IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

OREXIGEN THERAPEUTICS, INC., Plaintiff, v. ACTAVIS LABORATORIES FL, INC. Defendant.	Civil Action No. 15-451-RGA

TRIAL OPINION

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ANDREWS, U.S. DISTRICT JUDGE:

Plaintiff brought this patent infringement action on June 3, 2015, alleging that Defendant had infringed seven of Plaintiff's patents by filing Abbreviated New Drug Application ("ANDA") No. 208043 seeking to enter the market with a generic version of Plaintiff's Contrave product. (D.I. 1). On April 15, 2016, Plaintiff filed a First Amended Complaint alleging infringement of four patents. (D.I. 47). Prior to trial, Plaintiff withdrew one of the four patents (*see* D.I. 182), leaving three patents-in-suit: U.S. Patent Nos. 7,462,626 ("the '626 patent"), 7,375,111 ("the '111 patent"), and 8,916,195 ("the '195 patent"). The Court held a three day bench trial on June 5-7, 2017. (D.I. 178, 179, 180) ("Tr.").

Plaintiff's Contrave product is approved by the Food and Drug Administration ("FDA") for "chronic weight management in adults" who are obese or overweight and who have "at least one weight-related comorbidity," such as type 2 diabetes or hypertension. (D.I. 117-1 at 5, ¶ 4). Contrave is formulated as extended-release tablets with the active ingredients naltrexone hydrochloride and bupropion hydrochloride. (*Id.*, ¶ 3).

Bupropion was first approved by the FDA in 1996 for use as an antidepressant and in 1997 for use in smoking cessation treatment. (Tr. 422:11-13). Bupropion was known to have weight loss effects as early as 1995. (Tr. 422:18-424:11). The efficacy and safety of bupropion for weight loss had been studied extensively prior to 2003, the priority date for the invention claimed in the patents-in-suit. (Tr. 425:10-431:23). Naltrexone is an opioid agonist that is FDA approved for treating drug addiction. (Tr. 432:112-433:10). At least as early as 2002, naltrexone was known to reduce carbohydrate cravings in patients with diabetes. (Tr. 433:21-434:19).

The '626 patent is directed to methods of treating overweight or obesity using a combination of naltrexone and bupropion. Plaintiff asserts that Defendant induces infringement

of dependent claims 2, 15, 26, and 31 of the '626 patent. Claims 2 and 15 depend from independent claim 1, which reads:

> 1. A method of treating overweight or obesity, comprising diagnosing an individual as suffering from overweight or obesity by determining said individual has a body mass index of at least 25 kg/m2, and treating said overweight or obesity by administering to said individual a first compound and a second compound in order to treat said overweight or obesity, wherein said second compound is bupropion or a pharmaceutically acceptable salt thereof in an amount effective to induce weight loss in said individual, and said first compound is naltrexone or a pharmaceutically acceptable salt thereof in an amount effective to enhance weight loss activity of said bupropion or a pharmaceutically acceptable salt thereof.

('626 patent, claim 1). Dependent claim 2 adds the limitation that the naltrexone and bupropion "are administered together." Dependent claim 15 adds the limitation that the naltrexone and bupropion "are administered in a single oral dosage form."

Claim 26 depends from independent claim 25, which reads:

> 25. A method of treating overweight or obesity, comprising administering a weight loss effective amount of a first and second compound to an individual who has been diagnosed as suffering from overweight or obesity in order to treat said overweight or obesity, wherein said first compound is bupropion, or a pharmaceutically acceptable salt thereof, and said second compound is naltrexone, or a pharmaceutically acceptable salt thereof, and wherein the weight loss activity of said first and second compounds is enhanced compared to the administration of the same amount of either compound alone.

('626 patent, claim 25). Claim 26 adds the limitation that the naltrexone and bupropion "are administered together." Asserted claim 31 depends from claim 30, which is not asserted and which depends from claim 25. Claim 30 adds the limitation that the naltrexone and bupropion "are in a sustained-release formulation." Asserted claim 31 adds the limitation that the naltrexone and bupropion "are administered in a single oral dosage form."

The '111 patent is directed to compositions for use in weight loss treatments comprising a combination of sustained release formulations of bupropion and naltrexone. Plaintiff asserts that Defendant directly infringes claim 1 of the '111 patent. Claim 1 reads:

> 1. A composition for affecting weight loss comprising:
> (a) a sustained release formulation of bupropion or a pharmaceutically acceptable salt thereof in an amount effective to induce weight loss in an individual; and
> (b) a sustained release formulation of naltrexone or a pharmaceutically acceptable salt thereof in an amount effective to enhance the weight loss effect of the bupropion or salt thereof;
> wherein said composition is in a single oral dosage form fixed combination.

('111 patent, claim1).

The '195 patent is directed to methods of treating overweight or obesity using a combination of naltrexone and bupropion. Plaintiff asserts that Defendant directly infringes claim 11 of the '195 patent. Claim 11 reads:

> 11. A method of treating overweight or obesity having reduced adverse effects comprising orally administering daily about 32 mg of naltrexone and about 360 mg of bupropion, or pharmaceutically acceptable salts thereof, to a person in need thereof, wherein the bupropion or pharmaceutically acceptable salt thereof is administered as a sustained-release formulation, wherein the naltrexone or pharmaceutically acceptable salt thereof is administered as a sustained-release formulation, and wherein said sustained-release formulation of naltrexone has an in vitro naltrexone dissolution profile in a dissolution test of USP Apparatus 2 Paddle Method at 100 rpm in a dissolution medium of water at 37° C. of:
> a) between 39% and 70% of naltrexone released in one hour;
> b) between 62% and 90% of naltrexone released in two hours; and
> c) at least 99% in 8 hours;
> wherein about 16 mg of said sustained-release formulation of naltrexone or a pharmaceutically acceptable salt thereof is administered twice daily, and about 180 mg of said sustained-release formulation of bupropion or a pharmaceutically acceptable salt thereof is administered twice daily.

('195 patent, claim 11).

Defendant contends that it does not infringe any of the asserted claims. Defendant also argues that claim 11 of the '195 patent is invalid for lack of written description and all asserted claims of the '111 and '626 patents are invalid as obvious in view of the prior art.

