IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	CAAMTECH, INC.	Confirmation No.:
Serial No.:	17/620,855	Group No.:
Filing or 371(c) Date:	June 24, 2020	Examiner:

Entitled: IBOGAINE FORMULATIONS

THIRD-PARTY PRE-ISSUANCE SUBMISSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application:

1. U.S. Pat. Doc. No. US/2013/0131046 “Noribogaine compositions” (Published 23 May 2013)
2. U.S. Pat. Doc. No. US/2006/0229293 “Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C” (Published 06 April 2006)
3. Int’l Pat. Doc. No. WO/2015/134405 “THERAPEUTIC USES OF IBOGAINE AND RELATED COMPOUNDS” (Published 11 September 2015)
4. Israel Pat. Doc. No. IL/73585 “A PHARMACEUTICAL COMPOSITION CONTAINING AN IBOGA ALKALOID FOR TREATING OPIATE ADDICTION” (Published 29 April 1990)
5. U.S. Pat. Doc. No. US/2015/0258112 “METHODS AND COMPOSITIONS FOR TREATING DEPRESSION USING IBOGAINE” (Published 02 March 2015)
6. Int’l Pat. Doc. No. WO/2017/184531 “TREATMENT OF MOVEMENT-RELATED DISORDERS USING NORIBOGAINE” (Published 26 October 2017)
7. U.S. Pat. Doc. No. US/2016/0220579 “Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids” (Published 04 August 2016)
8. U.S. Pat. Doc. No. US/2013/0303756 “Methods and compositions for preparing noribogaine from voacangine” (Published 14 November 2013)
9. BÜCHI (1966) “The Total Synthesis of Iboga Alkaloids”, Journal of the American Chemical Society. 88(13):3099-3109.

10. NOLLER (2017) “Ibogaine treatment outcomes for opioid dependence from a twelve-month follow-up observational study”, The American Journal of Drug and Alcohol Abuse. 44(1):37-46.

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. 17/620,855 Pending Claims	References
1. A formulation comprising a combination comprising a first purified ibogaine derivative and a second ibogaine derivative.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
2. The formulation of claim 1, wherein the combination comprises the first purified ibogaine derivative and a second purified ibogaine derivative.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
3. The formulation of claim 1, wherein the combination comprises	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006)

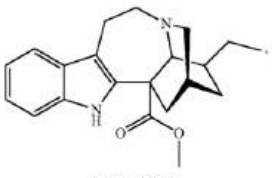
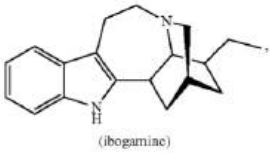
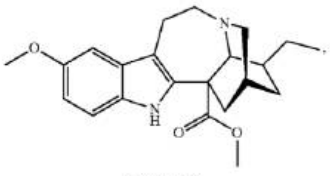
the first purified ibogaine derivative, a second purified ibogaine derivative, and a third ibogaine derivative.	From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
4. The formulation of claim 1, wherein the combination comprises the first purified ibogaine derivative, a second purified ibogaine derivative, and a third purified ibogaine derivative.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
5. The formulation of claim 1, wherein the first purified ibogaine derivative is selected from the group consisting of dihydroxyibogamine, dihydrocatharanthine,	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A composition comprising **one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective

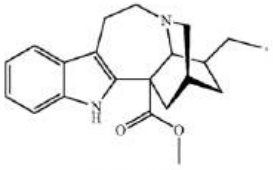
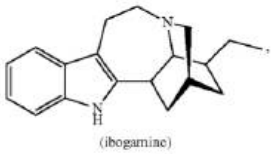
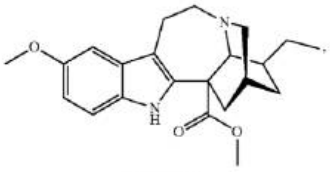
coronaridine, conopharyngine, conoflorine, catharanthine, iboxygaine, iboluteine, ibogamine, ibogaline, ibogaine, epiibogamine, isovoacangine, isovoacristine, kisantin, montanin, noribogaine, tabernanthine, tubotaiwine, voacristine, voacangine, voaluteine, and voacamine.	concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
6. The formulation of claim 1, wherein the combination is substantially free from a compound selected from the group consisting of dihydroxyibogamine, dihydrocatharanthine, coronaridine, conopharyngine, conoflorine, catharanthine, iboxygaine, iboluteine, ibogamine, ibogaline, ibogaine, epiibogamine, isovoacangine, isovoacristine, kisantin, montanin, noribogaine, tabernanthine, tubotaiwine, voacristine, voacangine, voaluteine, and voacamine.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention."
7. The formulation of claim 6, wherein the combination is substantially free from ibogaine.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective

	concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention. The amount of agent contained in a composition of this invention will depend in part on the desired results of the treatment, the stage of hepatitis C, its associated complications, and/or the health of the patient."
8. A method of treating addiction in a human in need of treatment, comprising the step of administering a therapeutically effective amount of a formulation of claim 1 to the human in need of treatment.	7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is contemplated that co-administration of **the iboga alkaloid with the opioid** prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, the **iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **paragraph [0161]** "**Noribogaine can be synthesized as described, for example in U.S. Patent Pub. Nos.** 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471." 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013)

	From **paragraph [0030]** "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**."
9. The method of claim 8, wherein the addiction is selected from the group consisting of opioid addiction, alcohol addiction, and nicotine addiction.	7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is contemplated that co-administration of **the iboga alkaloid with the opioid** prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, the **iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **paragraph [0161]** "**Noribogaine can be synthesized as described, for example in U.S. Patent Pub. Nos.** 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471." 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013) From paragraph [0030] "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**." 4. Israel Pat. Doc. No. IL/73585 "A PHARMACEUTICAL COMPOSITION CONTAINING AN IBOGA ALKALOID FOR TREATING OPIATE ADDICTION" (Published 29 April 1990) From **claim 1** "**A pharmaceutical composition for treating opiate addiction comprising an iboga alkaloid, a therapeutically active non-toxic salt thereof or a mixture thereof as active ingredient therein**."

	From **page 73585/3, paragraph 5** "**Pharmaceutical compositions according to the present invention comprise 98 to 99+ percent ibogaine or one of its salts with 1/4 to 2 percent ibogamine and/or tabernanthine or their salts**. The material will be administered in capsule form in dosage units of between 6mg/kg and 30mg/kg in the amount of 400mg to 200mg. In pill form, fillers such as lactose or starch may be used with various binding agents to maintain the integrity of the pill."
10. The method of claim 9, wherein the addiction is opioid addiction.	4. Israel Pat. Doc. No. IL/73585 "A PHARMACEUTICAL COMPOSITION CONTAINING AN IBOGA ALKALOID FOR TREATING OPIATE ADDICTION" (Published 29 April 1990) From **claim 1** "**A pharmaceutical composition for treating opiate addiction comprising an iboga alkaloid, a therapeutically active non-toxic salt thereof or a mixture thereof as active ingredient therein**." From **page 73585/3, paragraph 5** "Pharmaceutical compositions according to the **present invention comprise 98 to 99+ percent ibogaine or one of its salts with 1/4 to 2 percent ibogamine and/or tabernanthine or their salts**. The material will be administered in capsule form in dosage units of between 6mg/kg and 30mg/kg in the amount of 400mg to 200mg. In pill form, fillers such as lactose or starch may be used with various binding agents to maintain the integrity of the pill." 7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is contemplated that co-administration of **the iboga alkaloid with the opioid** prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, the **iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt."

	From **paragraph [0161]** "**Noribogaine can be synthesized as described, for example in U.S. Patent Pub. Nos.** 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471." 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013) From **paragraph [0030]** "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**."
11. A method of treating depression in a human in need of treatment, comprising the step of administering a therapeutically effective amount of a formulation of claim 1 to the human in need of treatment.	5. U.S. Pat. Doc. No. US/2015/0258112 "METHODS AND COMPOSITIONS FOR TREATING DEPRESSION USING IBOGAINE" (Published 02 March 2015) From **paragraph [0150]** "One aspect of this invention is directed to a kit of parts for the **treatment of depression** and/or PTSD c**omprising a composition comprising ibogaine, ibogaine derivative, or salt and/or solvate thereof as disclosed herein and a means for administering the composition to a patient in need thereof**. The **means for administration to a patient can include, for example, any one or combination of ibogaine, ibogaine derivative,** or pharmaceutically acceptable salt and/or solvate thereof" From **paragraph [0089]** "This **invention is not limited to any particular chemical form of ibogaine or ibogaine derivative**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **page 12** **[0088]** In one embodiment, the ibogaine derivative is:  (coronaridine)  (ibogamine)  (voacangine)

