October 1, 2024

VIA EMAIL

Samuel A.A. Levine, Director
James A. Kohm, Associate Director
Bureau of Consumer Protection
Federal Trade Commission
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John D. Jacobs, Attorney
Federal Trade Commission
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Re: Violations of Stipulated Order in *FTC v. Lunada Biomedical, Inc., et al.,* Case No. 15-cv-03380, C.D. Cal.

Dear Mr. Levine, Mr. Kohm, and Mr. Jacobs:

The marketer of the menopause supplement Amberen is violating the May 25, 2016 Stipulated Order entered in *FTC v. Lunada Biomedical, Inc., et al.* ("Order")[1] by continuing to market the brand's products as able to relieve the symptoms of menopause without competent and reliable scientific evidence to substantiate the claims. Truth in Advertising, Inc. (TINA.org) has catalogued more than 1,000 examples of marketing materials that violate the Order. Indeed, it appears that the Order has had no impact on the way Amberen is advertised to millions of women[2] seeking relief from menopausal symptoms. Unless prompt action is taken, there can be no doubt that the wrongdoing will continue.

A. Background

The Order permanently prohibits Lunada Biomedical, Inc. and its "successors and assigns"[3] – which include Alliance Pharmaceuticals, the current owner of the Amberen brand[4] (hereinafter "Defendants") – from, among other things, labeling and advertising Amberen or any other dietary supplement as able to:

> Relieve hot flashes, night sweats, irritability, mood swings, inability to concentrate, sleeplessness, lack of energy, decreased libido, stress, anxiety, weight gain, headache, or muscle or joint aches associated with menopause unless the representation is non-misleading and, at the time of making such representation, Defendants possess and rely upon competent and reliable scientific evidence that substantiates that the representation is true. For purposes of this

> Section, competent and reliable scientific evidence shall consist of human clinical testing of the Covered Product or of an Essentially Equivalent Product that is sufficient in quality and quantity, based on standards generally accepted by experts in the relevant disease, condition, or function to which the representation relates, when considered in light of the entire body of relevant and reliable scientific evidence, to substantiate that the representation is true. Such testing shall (1) be randomized, double-blind, and placebo-controlled; and (2) be conducted by researchers qualified by training and experience to conduct such testing.[5]

Since this Order was entered in 2016, Defendants' deceptive and unsubstantiated marketing for Amberen has continued unfettered despite receiving several reminders from regulators of the obligation to comply with FTC law. In fact, in April 2023, Alliance Pharmaceuticals received a Notice of Penalty Offenses Concerning Substantiation of Product Claims from the FTC.[6] That same month, the National Advertising Division (NAD) opened an investigation into the advertising for Amberen, specifically flagging, and requesting substantiation for, claims that the product is clinically proven to relieve 12 menopause symptoms. However, because all of the marketing claims at issue are the subject of the FTC's Order, NAD determined that it "was deprived of jurisdiction" and the inquiry was closed, underscoring the necessity of FTC action.[7]

B. Order Violations

Throughout its marketing materials, Amberen is touted as "clinically proven" to provide menopause and perimenopause relief and able to treat a variety of menopause symptoms, including hot flashes, night sweats, irritability, mood swings, inability to concentrate, sleeplessness, lack of energy, decreased libido, stress, anxiety, depression, weight gain, headaches, and muscle and joint aches. TINA.org has catalogued a sampling of more than 1,000 examples of such marketing materials, all of which were published after the Order was entered and none of which are substantiated by competent and reliable scientific evidence. These examples, which are not an exhaustive list of violative marketing materials for Amberen, are available at www.truthinadvertising.org/evidence/amberen-menopause-claims/. The following marketing materials are illustrative of TINA.org's findings.

Amberen Website[8]

Amberen PERIMENOPAUSE MENOPAUSE SYMPTOM SUPPORT SCIENCE RESULTS LEARN FIND IN STORE

Get Support | Hot Flashes

Experiencing out-of-nowhere heat? You're not alone. Caused by hormonal fluctuations and other physiological changes and occurring day or night, hot flashes often start intensely in the face, neck and chest area before spreading to other parts of the body. Hot flashes can also worsen from environmental factors, including stress, spicy food, caffeine, alcohol, tight clothing and hot weather.

Amberen PERIMENOPAUSE MENOPAUSE SYMPTOM SUPPORT SCIENCE RESULTS LEARN FIND IN STORE

Get Support | Mood Swings

Is your mood rapidly changing from one moment to the next? Hormonal shifts that arise during perimenopause and into menopause can lead to mood changes ranging from irritability and anxiety to sadness and anger.

Amberen PERIMENOPAUSE MENOPAUSE SYMPTOM SUPPORT SCIENCE RESULTS LEARN FIND IN STORE

Get Support | Difficulty Concentrating

Are you finding it impossible to stay focused? A loss of focus is among the common symptoms women often experience during menopausal transition. Hormonal changes, sleep problems, mood swings, as well as the natural aging process can also play a role, making it difficult to concentrate.

Amberen PERIMENOPAUSE MENOPAUSE SYMPTOM SUPPORT SCIENCE RESULTS LEARN FIND IN STORE

Get Support | Anxiety/Stress

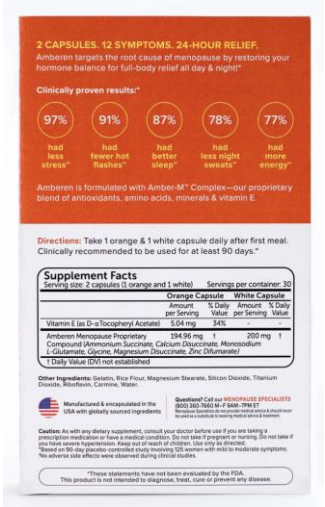
Feeling stressed out or anxious? Hormonal fluctuations during perimenopause and menopause can impact neurotransmitter levels in the brain, contributing to feelings of anxiety and stress. Other physical and emotional changes and sleep disturbances associated with entering menopause and external life stressors can also further exacerbate stress and anxiety levels.