I. MOTION TO STRIKE THE GADDE FAX

Plaintiff moves to strike Defendant's exhibits DTX-48 and DTX-180, a fax sent by Dr. Kishore Gadde to Orexigen on November 19, 2003 ("Gadde Fax" or "Fax"), as inadmissible hearsay. (D.I. 155 at 2). The Fax consists of a table which contains brief descriptions of patients Dr. Gadde treated for obesity in 1997 and 2000. (DTX-180 at GADDE0000010). According to the table, Dr. Gadde treated four patients in 1997 with a combination of fluoxetine and naltrexone and two patients in 2000 with a combination of bupropion and naltrexone. (*Id.*). Dr. Gadde testified at trial that he prepared the table in 2003 "by reviewing the patient charts." (Tr. 715:16-18, 768:19-21). The original patient charts were not produced as evidence in this case. (D.I. 155 at 3).

Defendant argues that the Gadde Fax is not hearsay because it qualifies as an adoptive admission under Federal Rule of Evidence 801(d)(2)(B).[1] (D.I. 159 at 2; Tr. 722:10-12). According to Defendant, Plaintiff shared the data in the Gadde Fax with the FDA to help demonstrate safety and efficacy of the combination of bupropion and naltrexone. (D.I. 159 at 2; Tr. 722:12-19). As support for this contention, Defendant produced a clinical study report submitted to the FDA as part of Orexigen's Investigational New Drug ("IND") Application for fluoxetine or bupropion SR in combination with naltrexone. (DTX-154). In relevant part, the

[1] In post-trial briefing, Defendant also argued that the Gadde Fax is admissible under Rule 801(d)(1)(B). (D.I. 159 at 6-7). This argument fails at least because Defendant seeks to admit the Gadde Fax itself as substantive evidence, rather than seeking to admit the Fax as a prior statement consistent with Dr. Gadde's testimony in court. Dr. Gadde testified that he had no contemporaneous recollection of the facts of the cases reported on in the Fax. (Tr. 789:6-14). In fact, Dr. Gadde testified directly from the Fax rather than from his independent recollection of the facts and events. (Tr. 715:16-719:10). Defendant cannot invoke Rule 801(d)(1)(B) to gain admission of a prior statement that is not actually offered as a prior consistent statement to in-court testimony.

report stated, "When naltrexone was added to fluoxetine or bupropion SR therapy, additional weight loss was observed in 2 of 6 patients; no adverse events other than nausea were reported (K Gadde, personal communication)." (DTX-154 at OREXC0748915).

During trial I found the Gadde Fax to be admissible as an adoptive admission, but allowed the parties to present additional arguments about its admissibility in post-trial briefing. (Tr. 731:1-4). I found that, while "not an absolute certainty," it was "a fair inference" that the paragraph Defendant pointed to was referring to the chart in the Gadde Fax. (Tr. 730:11-14). I also stated that it seemed clear that the paragraph's reference to additional weight loss referred to patients 2 and 3 on the fax, which are patients who received the fluoxetine/naltrexone combination therapy. (Tr. 728:15-729:2).

My opinion that the Gadde Fax is admissible as an adoptive admission has not changed. I think there is sufficient detail in the FDA report to support the inference that the "personal communication" referred to was the Fax. I disagree with Plaintiff's contention that this paragraph was merely a reference to the Fax and a repetition of the hearsay contained in the Fax. (D.I. 155 at 5-6). Orexigen presented this information to the FDA in support of its IND Application. I find it difficult to believe Orexigen would have done so if it did not believe in the trustworthiness of the contents of the communication. As to Plaintiff's argument that Defendant must show that each statement in the Fax was separately adopted (D.I. 155 at 7), I think this is satisfied by the statement that "additional weight loss was observed in 2 of 6 patients." It seems to me that this refers to the six patients reported in the Fax and I think the only reasonable interpretation is that the Fax was adopted in its entirety.

This does not mean, however, that the Gadde Fax is admissible as substantive evidence of anything that Dr. Gadde did in 1997 or 2000. The parties agreed that any allegations of public

use by Dr. Gadde in 2000 would be subject to the corroboration requirement for inventor testimony. (Tr. 950:17-23). Defendant stated at trial that the purpose of Dr. Gadde's testimony and the Gadde Fax was not to prove prior use, but to prove secondary considerations, such as motivation to combine. (Tr. 951:13-17). Defendant argued that motivation to combine was not subject to the corroboration requirement. (Tr. 954:17-955:5). As I discuss below, I disagree. The Gadde Fax is not admissible to show that Dr. Gadde treated patients with the combinations of drugs reported in the Fax in 1997 and 2000, or as evidence of anything that occurred prior to the date the Fax was prepared.

For the foregoing reasons, Plaintiff's Motion to Strike (D.I. 155) is denied. The Gadde Fax is admissible for the limited purpose of showing that Dr. Gadde shared the data reported in the Fax with Orexigen in 2003.

II. WRITTEN DESCRIPTION

The written description requirement contained in 35 U.S.C. § 112, ¶ 1 requires that the specification "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharm., Inc., v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (alteration in original). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "A party must prove invalidity for lack of written description by clear and convincing evidence." *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 682 (Fed. Cir. 2015).

Defendant argues that claim 11 of the '195 patent is invalid for lack of written description because the ranges given for the claimed dissolution profile "were improperly cobbled together" and were measured using a different method than that required by the claim. (D.I. 162 at 10).

Specifically, Defendant argues that the lower bounds of the dissolution ranges at one and two hours recited in the claim were not obtained using the USP Apparatus 2 Paddle Method required by the claim. (*Id.* at 10). Defendant further argues that there is no evidence in the specification as to which method was used to obtain the 99% dissolution profile stated in the claim for the eight hour range. (*Id.*). Finally, Defendant argues that the upper bounds of the one and two hour ranges were picked from "a boilerplate paragraph without any sensible reason or industry custom/practice for their random selection." (*Id.*).

Plaintiff responds that simply because the claims draw support from different parts of the specification does not mean that a person of ordinary skill would not believe that the inventor was in possession of the invention. (D.I. 164 at 30). Plaintiff also argues that there is no legal requirement that all claim limitations be set out in a single place in the specification. (*Id.* at 31). Plaintiff points to the prosecution history, which shows the applicant cited to specific portions of the specification as support for claim 11, resulting in a notice of allowance for this claim. (*Id.*).