12. The method of claim 11, wherein the depression is selected from the group consisting of a major depressive disorder and treatment resistant depression.	5. U.S. Pat. Doc. No. US/2015/0258112 "METHODS AND COMPOSITIONS FOR TREATING DEPRESSION USING IBOGAINE" (Published 02 March 2015) From **paragraph [0150]** "One aspect of this invention is directed to a kit of parts for the **treatment of depression** and/or PTSD c**omprising a composition comprising ibogaine, ibogaine derivative, or salt and/or solvate thereof as disclosed herein and a means for administering the composition to a patient in need thereof**. The **means for administration to a patient can include, for example, any one or combination of ibogaine, ibogaine derivative,** or pharmaceutically acceptable salt and/or solvate thereof" From **paragraph [0126]** "This invention provides, in certain embodiments, **a method of treating a patient suffering from major depressive disorder,** which comprises administering to the patient a therapeutically effective amount of **any of the compounds utilized herein** effective to treat the subject's major depressive disorder." From **paragraph [0089]** "This **invention is not limited to any particular chemical form of ibogaine or ibogaine derivative**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **page 12** **[0088]** In one embodiment, the ibogaine derivative is:  (coronaridine)  (ibogamine)  (voacangine)
13. The method of claim 11, comprising administering ibogaine and noribogaine.	6. Int'l Pat. Doc. No. WO/2017/184531 "TREATMENT OF MOVEMENT-RELATED DISORDERS USING NORIBOGAINE" (Published 26 October 2017) From **claim 22** "A pharmaceutical composition comprising **a therapeutically effective amount of an iboga alkaloid** or pharmaceutically acceptable salt or solvate thereof, at least one agent for **treating or preventing a neurodegenerative disease**, and a pharmaceutically acceptable excipient."

	From **paragraph [0003]** "Neurodegenerative diseases include, without limitation, Alzheimer's disease, **Parkinson's disease**, Huntington's disease, amyotrophic lateral sclerosis (ALS), prion diseases (e.g., Creutzfeldt- Jakob Disease), ataxia, spinocerebellar ataxia, spinal muscular atrophy, Friedreich's ataxia, Lewy body disease, and motor neuron diseases." From **paragraph [0172]** "**Parkinson's disease** is a progressive disorder caused by degeneration of nerve cells in the substantia nigra, which controls movement. Nerve cell degeneration **results in** a reduction in dopamine production, which causes tremor; muscle rigidity or stiffness of the limbs; gradual loss of spontaneous movement, including decreased mental skill or reaction time, voice changes or decreased facial expression; gradual loss of automatic movement, including decreased blinking, decreased frequency of swallowing, and drooling; a stooped, flexed posture, with bending at the elbows, knees and hips; an unsteady walk or balance; and **depression** or dementia." From **paragraph [0139]** "**"Treatment", "treating", and "treat" are defined as** acting upon a disease, disorder, or condition with an agent, such as iboga alkaloid or pharmaceutically acceptable salt or solvate thereof, t**o reduce or ameliorate harmful or any other undesired effects of the disease, disorder, or condition and/or its symptoms**." From **paragraph [0030]** "It must be noted that as used herein and in the appended claims, the singular forms **"a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a plurality of compounds.**" From **paragraph [0145]** "In one embodiment, **the iboga alkaloid is ibogaine**, **noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0130]** "**This invention is not limited to any particular chemical form of iboga alkaloid, and the drug may be given to patients either as a free base or as a pharmaceutically acceptable acid addition salt**. In the latter case, the hydrochloride salt is generally preferred, but other salts derived from organic or inorganic acids may also be used. Examples of such acids include, without limitation, those described below as "pharmaceutically acceptable salts" and the like."
14. The method of claim 12, comprising administering a composition comprising purified ibogaine.	6. Int'l Pat. Doc. No. WO/2017/184531 "TREATMENT OF MOVEMENT-RELATED DISORDERS USING NORIBOGAINE" (Published 26 October 2017) From **claim 22** "A pharmaceutical composition comprising **a therapeutically effective amount of an iboga alkaloid** or pharmaceutically