Amberen PERIMENOPAUSE MENOPAUSE SYMPTOM SUPPORT SCIENCE RESULTS LEARN FIND IN STORE

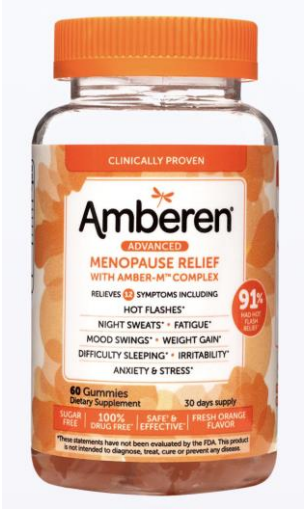
Get Support | Night Sweats

Waking up with damp sheets? Night sweats are a common symptom of overheating that often occurs during menopause and can be triggered by hormonal fluctuations, physiological changes and other environmental factors. Unlike a hot flash, night sweats occur only at night and include periods of intense sweating, which can amplify sleep problems and may exacerbate other menopausal symptoms.

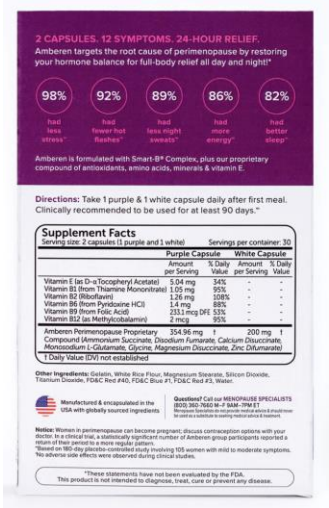
Product Packaging



"Control the CHANGE. Restore the BALANCE. ...Alleviates 12 Symptoms…clinically proven…regulates hormones….Amberen targets the root cause of menopause by restoring your hormone balance for full-body relief all day & night! …"



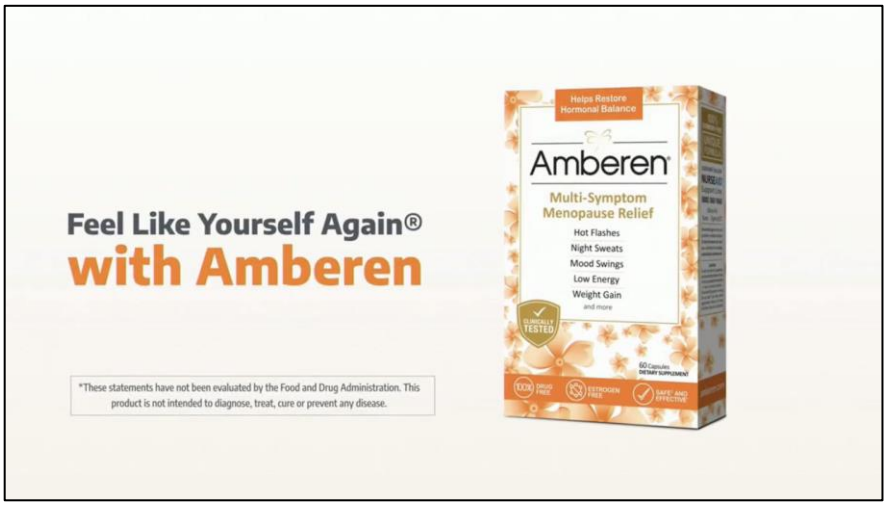
"Relieves 12 Symptoms including hot flashes[,] night sweats[,] fatigue[,] mood swings[,] weight gain[,] difficulty sleeping[,] irritability[,] anxiety & stress…Finally, clinically proven menopause symptom relief in a gummy supplement! … helping to regulate your hormone production…"



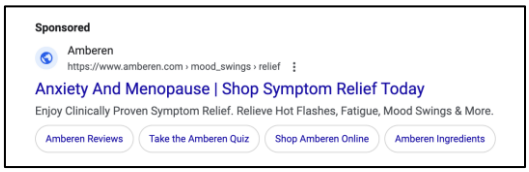
"Control the CHANGE. Restore the BALANCE… Alleviates 12 Symptoms…clinically proven…regulates hormones….Amberen targets the root cause of menopause by restoring your hormone balance for full-body relief all day & night! …"

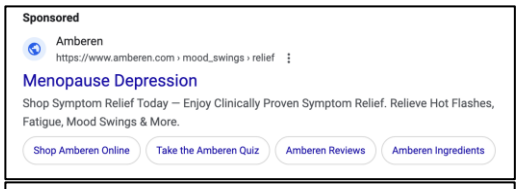
"Control the CHANGE. Restore the BALANCE…perimenopause support…Get focused support for energy, mood and occasional sleeplessness and help relieve hot flashes and night sweats with results in as little as four weeks…"

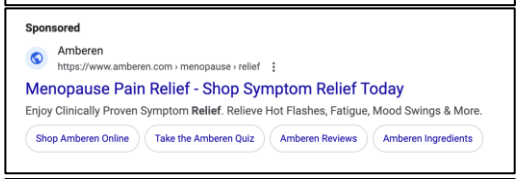
National Television Commercials[9]