Claim 11 of the '195 patent claims a method of treating overweight or obesity using a sustained released formulation of bupropion and naltrexone. Claim 11 includes the limitation that the naltrexone have a specific dissolution profile measured "in a dissolution test of USP Apparatus 2 Paddle Method at 100 rpm in a dissolution medium of water at 37°C." The dissolution profile recited requires "a) between 39% and 70% of naltrexone released in one hour; b) between 62% and 90% of naltrexone released in two hours; and c) at least 99% in 8 hours."

As support for the claimed dissolution profile, Plaintiff points to Table 10 in the specification. (*Id.* at 32). Table 10 provides dissolution data for naltrexone in one embodiment described in the specification. ('195 patent at 19:60-67). Table 10 indicates that, after one hour, 67% of naltrexone was released, after two hours, 85% of naltrexone was released, and after 8

hours, 99% of naltrexone was released. ('195 patent at 20:1-10). These values fall squarely within the ranges in claim 11. Defendant argues that this data is not relevant as it was not obtained using the USP Apparatus 2 method. (D.I. 162 at 11). In response, Plaintiff points to a portion of the specification that it argues constitutes a definition of a "standard dissolution test." (D.I. 164 at 32; '195 patent at 6:49:55).

I agree with Plaintiff that the specification would indicate to a person of ordinary skill that all of the dissolution data reported in the patent was obtained "using Apparatus 2 . . . at a spindle rotation speed of 100 rpm and a dissolution medium of water, at 37° C., or other test conditions substantially equivalent thereto." ('195 patent at 6:52-55). Plaintiff's expert, Dr. Treacy, testified that a person of ordinary skill would recognize that the inventors had possession of an embodiment representative of the invention, as described in Table 10. (Tr. 660:21-661:1). Dr. Treacy further testified that a person of ordinary skill "would find reasonable support for the claim limitations in the written description," specifically the upper and lower limits for each of the ranges. (Tr. 660:12-20). Dr. Treacy also opined that, in the context of the patent, a person of ordinary skill would understand that the inventors had possession of the claimed invention regardless of whether the USP Apparatus 2 method or a "substantially equivalent" method were used. (Tr. 663:3-9).

Defendant's expert, Dr. Mayersohn, testified at trial that the paddle method and the USP Apparatus 1 basket method were different in that the hydrodynamics were different and that a person of ordinary skill would expect the two methods to yield different results. (Tr. 602:23-604:20). Dr. Mayersohn did not, however, perform any actual tests on the tablets claimed in this patent. (Tr. 640:19-22). Furthermore, in his expert report, Dr. Mayersohn provided an opinion on obviousness for this claim in which he relied on a prior art reference that used the USP

Apparatus 1 basket method. (Tr. 637:8-640:13). It seems to me that Dr. Mayersohn's theoretical opinion that the methods would yield different results is at odds with his reliance on a prior art reference using the basket method to argue that claim 11, which specifies the paddle method, was obvious.

I do not think it matters whether the two methods would yield exactly the same results. I find credible Dr. Treacy's testimony that a person of ordinary skill would understand, in the context of the patent, that the inventors possessed the claimed invention. The embodiments disclosed in a patent are intended to be exemplary and it is clear to me that the inventors possessed at least one embodiment that falls squarely within the claimed ranges, as evidenced by Table 10. Furthermore, Defendant's emphasis on the purported differences between the two methods of measuring dissolution profiles seems to me to be misplaced as even its own expert was willing to favorably compare the two methods when it was to Defendant's benefit to do so. Therefore, whether the dissolution data reported in the specification was obtained using the basket method or the paddle method is not relevant to whether the inventors had possession of the invention.

Defendant also argues that the lower bounds of the one and two hour ranges lack written description support because they were pulled from Table 5, which reports data on specific embodiments which includes different amounts of the polymer excipient hydroxypropylmethyl cellulose ("HPMC"). (D.I. 162 at 12). Defendant contends that the data from the 15% HPMC formulation was "randomly selected" and "improperly picked from amongst a plethora of other possible options." (*Id.* at 12-13). I disagree. As Plaintiff points out, claim 11 calls for a "sustained-release formulation." (D.I. 164 at 34). Both Dr. Mayersohn and Dr. Treacy testified that the data from the 5% and 10% HPMC formulations indicated that both were "essentially

immediate release" and the 15% formulation was "the first one . . . where you see a sustained release profile." (Tr. 615:6-19, 655:10-17). For this reason, it seems clear that these are appropriate data points to support the claimed lower bounds for the one and two hour ranges.

Dr. Mayersohn's main criticism of using the data in Table 5 was that there was no eight-hour value and, in his opinion, the data provided indicated that the dissolution profile would plateau and never reach the claimed 99% at eight hours. (Tr. 615:20-616:3). I am not convinced. There is no data provided at all in Table 5 for the dissolution at eight hours. I do not think there is sufficient evidence to support Dr. Mayersohn's plateau theory to a clear and convincing standard for invalidating this patent claim. In contrast, as Plaintiff notes, there is an embodiment reported in Table 10 that has a dissolution profile falling squarely within the claimed ranges. (D.I. 164 at 32).

Defendant also argues that the inventor did not possess the eight-hour limitation by attempting to characterize this limitation as a range, wherein "at least 99%" necessarily "extends up to and includes 100%." (D.I. 162 at 13). Defendant suggests that to show the inventor possessed the invention, Plaintiff must establish written description support "for the upper end of the claimed range above 99%." (*Id.* at 15). I disagree. Dr. Treacy opined that "at least 99%" would be understood by a person of ordinary skill to mean "essentially complete dissolution." (Tr. 653:5-12). I find this testimony credible. It seems clear to me that "at least 99%" means "at least 99%" rather than "between 99% and 100%." I think it is sufficient that the inventors showed possession by disclosing an embodiment that falls squarely within all of the claimed ranges, including "at least 99%" at eight hours.

Defendant also criticizes the upper bounds of the one and two hour ranges as lacking written description support because these bounds come from "a boilerplate paragraph containing

multiple theoretical ranges." (D.I. 162 at 14). As an initial matter, there is no definitive evidence that these ranges were "theoretical." More importantly, I see nothing odd or invalidating about the inventors looking to different tables of dissolution data and other places in the specification to determine the ranges for the claimed dissolution profile. A single test on a single tablet could provide only a single data point at each time; rather, multiple tests are necessarily required to establish a range.