	acceptable salt or solvate thereof, at least one agent for **treating or preventing a neurodegenerative disease**, and a pharmaceutically acceptable excipient." From **paragraph [0003]** "Neurodegenerative diseases include, without limitation, Alzheimer's disease, **Parkinson's disease**, Huntington's disease, amyotrophic lateral sclerosis (ALS), prion diseases (e.g., Creutzfeldt- Jakob Disease), ataxia, spinocerebellar ataxia, spinal muscular atrophy, Friedreich's ataxia, Lewy body disease, and motor neuron diseases." From **paragraph [0172]** "Parkinson's disease is a progressive disorder caused by degeneration of nerve cells in the substantia nigra, which controls movement. Nerve cell degeneration results in a reduction in dopamine production, which causes tremor; muscle rigidity or stiffness of the limbs; gradual loss of spontaneous movement, including decreased mental skill or reaction time, voice changes or decreased facial expression; gradual loss of automatic movement, including decreased blinking, decreased frequency of swallowing, and drooling; a stooped, flexed posture, with bending at the elbows, knees and hips; an unsteady walk or balance; and **depression** or dementia." From **paragraph [0130]** "**This invention is not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base or as a pharmaceutically acceptable acid addition salt." From **paragraph [0030]** "It must be noted that as used herein and in the appended claims, the **singular forms "a", "an", and "the" include plural referents** unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0145]** "In one embodiment, **the iboga alkaloid is ibogaine**, noribogaine, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0126]** "It should be understood that where "ibogaine" is mentioned herein, one or more polymorphs of ibogaine can be utilized and are contemplated. Ibogaine is isolated from Tabernanth iboga, a shrub of West Africa. **Ibogaine can also be synthesized** using known methods."
15. The method of claim 11, comprising administering a composition comprising purified noribogaine.	6. Int'l Pat. Doc. No. WO/2017/184531 "TREATMENT OF MOVEMENT-RELATED DISORDERS USING NORIBOGAINE" (Published 26 October 2017) From **claim 22** "A pharmaceutical composition comprising **a therapeutically effective amount of an iboga alkaloid** or pharmaceutically acceptable salt or solvate thereof, at least one agent for **treating or**

	preventing a neurodegenerative disease, and a pharmaceutically acceptable excipient." From **paragraph [0003]** "Neurodegenerative diseases include, without limitation, Alzheimer's disease, **Parkinson's disease**, Huntington's disease, amyotrophic lateral sclerosis (ALS), prion diseases (e.g., Creutzfeldt- Jakob Disease), ataxia, spinocerebellar ataxia, spinal muscular atrophy, Friedreich's ataxia, Lewy body disease, and motor neuron diseases." From **paragraph [0172]** "Parkinson's disease is a progressive disorder caused by degeneration of nerve cells in the substantia nigra, which controls movement. Nerve cell degeneration results in a reduction in dopamine production, which causes tremor; muscle rigidity or stiffness of the limbs; gradual loss of spontaneous movement, including decreased mental skill or reaction time, voice changes or decreased facial expression; gradual loss of automatic movement, including decreased blinking, decreased frequency of swallowing, and drooling; a stooped, flexed posture, with bending at the elbows, knees and hips; an unsteady walk or balance; and **depression** or dementia." From **paragraph [0130]** "**This invention is not limited to any particular chemical form of iboga alkaloid, and the drug may be given to patients either as a free base or as a pharmaceutically acceptable acid addition salt**. In the latter case, the hydrochloride salt is generally preferred, but other salts derived from organic or inorganic acids may also be used. Examples of such acids include, without limitation, those described below as "pharmaceutically acceptable salts" and the like." From **paragraph [0030]** "It must be noted that as used herein and in the appended claims, the **singular forms "a", "an", and "the" include plural referents** unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0145]** "In one embodiment, **the iboga alkaloid is ibogaine**, **noribogaine,** an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0127]** "**Noribogaine can be prepared by demethylation of naturally occurring ibogaine. Demethylation may be accomplished by conventional techniques such as by reaction with boron tribromide/methylene chloride at room temperature followed by conventional purification**. See, for example, Huffman, et al, J. Org. Chem. 50: 1460 (1985), which incorporated herein by reference in its entirety. **Noribogaine can be synthesized as described, for example in** U.S. Patent Pub. Nos. 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471 (includes description of making