Google Ads

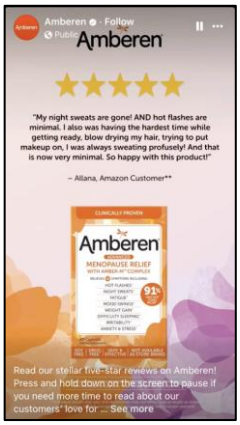




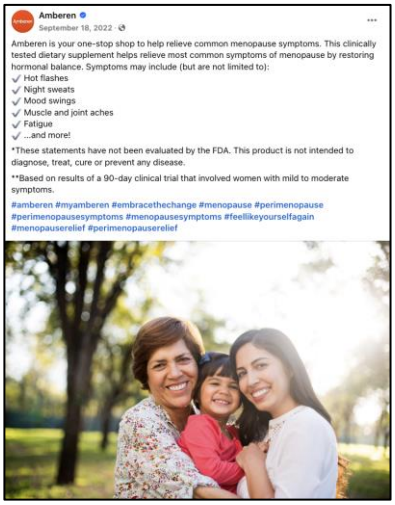


Amberen Social Media Platforms[10]

"It worked so well for me. The hot flashes completely stopped so I stopped taking it after 5-6 months. A few months later the hot flashes started again so I started taking this everyday again and the flashes lessened and completely stopped again…"

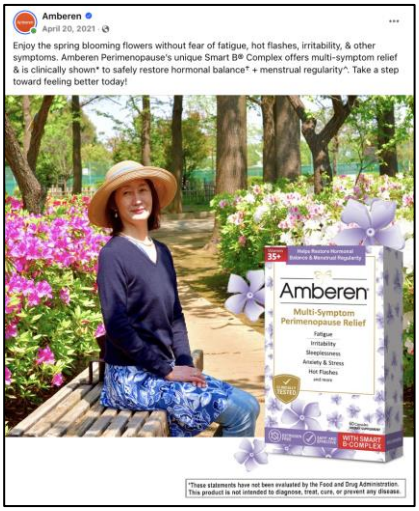


"My night sweats are gone! AND hot flashes are minimal. I also was having the hardest time while getting ready, blow drying my hair, trying to put makeup on, I was always sweating profusely! And that is now very minimal. So happy with this product!"



"Amberen is your one-stop shop to help relieve common menopause symptoms. This clinically tested dietary supplement helps relieve most common symptoms of menopause by restoring hormonal balance. Symptoms may include (but are not limited to): ✓Hot flashes ✓ Night sweats ✓Mood swings ✓ Muscle and joint aches ✓Fatigue ✓ ...and more!..."

"So how does Amberen work? As women age, natural changes to hormonal levels can lead to a drop in estrogen that may cause symptoms ranging from mild to severe. Unlike many supplements, Amberen targets the root cause of menopause by restoring hormonal balance for full-body relief…"



"Enjoy the spring blooming flowers without fear of fatigue, hot flashes, irritability, & other symptoms. Amberen Perimenopause's unique Smart B® Complex offers multi-symptom relief & is clinically shown to safely restore hormonal balance† + menstrual regularity^. Take a step toward feeling better today!"*

Influencer Marketing[11]

"30+ days ago I added Amberen supplements to my daily breakfast routine, to help me to manage my menopause symptoms. I am so excited to share that by simply adding 2 estrogen-free tablets to my breakfast routine, my sleeping habits have changed, I'm going to be bed at a regular time and waking up early and making it to the gym. My energy has increased and my days are so much more productive. Thank you @Amberen_official for choosing me as a partner."

All of these marketing materials violate the Order as they are not substantiated by competent and reliable scientific evidence.

The Amberen website lists two clinical trials as support for its marketing claims: (1) a 2016 clinical trial on Amberen Menopause Relief and (2) a 2020 clinical trial on Amberen Perimenopause Relief,[12] both of which are fatally flawed.

For starters, both trials were funded by the company and conducted by its employees. In addition, both trials examined homogenous populations during a relatively short intervention period. These material limitations, as well as others, are discussed in more detail below.

2016 Clinical Trial

The first clinical trial provided on the Amberen website is a 2016 clinical trial examining Amberen Menopause Relief.[13]

Clinical Trial: Amberen Menopause Relief (2016)

12-week, randomized, placebo-controlled, double-blind study with 125 women aged 42–60 with mild to moderate menopause symptoms.

Results

Amberen was shown to be a safe and well-tolerated supplement with no adverse side effects.‡ Compared to the placebo group, women who took Amberen reported significant improvements in many menopause symptoms∞:

This 90-day study contains numerous flaws that prevent it from properly substantiating Amberen's unqualified marketing claims, including but not limited to the following:

- **Inadequate and homogenous sampling:** The study examined only Caucasian women of Russian ancestry. As the researchers noted, "It is possible that these findings may not be similarly observed in studies of more diverse communities..."[14] In addition, all study participants were symptomatic postmenopausal women with mild to moderate vasomotor and psychosomatic menopausal symptoms; perimenopausal women and women with severe symptoms were not studied.

- **Method of administration:** While Amberen sells both Menopause Relief capsules and Menopause Relief gummies, the study only used capsules and did not ever examine the use of gummies.

- **Short intervention period:** The study was conducted for just 90 days. As the researchers noted, "the relatively short intervention study period … provides no information on the benefits of long-term use of [Amberen] or on the safety profile associated with long-term use. Further study is clearly needed to better assess the benefits and risks of long-term use of [Amberen]."[15]

- **Unbalanced study cohorts:** Women in the treatment group had more severe anxiety and more frequent hot flashes, depression, headaches, lack of sex drive and difficulty sleeping than women in the control group.[16] The heightened severity in anxiety in the treatment group is especially problematic as women with more anxiety show a higher response to a placebo.[17] Depression and hot flashes are also particularly susceptible to the placebo effect.[18]