Defendant suggests that all of the purported shortcomings it has identified in the disclosure of the claimed ranges necessarily lead to the conclusion that the patent fails to provide "blazemarks" that would direct a person of ordinary skill to select those specific bounds. (D.I. 162 at 15). The cases Defendant cites to support for this failure do not support its position. (*Id.* at 9). Most of Defendant's cases dealt with situations where an inventor had disclosed a large genus of possible compounds. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) ("simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-genuses"); *Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1367 (Fed. Cir. 2011) (finding lack of written description where patent claimed "rapamycin or a macrocyclic triene analog thereof" but specification "fail[ed] to disclose even a single member of either the genus of 'analogs' of rapamycin, or the more specific genus of 'macrocyclic triene analogs' of rapamycin"); *In re Ruschig*, 379 F.2d 990, 994 (C.C.P.A. 1967) (finding lack of written description where disclosure of genus encompassed "half million compounds within the scope of the broadest claim"). The instant case is not one of an inventor disclosing a large genus without any disclosure that certain of the species within the genus are preferred. I hold that Defendant has not proven by clear and convincing evidence that claim 11 of the '195 patent is invalid for lack of written description.

III. OBVIOUSNESS

Defendant argues that claims 26 and 31 of the '626 patent and claim 1 of the '111 patent are invalid as obvious over the prior art.[2] (D.I. 162 at 22, 27-28). Specifically, Defendant argues that a person of ordinary skill in the art would have been motivated to combine the teachings of the Jain and O'Malley references to administer the combination of naltrexone and bupropion for treating overweight and obesity with a reasonable expectation of success. (*Id.* at 28).

A. Legal Standard

A patent claim is invalid as obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103; *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406–07 (2007). The determination of obviousness is a question of law with underlying factual findings. *See Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1359-60 (Fed. Cir. 2012). "The underlying factual inquiries include (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art; and (4) any relevant secondary considerations . . . ." *Western Union Co. v. MoneyGram Payment Sys., Inc.*, 626 F.3d 1361, 1370 (Fed. Cir. 2010) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)).

A court is required to consider secondary considerations, or objective indicia of nonobviousness, before reaching an obviousness determination, as a "check against hindsight bias." *See In re Cyclobenzaprine Hydrochloride Extended–Release Capsule Patent Litig.*, 676

[2] As I discuss below, because I find that claims 26 and 31 of the '626 patent are valid and infringed, it is unnecessary for me to decide whether claims 2 and 15 are infringed. I find it equally unnecessary, therefore, to decide whether claims 2 and 15 are valid.

F.3d 1063, 1078-79 (Fed. Cir. 2012). Relevant secondary considerations include commercial success, long felt but unsolved needs, failure of others, praise, unexpected results, and copying, among others. *Graham*, 383 U.S. at 17-18; *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 662–63 (Fed. Cir. 2000); *Tex. Instruments, Inc. v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165, 1178 (Fed. Cir. 1993). Secondary considerations of nonobviousness are important because they "serve as insurance against the insidious attraction of the siren hindsight...." *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983).

A patentee is not required to present evidence of secondary considerations. *See Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092, 1101 (Fed. Cir. 2015). That said, if the patent challenger establishes a prima facie case of obviousness, "the patentee would be well advised to introduce evidence sufficient to rebut that of the challenger." *Id.* (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1360 (Fed. Cir. 2007)). There must be enough evidence, however, for a finding that a given secondary consideration exists by a preponderance of the evidence. *See Apple, Inc. v. Samsung Elec. Co., Ltd.*, 839 F.3d 1034, 1053 (Fed. Cir. 2016) (en banc). If there is, then the probative value of each secondary consideration will be considered in light of the evidence produced. That does not mean, though, that the burden of persuasion on the ultimate question of obviousness transfers to the proponent of the secondary consideration. *Pfizer, Inc.*, 480 F.3d at 1359. That burden stays always with the patent challenger. *Id.* at 1359–60.

A party asserting that a patent is invalid as obvious must "show by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361

(Fed. Cir. 2007). That "expectation of success need only be reasonable, not absolute." *Id.* at 1364. "Whether an ordinarily skilled artisan would have reasonably expected success . . . . is measured as of the date of the invention[] . . . ." *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1362 (Fed. Cir. 2009).

B. Findings of Fact

1. The level of ordinary skill in the art is a person with a Ph.D. in the pharmaceutical sciences or related field with at least three years of experience in pharmaceutical chemistry or drug development. Such a person would have access to researchers and clinicians as part of a project team. (Tr. 651:3-17, 587:19-588:6, 589:15-590:6).
2. The '111 and '626 patents are entitled to a priority date of no later than April 21, 2004, the filing date of U.S. Application No.10/828,795, which matured into the '111 and '626 patents.
3. The Gadde Fax is not prior art.
4. Jain and O'Malley are prior art.
5. Jain and O'Malley do not teach a person of ordinary skill in the art the combination of bupropion and naltrexone for the treatment of obesity or overweight.
6. The combination of bupropion and naltrexone for the treatment of obesity or overweight as disclosed in claims 26 and 31 of the '626 patent and claim 1 of the '111 patent would not have been obvious to a person of ordinary skill in the art.

C. Conclusions of Law

1. Priority Date of the '111 and '626 Patents

The '111 and '626 patents both claim priority to U.S. Provisional Application No. 60/466,838 ("the '838 provisional application"), filed on April 29, 2003. ('111 patent, cover; '626 patent, cover). Defendant asserts in post-trial briefing that Plaintiff failed to prove that the '838 provisional application "provided an adequate, enabling written description sufficient to demonstrate that the asserted claims are entitled to the '838 provisional's filing date." (D.I. 162 at 16). Defendant appears to be suggesting that Plaintiff had an affirmative duty to come forward with evidence supporting its claim to priority. I disagree. While the burden of establishing entitlement to the priority date of a provisional application rests with the party claiming priority, *see, e.g.*, *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1305 (Fed.

Cir. 2008), Plaintiff need not have met that burden in this case.