	noribogaine polymorphs), and U.S. PatentNo. 9,617,274, each of which is incorporated herein by reference in its entirety." 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013) From **paragraph [0030]** "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**."
16. The method of claim 8, comprising administering ibogaine and noribogaine to the brain of the human in need of treatment.	4. Israel Pat. Doc. No. IL/73585 "A PHARMACEUTICAL COMPOSITION CONTAINING AN IBOGA ALKALOID FOR TREATING OPIATE ADDICTION" (Published 29 April 1990) From **claim 1** "**A pharmaceutical composition for treating opiate addiction comprising an iboga alkaloid, a therapeutically active non-toxic salt thereof or a mixture thereof as active ingredient therein**." From **page 73585/3, paragraph 5** "Pharmaceutical compositions according to the **present invention comprise 98 to 99+ percent ibogaine or one of its salts with 1/4 to 2 percent ibogamine and/or tabernanthine or their salts**. The material will be **administered in capsule form in dosage units** of between 6mg/kg and 30mg/kg in the amount of 400mg to 200mg. In pill form, fillers such as lactose or starch may be used with various binding agents to maintain the integrity of the pill." 7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is contemplated that co-administration of **the iboga alkaloid with the opioid** prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, **the iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds."

	From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **paragraph [0184]** "In some embodiments, the **composition is formulated for oral, transdermal, internal, pulmonary, rectal, nasal, vaginal, lingual, intravenous, intraarterial, intramuscular, intraperitoneal, intracutaneous or subcutaneous delivery**." From **paragraph [0161]** "**Noribogaine can be synthesized as described, for example in U.S. Patent Pub. Nos.** 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471." 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013) From **paragraph [0030]** "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**."
17. The method of claim 8, comprising administering a composition of claim 1 intravenously to the human in need of treatment.	2. U.S. Pat. Doc. No. US/2006/0229293 "Compositions for the treatment of hepatitis C and methods for using compositions for the treatment of hepatitis C" (Published 06 April 2006) From **claim 1** "A **composition comprising one or more of ibogaine, ibogamine, tabernanthine, their nontoxic salts and/or the converted principal metabolite noribogaine** in a therapeutically effective concentration for the treatment of hepatitis C or hepatitis C-related complications." From **paragraph [0035]** "The **agents used in the compositions of this invention may be provided in the form of pure substances**, or as root bark of the natural plant containing the natural agents in concentrations between about 1 to 6 percent of which approximately fifty percent is ibogaine, or as concentrated plant extracts containing the natural agents in concentrations between about 5 to 40 percent of which one half is ibogaine. Doses of the root bark or total alkaloid extract would be extrapolated to correspond to doses of purified ibogaine in keeping with the dose recommendations and regimens for purified ibogaine and associated alkaloids as described in the present invention." From **paragraph [0039]** "The **compositions of this invention may also be administered as a solution and other oral or parenteral administration can be used**. For example, a compound with poor solubility in acidic media