- **Study results based on self-reported symptoms:** To evaluate Amberen's effect on menopausal symptoms, the study used two subjective self-assessments: the Greene Climacteric Scale, a self-reporting questionnaire that asks the degree to which participants experience 21 symptoms of menopause on a 4-point scale (0 = Not at all, 1 = A little, 2 = Quite a bit, 3 = Extremely), and the State-Trait Anxiety Inventory, a self-reporting questionnaire that asks the degree to which participants experience anxiety.[19] Self-reporting introduces several biases (e.g., social desirability bias, recall bias, measurement error basis) that can pose major problems in medical research if not properly accounted for.[20] None of these biases were addressed in the study. Further, the study's researchers noted that "a number of publications have highlighted that the simple measure of frequency and severity of vasomotor symptoms may not provide an overarching assessment of the overall efficacy of an intervention since the frequency/severity of vasomotor symptoms do not necessarily correlate with the degree of bother and quality of life of symptomatic menopausal women."[21]

- **Hormone "regulation" and "balancing" not observed:** Despite claiming throughout its marketing campaign that the reason Amberen can purportedly

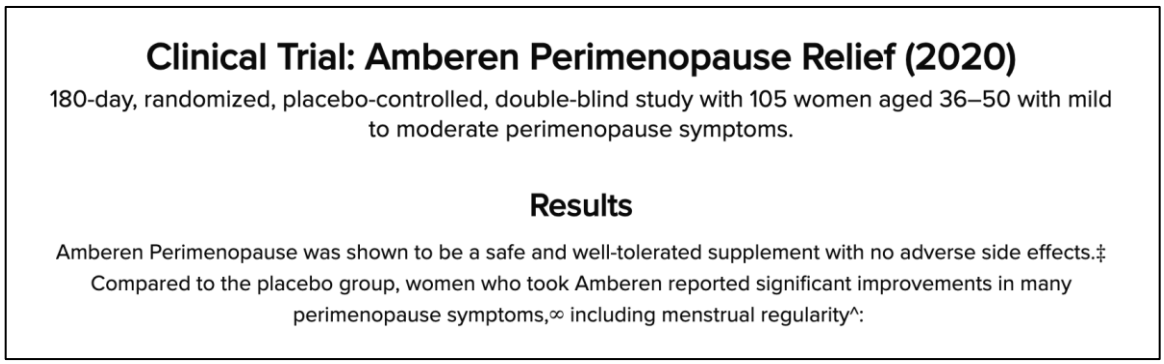
relieve 12 menopausal symptoms is its ability to "regulate" and "balance" hormones, the study only observed statistically significant changes in two of the four hormones measured (estradiol and leptin), and failed to establish that those changes caused any of the observed effects on menopausal symptoms. In fact, the study noted that "the mechanism of action of the [Amberen] regimen has not been entirely elucidated. Some may point to the observed increase in serum estradiol levels among [Amberen] users as the sole or major reason for the clinical benefits observed. However, it is important to recognize that the magnitude of increase in serum estradiol levels in this study is considerably less than that observed in conventional hormone therapy trials and that certain benefits, such as anxiety reduction, have not been historically associated with postmenopausal estrogen use. While the etiology of the observed increase in serum estradiol levels among [Amberen] users is not currently known, it is likely an indirect effect as the components of the [Amberen] regimen are not known to be involved in the hormone synthesis pathway."[22]

- **Biased researchers and company funding:** The study was funded by the manufacturer of Amberen at the time, and was conducted, in part, by a paid consultant for the company.

- **Study not accepted by The Menopause Society:** The Menopause Society (formerly The North American Menopause Society, or NAMS), the country's leading nonprofit organization comprised of nearly 3,000 members across different disciplines dedicated to promoting the health of menopausal women,[23] determined that this study was insufficient.[24] Specifically, The Menopause Society stated: "An ammonium succinate-based supplement (Amberen) was studied for the management of menopause symptoms in a manufacturer-sponsored clinical trial . . . Because of limited studies and the results being based on manufacturer-sponsored clinical trials, ammonium succinate is not recommended. (Level II; not recommended)."[25]

2020 Clinical Trial

The second clinical trial provided on the Amberen website is a 2020 clinical trial examining Amberen Perimenopause Relief.[26]



This study also contains numerous flaws that prevent it from properly substantiating Amberen's unqualified marketing claims, including but not limited to the following:

- **Inadequate and homogenous sampling:** The study sampling was small (only 105 participants completed the trial) and homogenous (all were white women or women of European descent, and all were 50 years of age or younger). Further, only perimenopausal women with mild to moderate symptoms were examined; menopausal/postmenopausal women and women with severe symptoms were not studied.

- **Short intervention period:** While the study included observations for 180 days, the treatment was only administered for 90 days. As the researchers noted in the 2016 study, described above, this short intervention study period does not provide information on the benefits of long-term use of Amberen products.

- **Hormones not impacted:** Despite a plethora of marketing claims regarding Amberen's effect on hormones, the study did not observe any statistically significant difference in hormones between the placebo group and the treatment group, and noted that "[i]t is still not clear what the exact mechanism of action for the [active ingredient] is."[27]

- **Study results based on self-reported symptoms:** Like the 2016 study, this study used subjective self-assessments to evaluated participants' menopause symptoms: the Greene Climacteric Scale, the State-Trait Anxiety Inventory, the Hospital Anxiety and Depression Scale, and the Well-being, Activity, and Mood test.

- **Biased researchers and company funding:** The study was funded by the manufacturer of Amberen at the time, and was conducted, in part, by a scientific advisor and a paid consultant for the company.

In short, neither of these studies properly substantiate claims that Amberen products can relieve the symptoms of perimenopause and menopause by balancing a women's hormones.