As an initial matter, a defendant raising a defense of invalidity based on anticipating prior art "has the burden of going forward with evidence that there is such anticipating prior art." *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1327 (Fed. Cir. 2008). Once the defendant has met its burden, the plaintiff "has the burden of going forward with evidence either that the prior art does not actually anticipate, or . . . that it is not prior art because the asserted claim is entitled to the benefit of a filing date prior to the alleged prior art." *Id.*

Here, Defendant did not come forward with prior art that would cause Plaintiff to present evidence that it is entitled to claim the priority date of its provisional application. First, Defendant's arguments that the '111 and '626 patents are invalid are limited to obviousness and lack of written description. (*See generally* D.I. 153). Defendant does not argue the '111 and '626 patents are invalid as anticipated by any prior art reference. Second, after the pretrial conference, Defendant represented to the Court that it would rely on one specific combination of references to support its obviousness defense as to the '111 and '626 patents. (*See* D.I. 123). That combination consisted of Jain, a peer reviewed paper from 2002, and O'Malley, a patent that issued on April 1, 2003. Defendant identified no other prior art references to support its obviousness defense, and in particular, none between April 29, 2003 and April 21, 2004. Thus, there was no need for Plaintiff to present evidence that it was entitled to an earlier priority date in order to prevent a particular reference from being treated as prior art. Further, although Defendant referred to Gadde in its letter to the Court (*id.* at 2, 5), Defendant did not indicate that it would rely upon the Gadde Fax as prior art,[3] and in any event, for the reasons stated below, I

[3] That Defendant did not seek to rely on the Gadde Fax as prior art is further supported by Defendant's representations at the pretrial conference on May 15, 2017. At the conference, in connection with Defendant's Motion *in Limine* #3, I asked Defendant whether it would "be relying on some art that is dated between April 29th of 2003 and April 21st of 2004." (D.I. 138 at 75:11-15). Defendant responded that it would drop that motion in

find that the Gadde Fax does not constitute prior art. Whether the '111 and '626 patents are entitled to the priority date of a provisional application is therefore immaterial under the circumstances of this case.

2. Scope and Content of the Prior Art

i. The Gadde Fax

Defendant argues that Dr. Gadde's work in 2000 treating patients with the combination of naltrexone and bupropion for weight loss, as documented in the Gadde Fax, constitutes prior art. (D.I. 162 at 31). I disagree. The contents of the Gadde Fax, the purported treatment of six patients in 1997 and 2000, were not corroborated at trial. (Tr. 950:17-951:3). Defendant suggests that no corroboration was necessary "because Dr. Gadde is a nonparty inventor with no interest in this litigation." (D.I. 162 at 31 n.7). It is true that the Federal Circuit has held that "corroboration is required only when the testifying inventor is asserting a claim of derivation or priority of his or her invention and . . . stands to directly and substantially gain by his or her invention being found to have priority over the patent claims at issue." *Thomson, S.A. v. Quixote Corp.*, 166 F.3d 1172, 1176 (Fed. Cir. 1999). The problem for Defendant in this case, however, is that Dr. Gadde did not testify to any independent recollection of any of the facts of the treatments he administered in 1997 or 2000. Rather, Dr. Gadde testified directly from the 2003 Fax. Dr. Gadde's 1997 and 2000 treatments, therefore, are not themselves prior art. The Gadde Fax is not evidence of anything more than the fact that Dr. Gadde shared with Orexigen the contents of the Fax in 2003.

ii. Jain

Jain is a peer reviewed paper published in 2002. (DTX-011). There is no dispute that

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light of my request that it identify the specific prior art on which it intended to rely. (*Id.* at 75:17-22). Accordingly, I dismissed Defendant's Motion *in Limine* #3 as moot. (*Id.* at 75:23-24).

Jain is prior art. Jain discloses a placebo-controlled study of sustained release bupropion for reducing weight and depressive symptoms in obese patients. (DTX-11, p.1049). Jain reports a placebo adjusted weight loss of 2.8%. (*Id.*; Tr. 852:23-24). Jain does not discuss naltrexone, nor does it suggest combining bupropion with naltrexone or any other drug. (Tr. 853:17-23). Jain further discloses that the mechanism of action of bupropion for weight loss was unknown. (DTX-11, p. 1055; Tr. 854:9-17).

iii. O'Malley

O'Malley is a U.S. Patent that issued on April 1, 2003. (DTX-18, cover). O'Malley issued from an application filed on September 16, 1999. (*Id.*). There is no dispute that O'Malley is prior art. O'Malley discloses the use of an opioid antagonist, such as naltrexone, during smoking cessation to minimize weight gain. (*Id.* at 1:14-21). O'Malley also discloses that the opioid antagonist may be administered "in combination with at least one withdrawal attenuating agent . . . such as clonidine, acamprosate, antihypertensives, antidepressants, antianxiety agents, agents which alter serotonergic function or other agents." (*Id.* at 4:25:33). One of the antidepressants disclosed in O'Malley is bupropion. (*Id.*, claims 1, 4, and 19).

3. Comparing Prior Art and Claimed Subject Matter

Defendant argues that it would have been obvious to a person of ordinary skill in the art to combine bupropion and naltrexone for treating overweight and obesity because both bupropion and naltrexone were known to cause weight loss. (D.I. 162 at 17). Defendant further argues that the combination of bupropion and naltrexone for the purposes of weight loss had also been disclosed prior to the priority date of the '111 and '626 patents. (*Id.* at 18).

Plaintiff responds by arguing that Defendant's obviousness analysis suffers from impermissible hindsight bias. (D.I. 164 at 15). Plaintiff argues that "there were dozens of

different biological targets for weight loss with a wide range of pharmacological agents that could be considered for each of those targets." (*Id.*). Plaintiff contends that Defendant "starts with bupropion because the ultimate invention had bupropion," and argues that assuming a person of ordinary skill "would necessarily focus on improving bupropion" constitutes improper hindsight bias. (*Id.*).