	may show poor or erratic bioavailability when absorbed orally. **Further, intravenous administration requires that a drug be administered in a soluble form**." 7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is contemplated that co-administration of **the iboga alkaloid with the opioid** prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, the **iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt." From **paragraph [0184]** "In some embodiments, the **composition is formulated for oral, transdermal, internal, pulmonary, rectal, nasal, vaginal, lingual, intravenous, intraarterial, intramuscular, intraperitoneal, intracutaneous or subcutaneous delivery**."
18. The method of claim 8, comprising administering between 1 to 100 mg/kg of total ibogaine derivatives to the human in need of treatment.	3. Int'l Pat. Pub. Pub. No. WO/2015/134405 "THERAPEUTIC USES OF IBOGAINE AND RELATED COMPOUNDS" (Published 11 September 2015) From **paragraph [0008]** "This **invention provides noribogaine compositions which** are enantiomerically enriched and substantially free of ibogaine. Such compositions **provide a significant breakthrough in the treatment of addiction** and/or pain..." From **paragraph [0002]** "This **invention relates generally to the use of each of ibogaine, an ibogaine derivative,** or a pharmaceutically acceptable salt and/or solvate thereof at a dosage that provides a therapeutic serum concentration for treating or preventing a disease or disorder in a patient."

	From **paragraph [0155]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a plurality of compounds**." From **paragraph [0177]** "Unless specified otherwise, **"ibogaine" as used herein refers to ibogaine, ibogaine derivative, or a pharmaceutically acceptable salt and/or solvate thereof**." From **paragraph [0195]** ""**Treatment", "treating", and "treat" are defined as acting upon a disease, disorder, or condition with ibogaine to reduce or ameliorate harmful or any other undesired effects of the disease, disorder, or condition and/or its symptoms**. "Treatment," as used herein, covers the treatment of a human patient, and includes: (a) reducing the risk of occurrence of the condition in a patient determined to be predisposed to the condition but not yet diagnosed as having the condition, (b) impeding the development of the condition, and/or (c) relieving the condition, i.e., causing regression of the condition and/or relieving one or more symptoms of the condition. "Treating" or "treatment of a condition or patient refers to taking steps to obtain beneficial or desired results, including clinical results such as the reduction of symptoms. **For purposes of this invention, beneficial or desired clinical results include, but are not limited to: treating nicotine addiction; treating, preventing, and/or attenuating cravings for nicotine; and preventing relapse of nicotine use. This includes reducing or eliminating smoking in the patient, and/or reducing or eliminating symptoms of withdrawal, cravings, and the like. For some purposes of this invention, beneficial or desired clinical results include, but are not limited to: treating substance addiction; treating, preventing, and/or attenuating acute withdrawal symptoms**." From **paragraph [0340]** "In one embodiment, the therapeutically effective amount of **the compound is about 3 mg/kg body weight** per day. In one embodiment, the therapeutically effective amount of the compound is about 2 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.5 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.4 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.3 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.2 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.1 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1 mg/kg body weight per day."

19. The method of claim 18, comprising administering between 2 to 25 mg/kg of total ibogaine derivatives to the human in need of treatment.	3. Int'l Pat. Pub. Pub. No. WO/2015/134405 "THERAPEUTIC USES OF IBOGAINE AND RELATED COMPOUNDS" (Published 11 September 2015) From **paragraph [0008]** "This **invention provides noribogaine compositions which** are enantiomerically enriched and substantially free of ibogaine. Such compositions **provide a significant breakthrough in the treatment of addiction** and/or pain..." From **paragraph [0155]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a plurality of compounds**." From **paragraph [0177]** "Unless specified otherwise, **"ibogaine" as used herein refers to ibogaine, ibogaine derivative, or a pharmaceutically acceptable salt and/or solvate thereof**." From **paragraph [0195]** ""**Treatment", "treating", and "treat" are defined as acting upon a disease, disorder, or condition with ibogaine to reduce or ameliorate harmful or any other undesired effects of the disease, disorder, or condition and/or its symptoms**. "Treatment," as used herein, covers the treatment of a human patient, and includes: (a) reducing the risk of occurrence of the condition in a patient determined to be predisposed to the condition but not yet diagnosed as having the condition, (b) impeding the development of the condition, and/or (c) relieving the condition, i.e., causing regression of the condition and/or relieving one or more symptoms of the condition. "Treating" or "treatment of a condition or patient refers to taking steps to obtain beneficial or desired results, including clinical results such as the reduction of symptoms. **For purposes of this invention, beneficial or desired clinical results include, but are not limited to: treating nicotine addiction; treating, preventing, and/or attenuating cravings for nicotine; and preventing relapse of nicotine use. This includes reducing or eliminating smoking in the patient, and/or reducing or eliminating symptoms of withdrawal, cravings, and the like. For some purposes of this invention, beneficial or desired clinical results include, but are not limited to: treating substance addiction; treating, preventing, and/or attenuating acute withdrawal symptoms**." From **paragraph [0340]** "In one embodiment, the therapeutically effective amount of **the compound is about 3 mg/kg body weight** per day. In one embodiment, the therapeutically effective amount of the compound is about 2 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.5 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is