It is also incredibly problematic that the company, while featuring women of various races and ethnicities in its marketing campaign, as shown in the examples above, only studied white women (or women of European descent) in both of its clinical trials. The exclusion of all other races and ethnicities is troubling not only because the company's unqualified marketing for its "clinically proven"[28] supplements is directed at all women, but also because women of different races experience menopause differently.[29] For example, Black women can have more severe hot flashes and other hallmark menopause symptoms than white women.[30] And Black and Hispanic women generally reach menopause earlier than, and experience certain menopause symptoms almost twice as long as, Japanese, Chinese and white women.[31] And among Asian women, there are more than 30 different sub-ethnic groups that have variations in their menopausal symptom experiences.[32]

In addition to the two studies listed on the Amberen website, Defendants also reference – in connection with its Amberen Energy | Mood | Sleep Gummies, which contain 60mg of Pycnogenol – "a clinical study supporting the beneficial impact on energy, mood and sleep in perimenopausal and menopausal women."[33]

> **Ingredients**
> Amberen Energy | Mood | Sleep is formulated with Pycnogenol®, an extract of French Maritime Pine Bark with a clinical study supporting the beneficial impact on energy, mood and sleep in perimenopausal and menopausal women.* Pycnogenol® is a registered trademark of Horphag Research. Use of this product may be protected by one or more U.S. patents and other international patents.

While there are several serious issues with this study, the most problematic flaws are (1) the failure to include any menopausal women in the study (while Amberen markets the product to perimenopausal and menopausal women alike), and (2) the pronounced placebo effect observed, resulting in both the treatment group *and* the placebo group experiencing significant improvement in vasomotor symptoms, sleep problems and tiredness after 12 weeks.[34]

In short, eight years after the FTC's Order, Amberen still does not have the necessary substantiation for its menopause health claims.

C. Conclusion

It is estimated that women spend over $10 billion annually on nonmedical treatments for their menopause symptoms.[35] Defendants are not only capitalizing on this susceptible population, but turning a blind eye to the FTC's authority and Order in the process. As FTC Commissioner Slaughter once stated, "if we're not following up on our orders, then why have them in the first place."[36] It appears that the Defendants have been violating the FTC Order from the moment it was executed. As such, TINA.org urges the FTC to reopen its Amberen investigation and take appropriate enforcement action.

Sincerely,

Laura Smith, Esq.
Legal Director
Truth in Advertising, Inc.

Bonnie Patten, Esq.
Executive Director
Truth in Advertising, Inc.

Cc via email: Chris Chrysanthou, Group General Counsel, Alliance Pharmaceuticals
Ann Oxenham, U.S. Food and Drug Administration
Cara Welch, U.S. Food and Drug Administration

[1] Stipulated Order for Permanent Injunction and Monetary Judgment Against All Defendants, *Fed.Trade Comm'n v. Lunada Biomedical, Inc.*, No. 2:15-cv-03380 (C.D. Cal. May 25, 2016), ECF No. 99, https://www.ftc.gov/system/files/documents/cases/160525lunadastip.pdf.

[2] While TINA.org understands and appreciates that individuals who do not identify as women may also experience menopause, the term women is used to reflect the marketing at issue.

[3] Stipulated Order, *supra* note 1, at para 1.

[4] After the Order was entered, Lunada Biomedical, Inc. changed its name to Biogix. *See* Viktor E. Radzinsky et al., *Succinate-Based Dietary Supplement for Menopausal Symptoms: A Pooled Analysis of Two Identical Randomized, Double-Blind, Placebo-Controlled Clinical Trials,* 2019 Obstetrics and Gynecology Int'l 1, 8 (2019), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6875258/pdf/OGI2019-1572196.pdf ("Biogix, Inc. is the manufacturer of Amberen"); Anna Skylar, LinkedIn, https://www.linkedin.com/in/anna-skylar-0844b520/ ("Biogix, Inc. (formerly Lunada Biomedical)"). Biogix was then acquired in 2020 by Alliance Pharmaceuticals, the current owner of the Amberen brand. Alliance Pharma, Acquisition of Biogix Inc. (Dec. 20, 2019), https://www.alliancepharmaceuticals.com/investors/investor-news/latest-updates/2020/acquisition-of-biogix-inc/ ("Alliance Pharma plc…, the international healthcare group, is pleased to announce that it has today completed the acquisition of 100% of the share capital of Biogix Inc…, a privately held, US-based consumer healthcare company, for a total consideration of US$110.0 million … paid for in cash from the Group's existing financial resources.")

[5] Stipulated Order, *supra* note 1, at 6-7.

At the time of the FTC's action, Defendants sold one Amberen menopause product (Amberen Menopause Relief, which contained the same active ingredients as today's Amberen Advanced Menopause Relief products), two weight-loss products and a vein health product.
Amberen Menopause Relief, http://www.amberen.com/amberen-menopause-relief/ [https://web.archive.org/web/20150515061814/http://www.amberen.com/amberen-menopause-relief/]; Amberen, http://www.amberen.com/ [https://web.archive.org/web/20150314232937/http://www.amberen.com/]; Amberen Menopause Relief Ingredients, http://www.amberen.com/ingredients-amberen-menopause-relief [https://web.archive.org/web/20150512212617/http://www.amberen.com/ingredients-amberen-menopause-relief].

In addition, the scientific evidence relied upon by Defendants at the time of the FTC's action included a 2001clinical trial conducted in Russia (referred to as the "2001 Russian Study" in the FTC's action), a 2012 clinical trial conducted in Los Angeles (referred to as the "Medicus Study" in the FTC's action), observational studies conducted in Russia in 2001-2004, a 2015 clinical trial commissioned by Lunada's Russian supplier in 2015, and a 2015 clinical trial advisory paper. *See*
First Amended Complaint for Permanent Injunction and Other Equitable Relief, *Fed. Trade Comm'n v. Lunada Biomedical, Inc.*, No. 2:15-cv-03380 (C.D. Cal. Dec. 2, 2015), https://www.ftc.gov/system/files/documents/cases/151202lunadacmpt.pdf; Defendants' Opposition to Plaintiff's Motion for Leave to File a First Amended Complaint for Permanent Injunction and Other Equitable Relief, *Fed. Trade Comm'n v. Lunada Biomedical, Inc.*, 2:15-cv-03380 (C.D. Cal. Nov. 9, 2015); Defendants' Notice of Motion and Motion to Dismiss or, in the Alternative, for Partial Summary Judgment, *Fed. Trade Comm'n v. Lunada Biomedical, Inc.*, No. 2:15-cv-03380 (C.D. Cal. Dec. 21, 2015).

