*e.g.*, 1, 1.5, 2, or 2.5 times higher) than the average drug concentration (C_{ave}) in the range of 1-8 ng/mL (*e.g.*, 4 ng/mL). In an example, the pharmaceutical product provides a mean

maximum drug concentration (C_{max}) in plasma at steady state of 11 ng/ml, following an injected dose of 10mg once weekly, which is no more than 3 times higher than the average drug concentration (C_{ave}) of 4 ng/mL.

In an example, the minimum drug concentration (C_{min}) in plasma at steady state is in the range of 1-3 ng/mL (*e.g.*, 1.88 ng/mL) at the time of dosing. In an example, the mean accumulation index is in the range of 1-3 (*e.g.*, 1.48), and the mean fluctuation factor is in the range of 180-210% (*e.g.*, 199%). In an example, the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, profile in plasma at steady state provides drug coverage over a one-week (*e.g.*, a 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 day) dosing interval.

In an example, the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection, described herein, is optimized to allow for the neutral diacyl lipid and/or tocopherol and phospholipid components to be formulated in a wide range of proportions. In an example, the pharmaceutical product has a greater proportion of neutral diacyl lipid and/or tocopherol to phospholipid than was previously achievable without risking phase separation and/or unacceptably high viscosities in the formulation. In an example the ratio of neutral diacyl lipid and/or tocopherol to phospholipid is 1:1, or a ratio that is between 0.5 to 1.0, 0.7 to 1.0, or 1 to 0.5, or 1 to 0.7.

Methods described herein allow for more precise and accurate levels of alcohol in the preparations. The level of alcohol may affect release kinetics, *e.g.*, burst profile. Levels that are

too high may impact, e.g., negatively impact, release kinetics, *e.g.*, burst profile. Control of the level of alcohol thus may allow for a more predictable and repeatable achievement of an optimized release profile. The level of alcohol may also affect pre-injection viscosity, with higher levels of alcohol resulting in lower viscosity. Thus, defined and repeatable levels of alcohol may allow for optimized performance. Described herein are methods that combine the addition of a known amount of alcohol with steps to minimize or control the level of loss by evaporation. In an example, a method of making a pharmaceutical product described herein comprises the use of a controlled amount of alcohol to make the pharmaceutical product. In an example, the pharmaceutical product is prepared so as to reduce or control evaporation, *e.g.*, by the use of a closed vessel (thus reducing or controlling evaporation). The use of a closed vessel may allow for tight regulation of the amount of alcohol that is used to make the pharmaceutical product, and may improve the reproducibility of the pharmaceutical product. Preventing loss from evaporation is an important feature to reduce variability between batches of the pharmaceutical product, and between individual dosage units within a batch. Since the formulation may be used to deliver setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection *in vivo*, it is important that each batch of the pharmaceutical product contain a similar amount of the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; or an $MC4RA_P$, at a similar concentration.

Disclosed herein, *inter alia*, is a specified order in which components are added to the preparation. The specified order may have a significant effect on the solubility of the components with one another, *e.g.*, the solubility of the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an $MC4RA_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11) as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical

ingredient for injection in the preparation. In an example, a method of making the pharmaceutical product described herein comprises a specified order of addition of components to make the pharmaceutical product. In an example, setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection is contacted with one or more of the other components after the setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection is contacted with alcohol. The method may further optimize the time required for making the preparation. The pharmaceutical product of setmelanotide; setmelanotide as sole active pharmaceutical ingredient formulated for injection; setmelanotide as the sole active ingredient; setmelanotide as the active pharmaceutical ingredient; setmelanotide as the active pharmaceutical ingredient for injection; or an MC4RA$_P$ (*e.g.*, BIM-22511, BIM-22287, BIM-22512, 001152C, 001543C, 001003C, 001574C, 001555C, 001554C, 001556C, 001358C, 001576C, 001364C, 001258C, or MC4R-11), as the sole active ingredient, as the sole active ingredient for injection, as the active pharmaceutical ingredient, or as the active pharmaceutical ingredient for injection resulting from a specific order of addition of components has a low viscosity and an amount of alcohol that is compatible with *in vivo* use.

In examples, the control of alcohol content and the order of addition can be combined. In another aspect, there is provided a plurality of preparations of a pharmaceutical product, comprising setmelanotide as sole active pharmaceutical ingredient formulated for injection, each

preparation of the plurality having an amount of EtOH that falls within a predetermined range, optionally wherein the plurality of preparations is made by the method as defined above.

In another aspect, there is provided a composition for use in a method of providing setmelanotide as sole active pharmaceutical ingredient formulated for injection to a subject, comprising administering to the subject an effective amount of the injectable composition as defined above, or a unit dosage as defined above.

In another aspect, there is provided the use of an effective amount of the injectable composition as defined above, or a unit dosage as defined above, in the manufacture of a medicament for providing setmelanotide as sole active pharmaceutical ingredient formulated for injection to a subject.

The disclosure contemplates all combinations of any one or more of the foregoing aspects and/or examples, as well as combinations with any one or more of the examples set forth in the detailed description and examples.