Defendant's expert, Dr. Ahima, opined that Jain disclosed that sustained release bupropion was effective and well-tolerated. (Tr. 430:22-431:2). Plaintiff's expert, Dr. Seeley, disagreed, pointing to the "relatively modest" placebo-adjusted weight loss of 2.8%. (Tr. 852:22-24). This modest weight loss was insufficient to meet FDA requirements of five percent placebo adjusted weight loss. (Tr. 851:5-11). Dr. Seeley also testified that bupropion was "known to have seizure risks." (Tr. 853:3-16). Defendant cites to additional prior art disclosing that bupropion was effective for weight loss, including papers by Anderson and Gadde. (D.I. 162 at 23; Tr. 425:16-426:21, 428:3-17; DTX-9; DTX-10). Dr. Seeley responded by pointing to a statement in the Gadde reference that the "seizure risks complicates [bupropion's] use in obesity." (Tr. 877:7-8; DTX-9, p.550). The Gadde paper concludes that, "Alternative norepinephrine and dopamine uptake inhibitor drugs should be investigated as adjunctive therapies in weight management." (Tr. 877:8-11; DTX-9, p. 550). Dr. Seeley opined that a person of ordinary skill would understand the Gadde reference as "teach[ing] away from using bupropion as a weight loss therapy." (Tr. 877:14-17).

Dr. Seeley also testified to the many different biological targets for treating obesity. (Tr. 849:17-850:23; PTX-112). Dr. Seeley opined that each of these biological targets would involve different pharmacological agents. (Tr. 850:17-23). According to Dr. Seeley, the limited effectiveness of bupropion, combined with the fact that the mechanism of action of bupropion

was unknown, would discourage a person of ordinary skill from considering bupropion as a starting point in developing a new weight loss drug. (Tr. 854:6-22).

I agree with Plaintiff that Defendant's suggestion that bupropion would be an obvious choice for further study in the treatment of overweight and obesity suffers from impermissible hindsight bias. It seems clear that the weight loss effects of bupropion were known to be relatively modest at best. There is also no dispute that the prior art references reported potential risks associated with bupropion, including the risk of seizure. Based on the lack of knowledge of the mechanism of action, combined with the modest effectiveness, I do not think a person of ordinary skill would have found bupropion to be an obvious starting point for further study.

Defendant next argues that it would have been obvious to combine bupropion with naltrexone to enhance bupropion's weight loss effects. (D.I. 162 at 18). According to Defendant, naltrexone was known to cause weight loss and the combination of bupropion and naltrexone had already been used for weight loss. (*Id.* at 17-18). Plaintiff responds that the literature does not disclose that naltrexone alone was effective for weight loss. (D.I. 164 at 18). Plaintiff further argues that the prior art references Defendant cites in support of the combination do not actually disclose the use of the combination for weight loss. (*Id.* at 19).

Defendant relies on the Atkinson and Bernstein references as support for its argument that naltrexone was known to cause weight loss. (D.I. 162 at 17; Tr. 440:4-21, 438:12-20). Dr. Ahima testified that Atkinson disclosed "a small but significant weight loss in women, not the men" in a study of sixty obese patients given naltrexone for eight weeks. (Tr. 440:15-19; DTX-97, p.419). Dr. Ahima further testified that Bernstein disclosed "significant reductions in carbohydrate cravings" in patients treated with naltrexone. (Tr. 438:12-20; DTX-13 at ¶ 15).

Plaintiff's expert, Dr. Seeley, pointed out that Bernstein does not disclose weight loss,

only curbing carbohydrate cravings. (Tr. 878:13-21). Dr. Seeley further testified that Atkinson disclosed a body weight increase in men taking naltrexone. (Tr. 881:1-18). According to Dr. Seeley, a person of ordinary skill reading Defendant's prior art references would conclude that "naltrexone is not a very effective weight loss agent by itself." (Tr. 882:3-9). Dr. Seeley further opined that the references "teach away from the use of naltrexone." (Tr. 882:10-12).

I agree with Plaintiff that the prior art cited by Defendant does not teach a person of ordinary skill that naltrexone was effective for weight loss. The Bernstein reference in particular was not directed to weight loss and did not disclose weight loss effects of naltrexone. I do not think a disclosure of effectiveness for curbing carbohydrate cravings, without more, would inform a person of ordinary skill that naltrexone was effective for weight loss in overweight or obese individuals. Furthermore, Atkinson's disclosure of a small weight loss in women is counterbalanced by its disclosure of an increase in body weight in men. I do not think either of these references, individually or in combination, teaches a person of ordinary skill that naltrexone is effective for weight loss.

Finally, Defendant argues that the prior art disclosed the use of the combination of bupropion and naltrexone for weight loss. (D.I. 162 at 18). Defendant cites to the Dante and O'Malley patents as support for this contention. (*Id.*; DTX-16; DTX-18). Dr. Ahima testified that Dante discloses the use of the combination "decreases cravings for sugar and carbohydrates." (Tr. 445:10-18). Dr. Ahima further testified that the combination of bupropion and naltrexone was disclosed in O'Malley as effective for reducing weight gain during smoking cessation treatment. (Tr. 448:22-449:17).

Plaintiff responds by pointing out that neither of these references disclose the use of the combination of bupropion and naltrexone for weight loss. (D.I. 164 at 19). Dr. Seeley testified

that Dante disclosed compositions and methods of treatment for depression, not weight loss. (Tr. 869:21-870:3; DTX-16). According to Dr. Seeley, Dante does not disclose weight loss using a combination of bupropion and naltrexone, Dante does not disclose naltrexone enhancing bupropion's weight loss effectiveness, and the only discussion related to weight management in Dante is of weight gain associated with tricyclic antidepressants, a different category of antidepressants than bupropion. (Tr. 870:7-23).

Dr. Seeley further testified that O'Malley is directed to smoking cessation treatments, not weight loss. (Tr. 856:14-857:5). Dr. Seeley explained that O'Malley does not contain a single disclosure of weight loss. (Tr. 857:3-5). Rather, O'Malley discloses a single example of minimizing weight gain during smoking cessation therapy and that the single example did not use the combination of naltrexone and bupropion. (Tr. 857:6-22). Dr. Seeley explained that a person of ordinary skill would read O'Malley to disclose that bupropion was used to treat the depressive symptoms smokers have when they stop smoking. (Tr. 858:14-859:4). Dr. Seeley further explained that naltrexone was used "as an adjunct for smoking cessation therapy . . . to block [the] rewarding ability [of nicotine], making it less likely that you're going to pick up a cigarette again." (Tr. 859:17-23). According to Dr. Seeley, there is no disclosure of naltrexone enhancing bupropion's weight loss effects. (Tr. 860:7-861:17). Rather, the only enhancement disclosed in O'Malley is the enhancement of smoking cessation treatments. (Tr. 863:6-20).