[6] List of April 2023 Recipients of the FTC's Notice of Penalty Offenses Concerning Substantiation of Product Claims, https://www.ftc.gov/system/files/ftc_gov/pdf/Published-list-Recipients.pdf.

[7] Alliance Pharmaceuticals Ltd. Case #7209 (Nat'l Advert. Div. Apr. 24, 2023).

Of note, this was not the first time Amberen was the subject of self-regulatory action. In 2010, the Electronic Retailing Self-Regulation Program (ERSP) recommended that certain marketing claims for the product be discontinued, including weight-loss claims. Press Release, Elec. Retailing Self-Regul. Program, Lunada Biomedical Participates in ERSP Forum (Apr. 12, 2010); Lunada Biomedical Amberen Dietary Supplement Case #239 (Nat'l Advert. Div. Apr. 2, 2010).

In 2012, NAD investigated a challenge by the Council for Responsible Nutrition (CRN) regarding the marketing for Amberen and recommended that Lunada Biomedical modify or discontinue a number of advertising claims, including claims that Amberen is an "all in one solution" and that Amberen can achieve "balanced production and circulation of hormones throughout your body." Press Release, Nat'l Advert. Div., NAD Recommends Lunada Discontinue Certain Claims for 'Amberen,' Marketed to Menopausal Women (June 6, 2012); Lunada Biomedical, Inc. Amberen Case #5466 (Nat'l Advert. Div. May 24, 2012).

In 2013, ERSP reinvestigated the marketing for Amberen. During the pendency of the inquiry, it was reported that Lunada voluntarily discontinued all of the consumer testimonials at issue regarding weight loss and also had voluntarily modified the claim that "Amberen is the only product clinically proven to promote weight loss during menopause without additional exercise or restrictive dieting." ERSP also determined that claims that Amberen balances hormones and relieves night sweats and moodiness should be discontinued or modified. Lunada Biomedical disagreed with the recommendation but said it would "take into consideration ERSP recommendations" in future advertising. Lunada Biomedical Amberen Dietary Supplement Case #309 (Nat'l Advert. Div. Feb. 14, 2013).

[8] Amberen Advanced Menopause Relief Capsules, https://amberen.com/products/amberen-menopause-1-month-supply; Amberen Advanced Perimenopause Relief Capsules, https://amberen.com/products/amberen-advanced-perimenopause-relief-capsules; Amberen, https://amberen.com/; Amberen Hot Flashes Collection, https://amberen.com/collections/hot-flashes; Amberen Mood Swings Collection, https://amberen.com/collections/mood-swings; Amberen Difficulty Concentrating Collection, https://amberen.com/collections/difficulty-concentrating; Amberen Anxiety/Stress Collection, https://amberen.com/collections/anxiety-stress.

[9] Amberen TV Spot, 'Number One Menopause Supplement,' https://www.ispot.tv/ad/2cGS/amberen-number-one-menopause-supplement.

[10] Amberen (@amberen_official), Instagram (Nov. 12, 2023), https://www.instagram.com/p/Czj44kyune_/; Amberen, Facebook Reels, https://www.facebook.com/reel/261207766402512; Amberen, Facebook (Apr. 12, 2024), https://www.facebook.com/photo/?fbid=820494886781761&set=pb.100064637713810.-2207520000; Amberen, Facebook (Sept. 18, 2022), https://www.facebook.com/photo/?fbid=5324330977662008&set=a.165419280219896; Amberen, Facebook (Apr. 2021), https://www.facebook.com/photo/?fbid=3789130151182106&set=a.165419280219896.

[11] @madukessharon, Instagram (Dec. 28, 2022), https://www.instagram.com/p/CmuXiPIqcqY/.

[12] Amberen Clinical Research, https://amberen.com/collections/clinical-research.

[13] *Id.*

The 2016 clinical trial referenced on the Amberen website is actually a compilation of two separate but effectively identical studies. Viktor E. Radzinsky et al., *Succinate-Based Dietary Supplement for Menopausal Symptoms: A Pooled Analysis of Two Identical Randomized, Double-Blind, Placebo-Controlled Clinical Trials*, 2019 Obstetrics and Gynecology Int'l 1, 1 (2019), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6875258/pdf/OGI2019-1572196.pdf ("Raw data were pooled from two identical randomized, multicenter, double-blinded, placebo-controlled, 90-day clinical trials."). *See also* Kuznetsova I.V. et al., *Efficiency of Alternative Therapy in Perimenopausal and*

Postmenopausal Women, Obstetrics and Gynecology (Moscow) (2016), https://en.aig-journal.ru/articles/Effektivnost-alternativnoi-terapii-u-jenshin-v-perimenopauze-i-postmenopauze.html; V. E. Radzinskii et al., *Treatment of Climacteric Symptoms with an Ammonium Succinate-Based Dietary Supplement: A Randomized, Double-Blind, Placebo-Controlled Trial*, 32 Gynecological Endocrinology 64 (2016), https://www.tandfonline.com/doi/full/10.1080/09513590.2016.1232686.