	about 1.4 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.3 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.2 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1.1 mg/kg body weight per day. In one embodiment, the therapeutically effective amount of the compound is about 1 mg/kg body weight per day."
20. The method of claim 16, comprising administering a composition comprising purified ibogaine and purified noribogaine to the brain of the human in need of treatment.	7. U.S. Pat. Doc. No. US/2016/0220579 "Methods and compositions for potentiating the action of opioid analgesics using iboga alkaloids" (Published 04 August 2016) From **paragraph [0020]** "In one embodiment, it is **contemplated that co-administration of the iboga alkaloid** with the opioid prevents, inhibits or **attenuates dependence on and/or addiction** to the opioid analgesic..." From **paragraph [0191]** "In one embodiment, the **iboga alkaloid is ibogaine, noribogaine**, an ibogaine derivative, noribogaine derivative, or prodrug, salt or solvate thereof." From **paragraph [0064]** "It must be noted that as used herein and in the appended claims, **the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise**. Thus, for example, reference to "a compound" includes a plurality of compounds." From **paragraph [0163]** "This invention is **not limited to any particular chemical form of iboga alkaloid**, **and the drug may be given to patients either as a free base, solvate, or as a pharmaceutically acceptable acid addition salt**. In the latter case, the hydrochloride salt is generally preferred, but other salts derived from organic or inorganic acids may also be used." From **paragraph [0184]** "In some embodiments, the **composition is formulated for oral, transdermal, internal, pulmonary, rectal, nasal, vaginal, lingual, intravenous, intraarterial, intramuscular, intraperitoneal, intracutaneous or subcutaneous delivery**." From **paragraph [0160]** "**Ibogaine can also be synthesized using known methods**. See, e.g., **Büchi, et al. (1966), J. Am. Chem Society, 88(13), 3099-3109**." From **paragraph [0161]** "**Noribogaine can be synthesized as described, for example in U.S. Patent Pub. Nos.** 2013/0165647, **2013/0303756**, and 2012/0253037, PCT Patent Publication No. WO 2013/040471." 9. **BÜCHI (1966)** "The Total Synthesis of Iboga Alkaloids" Journal of the American Chemical Society. 88(13):3099-3109.

	From **page 3103** "Reduction with zinc and acetic acid followed by Wolff-Kishner reduction yielded a **readily separable mixture of ibogaine** and its C4 epimer. **Infrared and mass spectra of racemic ibogaine were identical with those of the natural material**" 8. U.S. Pat. Doc. No. **US/2013/0303756** "Methods and compositions for preparing noribogaine from voacangine" (Published 14 November 2013) From **paragraph [0030]** "This invention is directed to methods and compositions comprising noribogaine and, in particular, methods and compositions comprising **highly pure noribogaine**." 10. NOLLER (2017) "Ibogaine treatment outcomes for opioid dependence from a twelve-month follow-up observational study" The American Journal of Drug and Alcohol Abuse. 44(1):37-46. From **page 39** "**All participants were orally administered staggered doses of ibogaine HCL** (200 mg capsules). Initially, both providers imported ibogaine HCL (98.5%) from a European manufacturer through a registered New Zealand pharmaceutical importer. Subsequently Provider 2 switched to using Remogen™, a Canadian product, **assessed by HPLC as 99.5% pure ibogaine HCl**. Of 14 participants, 42.9% received Remogen™." From **page 37** "A **single ibogaine treatment** reduced opioid withdrawal symptoms and **achieved opioid cessation or sustained reduced use in dependent individuals** as measured over 12 months."

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