I find Dr. Seeley's testimony and explanations credible. I do not think that Dante and O'Malley teach a person of ordinary skill that the combination of naltrexone and bupropion is effective for weight loss. Neither of these references teach a person of ordinary skill anything about weight loss and neither of them indicate that naltrexone enhances bupropion's effectiveness for weight loss. Defendant's argument, it seems to me, is a classic case of

hindsight bias. Defendant begins with the combination Plaintiff ultimately patented and then seeks to justify that combination by combining prior art references that simply would not guide a person of ordinary skill to choose this combination.

Defendant argues that a person of ordinary skill would have been motivated to combine the teachings of Jain and O'Malley to arrive at the combination of bupropion and naltrexone for weight loss. (D.I. 162 at 28). Defendant's rationale is based on a person of ordinary skill reaching the conclusion that naltrexone was effective for weight loss and that the combination had been previously used in connection with weight loss. (*Id.*). I have already determined that neither of these conclusions are supported by Defendant's prior art references. It seems clear that the prior art disclosed that naltrexone was not effective for weight loss, at least because it caused weight gain in the men involved in the study. Furthermore, Defendant's prior art does not disclose the use of the combination for weight loss, nor does it disclose any enhancement of bupropion's effectiveness for weight loss. I fail to see how the combination of Jain and O'Malley, in the absence of impermissible hindsight bias, would motivate a person of ordinary skill to pursue the combination of bupropion and naltrexone for weight loss.

As I have determined that the Gadde Fax is not prior art and cannot serve as evidence of prior use by Dr. Gadde, I need not consider whether the disclosure of his alleged treatment of two patients in 2000 with the combination of bupropion and naltrexone with "questionable benefit" and "no additional benefit" would have served as motivation to combine or would have provided a reasonable expectation of success.

4. Secondary Considerations

"[S]econdary considerations, when present, must be considered in determining obviousness." *Ruiz*, 234 F.3d at 667; *see also Cyclobenzaprine*, 676 F.3d at 1076 ("[E]vidence

on these secondary considerations is to be taken into account *always*, not just when the decisionmaker remains in doubt after reviewing the art." (quoting *Cable Elec. Prods. v. Genmark, Inc.*, 770 F.2d 1015, 1026 (Fed. Cir. 1985))).

Plaintiff presented evidence of unexpected results and failure of others. (D.I. 164 at 27). Plaintiff argues that the synergistic effect of the combination treatment was unexpected based on what was known from the prior art about using the two drugs individually for weight loss. (*Id.*). Defendant criticizes the single study Plaintiff points to as not being probative of non-obviousness because "it is not commensurate with the scope of the asserted claims." (D.I. 162 at 33). According to Defendant, the claims do not require synergy, only that naltrexone enhance the effectiveness of bupropion. (*Id.*). Defendant further argues that the study only showed synergy for 400 mg of bupropion with 36 mg of naltrexone and that the other combinations reported in the study were "merely additive." (*Id.*). I am not persuaded. As I concluded above, a person of ordinary skill would not have expected the combination of bupropion and naltrexone to have any enhanced effectiveness compared to bupropion alone. Therefore, it seems to me that even a limited study showing synergy for some combinations of the two drugs would necessarily constitute unexpected results.

Plaintiff argues that there had been "numerous failures in the field of safe and effective obesity medications." (D.I. 164 at 27). Plaintiff presented evidence that "by the time of invention . . . there were only two FDA drugs approved for the long-term treatment of obesity" and "at least seven other drugs that were being developed for the treatment of obesity had failed." (*Id.* at 28). Defendant counters that, rather than showing failure of others, the record shows evidence of success of others. (D.I. 162 at 34). Defendant again cites to the work of O'Malley, Dante, and Dr. Gadde as support for its contention that others had been successful in

using the combination of naltrexone and bupropion for weight loss. (*Id.*). As I stated above, I disagree that there was any disclosure in O'Malley or Dante showing the use of the combination for weight loss and I am dubious about the claim that Dr. Gadde's results in treating two patients showed success. Defendant also argues that "there were and are a number of FDA-approved weight loss drugs" that are more effective and that carry a lower risk of side effects than the bupropion-naltrexone combination. (*Id.*). Defendant's claim that there were "a number of" other weight loss drugs is belied by the fact that it can only name two other approved weight loss drugs. (*Id.*). I do not think these two other drugs rebut Plaintiff's showing that many others had tried and failed to obtain FDA approval for weight loss drugs.[4]

For the reasons given above, I find that Defendant has not met its burden of proving by clear and convincing evidence that claims 26 and 31 of the '626 patent and claim 1 of the '111 patent are obvious.

IV. INFRINGEMENT

Plaintiff asserts that Defendant directly infringes claim 1 of the '111 patent and indirectly infringes claim 11 of the '195 patent and claims 2, 15, 26, and 31 of the '626 patent. During discovery, Defendant never alleged that its proposed ANDA product did not meet the following claim limitations: 1) "bupropion . . . effective to induce weight loss" in the '626 and '111 patents; 2) "naltrexone . . . effective to enhance the weight loss effect of the bupropion" in the '626 and '111 patents; and 3) "sustained release" in the '111 and '195 patents. (D.I. 129 at 4). In the pre-trial order, Defendant attempted to raise new non-infringement defenses, including by alleging failure of proof of these three limitations. (*Id.* at 3). In an order dated May 19, 2017, I

[4] In post-trial briefing, Defendant for the first time argued that Plaintiff's Contrave product has not been commercially successful and that Dr. Gadde's 2000 treatment of two patients constitutes simultaneous invention. (D.I. 162 at 35-36). As Defendant failed to make these arguments at trial, I decline to consider either of them. Even if I were to consider them, I would be dubious about the merits of both arguments.

held that Defendant had waived the right to contest these three limitations. (*Id.* at 5).