Of note, while the Amberen website only describes two clinical trials on its Clinical Research webpage, the company references – in certain places – "5 clinical trials." *See, e.g.,* Amberen Science Collection, https://amberen.com/collections/science. As noted above, the 2016 clinical trial cited is actually a compilation of two separate trials. In addition, Amberen relied on at least two clinical trials at the time of the FTC's action, both of which the Commission rejected. *See* supra fn. 5.

[14] Radzinsky, *supra* note 4, at 8.

[15] *Id*. at 8.

[16] *Id.* at 3 ("For some parameters, statistically significant differences were found at baseline between the SBDS and placebo groups (Greene questions 3, 9, 15, 19, and 21; trait and actual anxiety; estradiol).")

[17] The N. Am. Menopause Soc'y, *NAMS Position Statement*, 30 Menopause 573, 574 (2023), https://www.menopause.org/docs/default-source/professional/2023-nonhormone-therapy-position-statement.pdf ("Individual panel members reviewed and evaluated the evidence on the different therapies for which they had special expertise, with the knowledge that trials of nonhormone treatments of VMS have a placebo improvement rate of 20% to 66%, and women with more anxiety show higher response to placebo.").

[18] Margaret Diana van Die et al., *Predictors of Placebo Response in a Randomized, Controlled Trial of Phytotherapy in Menopause*, 16 Menopause 792 (2009), https://pubmed.ncbi.nlm.nih.gov/19587583/ ("The magnitude of the placebo response is found to be partly dependent on the condition, with depression, anxiety, and pain found to be particularly susceptible to the placebo effect. In studies of antidepressant medications, placebo response rates average approximately 30%, ranging from 12% to more than 50%, and have been observed to be on the increase. In RCTs of hormone therapy for vasomotor symptoms in menopause, the placebo response rate averages 51%."); Ellen W. Freeman et al., *Placebo Improvement in Pharmacologic Treatment of Menopausal Hot Flashes: Time Course, Duration, and Predictors*, 77 Psychosom Med. 167 (2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4333078/pdf/nihms644591.pdf ("Placebo effects are expected in hot flash treatment. A Cochrane review of 9 placebo-controlled trials of oral estrogen therapy for menopausal hot flashes clearly indicated the efficacy of hormone therapy but also showed that those with placebo treatment had a mean reduction of 58% in hot flash frequency. A pooled analysis of 10 clinical trials of non-hormonal pharmacologic therapies for menopausal hot flashes showed that responses to placebo ranged from 27% to 52%"); Shelby Cefaratti-Bertin, *Magnitude of Placebo Response Identified in Drug for Treatment of Hot Flashes*, Baylor U., Aug. 28, 2023, https://news.web.baylor.edu/news/story/2023/magnitude-placebo-response-identified-drug-treatment-hot-flashes ("The results demonstrated that the placebo response accounted for the majority of treatment responses for reductions in both hot flash frequency and severity: •79% of the mean treatment response for hot flash frequency is accounted for by a placebo response, resulting in a mean true drug effect of 21% at most. • Additionally, 68% of the mean treatment response for hot flash severity is accounted for by a placebo response, resulting in a maximum true drug effect of 32%.").

[19] Jean Hailes For Women's Health Menopause Symptom Greene Climacteric Scale, https://www.jeanhailes.org.au/uploads/Health-professionals/Menopause_symptom_scale_Greene_Climacteric.pdf; State Trait Anxiety Inventory, https://www.advancedassessments.co.uk/resources/Mental-Health-Test.pdf.

[20] Alaa Althubaiti, *Information Bias in Health Research: Definition, Pitfalls, and Adjustment Methods*, 9 J. Multidisciplinary Healthcare 211, 212-4 (2016),

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4862344/; Pauline M. Maki & Rebecca C. Thurston, *Menopause and Brain Health: Hormonal Changes Are Only Part of the Story*, 11 Frontiers in Neurology 1, 3 (2020), https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2020.562275/full.

[21] Radzinsky *supra* note 4.

[22] *Id.* It is also important to note that while Amberen is marketed to all women, the study cautioned that "women who should not use estrogen (e.g., with history of estrogen-positive breast cancer) may not wish to use the [Amberen] regimen for the relief of menopausal symptoms." This fact is not disclosed in any of the Amberen marketing materials reviewed by TINA.org.

[23] The Menopause Society: About Us, https://www.menopause.org/About-NAMS.

[24] The N. Am. Menopause Soc'y, *NAMS Position Statement*, 30 Menopause 573 (2023), https://www.menopause.org/docs/default-source/professional/2023-nonhormone-therapy-position-statement.pdf.

[25] *Id.*

[26] Amberen Clinical Research, https://amberen.com/collections/clinical-research; Vera A. Kachko et al., *Clinical Evaluation of Effectiveness and Safety of Combined Use of Dietary Supplement Amberen® and Smart B® in Women with Climacteric Syndrome in Perimenopause*, 41 Advances in Therapy 3183 (2024), https://pubmed.ncbi.nlm.nih.gov/38904899/.

[27] *Id.*

[28] Amberen, Facebook (Dec. 5, 2023), https://www.facebook.com/photo/?fbid=741901691307748&set=pb.100064637713810.-2207520000; Amberen Advanced Menopause Relief Capsules, https://amberen.com/products/amberen-menopause-1-month-supply; Amberen Advanced Perimenopause Relief Capsules, https://amberen.com/products/amberen-advanced-perimenopause-relief-capsules.

[29] Alisha Haridasani Gupta, *How Menopause Affects Women of Color*, N.Y. Times, Aug. 23, 2023 (updated Sept. 4, 2023), https://www.nytimes.com/2023/08/23/well/live/menopause-symptoms-women-of-color.html#:~:text=But%20researchers%20have%20found%20that,and%20anxiety%20than%20hot%20flashes.