What is claimed is:

1. An injectable composition or preparation comprising:

a) glycerol dioleate (GDO);

b) phosphatidylcholine:

c) an alcohol;

d) setmelanotide as the sole active pharmaceutical ingredient; and

e) optionally, a polar solvent.

2. The injectable composition of claim 1, wherein

(i) the alcohol comprises ethanol; and

(ii) the polar solvent comprises a citrate buffer.

3. The injectable composition of claim 1 or 2, wherein the injectable composition is provided in a device chosen from: a manual syringe, or an auto-injector.

4. The injectable composition of any of the preceding claims, wherein the pharmaceutical product comprises an anti-microbial or microbial-static agent.

5. The injectable composition of any of the preceding claims, wherein the ratio, by weight, of a:b is 70:30 to 40:60.

6. The injectable composition of any of claims 1-4, comprising, per one milliliter of composition:

420 +/- 20% mg glycerol dioleate (GDO);

420 +/- 20% mg soybean phosphatidylcholine;

105 +/- 20% mg ethanol;

20 +/- 20% mg citrate buffer; and

30 +/- 20% mg setmelanotide.

7. The injectable composition of any of claims 1-4, comprising:

(i) neutral diacyl lipid of component a at 20-80%, 30-70%, 33-60%, or 38-43% by weight, of components a, b, and c; components a, b, c, and e; or components a, b, c, d, and e of the composition;

(ii) phospholipid of component b at is 20-80%, 30-70%, 33-60%, or 38-43% by weight, of components a, b, and c; components a, b, c, and e; or components a, b, c, d, and e of the composition;

(iii) alcohol of component c at 0.1 -35%, 5 -20%, 8-15 %, or 9-11 % by weight, of components a, b, and c; components a, b, c, and e; or components a, b, c, d, and e of the composition;

(iv) polar solvent of component e, at 0.5-10%, 1-5%, or 1-3% by weight, of components a, b, and c; components a, b, c, and e; or components a, b, c, d, and e of the composition; and

(v) setmelanotide, at 0.1 -10%, 0.2 -8%, 0.5-6%, 1-4% by weight, of components a, b, and c; components a, b, c, and e; or components a, b, c, d, and e of the composition.

8. The injectable composition of any one of the preceding claims, which, upon contact with an aqueous environment, forms or is capable of forming, at least one liquid crystalline structure.

9. The injectable composition of any of the preceding claims, wherein the viscosity is:

(i) low enough to be comfortably delivered with a device, optionally wherein the device is a syringe with a narrow needle;

(ii) low enough that, upon injection, the initial burst of setmelanotide; from the pharmaceutical product after subcutaneous injection gives a ratio of maximum concentration (C_{max}) in plasma to minimum concentration (C_{min}) in plasma before a next dose is administered, of less than 8; or

(iii) low enough that, upon injection, the pharmaceutical product provides a low initial release of setmelanotide.

10. The injectable composition of any of the preceding claims, wherein the injectable composition is to be injected into a subject, and:

(i) the initial burst of setmelanotide, from the pharmaceutical product after subcutaneous injection gives a ratio of maximum concentration (C_{max}) in plasma to minimum concentration (C_{min}) in plasma before a next dose is to be administered, of less than 8; or

(ii) the pharmaceutical product is to provide a low initial release of setmelanotide.

11. A unit dosage form comprising the composition of any of the preceding claims, wherein:
(i) the unit dosage form comprises at least 2, 1.8, 1.6, 1.4, 1.2, 1, 0.8, 0.6, 0.4, or 0.2 mL of the composition; and/or
(ii) the unit dosage form is disposed in a liquid tight enclosure, optionally, a vial or a cartridge; and/or;
(iii) the unit dosage form is disposed in an injection device, optionally a manual syringe, or an auto-injector; and/or
(iv) the unit dosage form comprises 10-70; 20-60, 25-50; 25-40; or 25-35 mg of setmelanotide.

12. A method of making a preparation or composition formulated for injection, comprising setmelanotide as sole active pharmaceutical ingredient , comprising:

i) providing a mixture of setmelanotide, a first amount of EtOH, and one or more of components:

a) a neutral diacyl lipid and/or a tocopherol;

b) a phospholipid;

c) an alcohol;

d) a polar solvent, and

ii) adding a second amount of EtOH,

thereby making a preparation or composition, formulated for injection, comprising setmelanotide as sole active pharmaceutical ingredient.

13. A plurality of preparations of a pharmaceutical product, comprising setmelanotide as sole active pharmaceutical ingredient formulated for injection, each preparation of the plurality having an amount of EtOH that falls within a predetermined range, optionally wherein the plurality of preparations is made by the method of claim 12.

14. A composition for use in a method of providing setmelanotide as sole active pharmaceutical ingredient formulated for injection to a subject, comprising administering to the subject an effective amount of the injectable composition of any one of claims 1 to 10, or a unit dosage of claim 11.

15. Use of an effective amount of the injectable composition of any one of claims 1 to 10, or a unit dosage of claim 11, in the manufacture of a medicament for providing setmelanotide as sole active pharmaceutical ingredient formulated for injection to a subject.