[30] *See, e.g.,* The Menopause Society, Race Matters When Prescribing Hormone Therapy for Menopausal Women, Sept. 27, 2023, https://menopause.org/wp-content/uploads/press-release/racial-disparities-among-menopausal-women-with-psychiatric-conditions.pdf; Alisha Haridasani Gupta, *Study Shows the Staggering Cost of Menopause for Women in the Work Force*, N.Y. Times, Apr. 28, 2023 (updated May 8, 2023), https://www.nytimes.com/2023/04/28/well/live/menopause-symptoms-work-women.html#:~:text=There%20are%2C%20according%20to%20U.S.,of%20the%20Mayo%20Clinic%20study ("Though a majority of survey participants were white, the researchers found that menopause can have a greater effect on Black and Hispanic working women, Dr. Kling said. "Black women tended to have more menopausal symptoms," she said. "And higher percentages of Black women and Hispanic women reported adverse work outcomes related to menopausal symptoms compared to white women."); Jeane Ann Grisso et al., *Racial Differences in Menopause Information and the Experience of Hot Flashes*, 14 J. Gen. Internal Med. 98, 98 (2008), https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1525-1497.1999.tb00004.x?sid=nlm – ("African-American women (53%) were more likely than white American women (29%) to have experienced hot flashes ($p < .001$)."); Ellen B. Gold et al., *Longitudinal Analysis of the Association Between Vasomotor Symptoms and Race/Ethnicity Across the Menopausal Transition: Study of Women's Health Across the Nation*, 96 Am. J. Pub. Health 1226, 1230 (2006), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1483882/ ("Compared with White women, significantly

more African American women and fewer (although not significantly fewer) women from the other 3 racial/ethnic groups reported vasomotor symptoms."); What to Know About Racial Disparities in Menopause, https://www.healthline.com/health/menopause/racial-disparities#symptoms ("Research suggests that Black women are more likely than white women to experience bothersome VMS such as hot flashes. Studies have found that approximately half of Black women have VMS during perimenopause, compared with one-third of white women. These symptoms are also more likely to be more bothersome and last longer for Black women than for white women. Compared with white women, Black women are also more likely to experience sleep disturbances such as insomnia during the menopausal transition and may have more trouble staying asleep at night.")

[31] *See* Gupta, *supra* note 30; Ellen B. Gold et al., *Factors Associated with Age at Natural Menopause in a Multiethnic Sample of Midlife Women*, 153 Am. J. Epidemiology 865 (2001), https://academic.oup.com/aje/article/153/9/865/124589?login=false; Pangaja Paramsothy et al., *Duration of the Menopausal Transition is Longer in Women with Young Age at Onset: The Multi-Ethnic Study of Women's Health Across the Nation*, 24 Menopause 142 (2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5266650/; Chihiro Ishikawa et al., A*sia's Menopause Challenge: The Economic Case for Better Female Health*, Nikkei Asia, Mar. 6, 2024, https://asia.nikkei.com/Spotlight/The-Big-Story/Asia-s-menopause-challenge-The-economic-case-for-better-female-health.

[32] Eun-Ok Im et al., *Sub-Ethnic Differences in the Menopausal Symptom Experience: Asian American Midlife Women*, 21 J. Transcultural Nursing 123 (2010), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2838208/.

[33] Amberen Energy Mood Sleep Gummies, https://amberen.com/products/amberen-energy-mood-sleep-gummies.

The same webpage states, at the very bottom, "Clinical studies show[ing] that 60mg of Pycnogenol® helps relieve low energy, mood swings, occasional sleeplessness, together with hot flashes and night sweats for perimenopausal women." Defendants do not link to or otherwise provide these purported studies but TINA.org's research indicates that there are two studies that examined the impact of 60 mg of Pycnogenol on women's health, only one of which examined perimenopausal women. *See* Franziska Weichmann & Peter Rohdewald, *Pycnogenol® French Maritime Pine Bark Extract in Randomized, Double-Blind, Placebo-Controlled Human Clinical Studies*, Frontiers Nutrition (2024), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11096518/; Nobutaka Suzuki et al., *French Maritime Pine Bark Extract Significantly Lowers the Requirement for Analgesic Medication in Dysmenorrhea: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study*, 53 J. Reprod. Med. 338 (2008), https://pubmed.ncbi.nlm.nih.gov/18567279/ https://pubmed.ncbi.nlm.nih.gov/18567279/; Takafumi Kohama & Masako Negami, *Effect of Low-Dose French Maritime Pine Bark Extract on Climacteric Syndrome in 170 Perimenopausal Women: A Randomized, Double-Blind, Placebo-Controlled Trial*, 58 J. Reprod. Med. 39 (2013), https://pubmed.ncbi.nlm.nih.gov/23447917/.

[34] In addition to its failure to include menopausal women and the pronounced placebo effect observed, the study also used capsules rather than gummies, and used subjective self-assessments to evaluate participants' symptoms. Takafumi Kohama & Masako Negami, *Effect of Low-Dose French Maritime Pine Bark Extract on Climacteric Syndrome in 170 Perimenopausal Women: A Randomized, Double-Blind, Placebo-Controlled Trial*, 58 J. Reprod. Med. 39 (2013), https://pubmed.ncbi.nlm.nih.gov/23447917/.

[35] Jennifer Sauer et al., *The Economic Impact of Menopause: A Survey of Women 35+ and Employers*, AARP Research (Jan. 2024), https://www.aarp.org/pri/topics/work-finances-retirement/employers-workforce/menopause-workplace/.

[36] *Strengthening the Federal Trade Commission's Authority to Protect Consumers*, *Hearing Before Senate Comm. on Com., Sci., and Transp.*, 117th Congress, at 1:58:12 (Apr. 20, 2021),

https://www.commerce.senate.gov/2021/4/strengthening-the-federal-trade-commission-s-authority-to-protect-consumers.