A. Legal Standard

A patent is infringed when a person "without authority makes, uses, offers to sell, or sells any patented invention, within the United States . . . during the term of the patent . . . ." 35 U.S.C. § 271(a). A two-step analysis is employed in making an infringement determination. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). First, the court must construe the asserted claims to ascertain their meaning and scope. *See id.* The trier of fact must then compare the properly construed claims with the accused infringing product. *See id.* This second step is a question of fact. *Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1353 (Fed. Cir. 1998). "Literal infringement of a claim exists when every limitation recited in the claim is found in the accused device." *Kahn v. Gen. Motors Corp.*, 135 F.3d 1472, 1477 (Fed. Cir. 1998). "If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law." *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000). The patent owner has the burden of proving infringement by a preponderance of the evidence. *See SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

35 U.S.C. § 271(b) provides that "[w]hoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "In order to prevail on an inducement claim, the patentee must establish first that there has been direct infringement, and second that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *ACCO Brands, Inc. v. ABA Locks Mfrs. Co.*, 501 F.3d 1307, 1312 (Fed. Cir. 2007) (internal quotation marks omitted). In other words, "inducement requires evidence of culpable conduct, directed to encouraging another's infringement, not merely that the inducer

had knowledge of the direct infringer's activities." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc). "[S]pecific intent may be inferred from circumstantial evidence where a defendant has both knowledge of the patent and specific intent to cause the acts constituting infringement." *Ricoh Co. v. Quanta Computer Inc.*, 550 F.3d 1325, 1342 (Fed. Cir. 2008). "[L]iability for induced infringement can only attach if the defendant knew of the patent and knew as well that 'the induced acts constitute patent infringement.'" *Commil USA, LLC v. Cisco Sys., Inc.*, 135 S. Ct. 1920, 1926 (2015) (quoting *Global–Tech Appliances, Inc. v. SEB S.A.*, 131 S. Ct. 2060, 2068 (2011)). The knowledge requirement may be satisfied by showing actual knowledge or willful blindness. *See Global–Tech,* 131 S. Ct. at 2068 (2011).

In Hatch-Waxman cases alleging that a proposed drug label will induce infringement by physicians, "The pertinent question is whether the proposed label instructs users to perform the patented method." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). "The label must encourage, recommend, or promote infringement." *Takeda Pharm. USA, Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015). "The mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient for inducement." *Id.* Rather, "specific intent and action to induce infringement must be proven." *Id.* Even where a proposed label does not explicitly track the language of a claimed method, a package insert containing directives that will "inevitably lead some consumers to practice the claimed method" provides sufficient evidence for a finding of specific intent. *See AstraZeneca*, 633 F.3d at 1060; *see also Abraxis Bioscience, Inc. v. Navinta, LLC*, 630 F. Supp. 2d 553, 570 (D.N.J. 2009) ("Statements in a package insert that encourage infringing use of a drug product are alone sufficient to establish intent to encourage direct infringement."), *rev'd and vacated on other grounds*, 625 F.3d 1359 (Fed. Cir. 2010).

B. Divided Infringement

Defendant contends that all of the asserted claims of the '626 patent require two steps, diagnosing and administering, that are each performed by a different actor, the doctor and the patient. (D.I. 172 at 8-10). According to Defendant, since the doctor diagnoses and the patient administers, there can be no infringement of these claims unless the patient is under the "control" of the doctor. (*Id.* at 11-14).

As an initial matter, I find that claims 26 and 31, which depend from claim 25, of the '626 patent involve the single step of administering the drug to a patient who has already been diagnosed. Defendant attempts to create an additional step in this method claim based on the fact that claim 25 requires that the drug is to be administered "to an individual who has been diagnosed as suffering from overweight or obesity." According to Defendant, "an obesity/overweight diagnosis is an explicit requirement of all of the '626 claims that will always be performed before the administering step." (D.I. 172 at 10) (emphasis omitted). I agree that a diagnosis is required, but I disagree that this comprises a step in the method claim. A plain reading of this claim limitation indicates that the individual will already be diagnosed prior to the method being performed. The method itself requires only the single step of administering the drug.

I also disagree with Defendant's assertion that Plaintiff "unequivocally admitted that the asserted claims of the '626 patent require a diagnosing step." (D.I. 172 at 10). Plaintiff made no such admission. Rather, Plaintiff stated only that some of the claims require "diagnosing" while other claims require "an individual who has been diagnosed." (D.I. 131, Ex. 17B at 1). This restatement of the precise language of the claims is not an admission of anything.

There is no dispute that claims 2 and 15, which both depend from claim 1, involve both a

diagnosing step and an administering step. There is also no dispute that the diagnosing step is performed by the doctor, but the administering step, which I have construed as "delivering into the body" is performed by the patient, who takes the pills each day outside of the presence of the doctor. The parties dispute whether the patient's actions in self-administering the drug are attributable to the physician who performed the diagnosing step. I do not think it is necessary for me to decide this issue. Having found that all of the asserted claims of the '626 patent are not invalid and that claims 26 and 31 are infringed, I think the question of divided infringement presented by claims 2 and 15 is moot. I cannot conceive of any circumstances in which an additional finding of either infringement or non-infringement of claims 2 and 15 would have any impact on the outcome of this case. Therefore, I decline to decide whether the administering step in independent claim 1 is attributable to the physician.

C. Infringement of the '111 Patent

Plaintiff asserts that Defendant directly infringes claim 1 of the '111 patent. Prior to trial, the only non-infringement argument raised by Defendant as to the '111 patent was that it could not be infringed because it was invalid. (D.I. 129 at 3). By order dated May 19, 2017, I held that Defendant would not be allowed to raise new non-infringement arguments for the first time at trial. (*Id.*).

1. Findings of Fact

1. Defendant has not disputed infringement of claim 1 of the '111 patent. (Tr. 98:24–99:3, 499:8–17).
2. Defendant's ANDA Product is a composition for affecting weight loss. (PTX-022.0001; Tr. at 97:14–23).
3. Defendant's ANDA Product contains sustained-release naltrexone and bupropion. (PTX-022.0002; Tr. at 92:8–14, 95:14–96:8).
4. Defendant's ANDA Product contains bupropion in an amount effective to induce weight loss. (PTX-022.0005–.0006, .0028, .0039–.0040; Tr. 77:6–23, 90:7–21, 93:11–19, 97:14–23, 152:23–153:3).
5. Defendant's ANDA Product contains naltrexone in an amount effective to enhance weight

loss activity of the bupropion. (PTX-022.0005, .0028, .0039–.0040; Tr. 78:2–14, 78:19–79:18, 90:7–91:12, 92:15–93:8, 93:11–19; 94:10–23, 97:24–98:13, 114:11–24, 152:23–153:3).

6. Defendant's ANDA Product is a single oral dosage form fixed combination. (PTX-022.0002; Tr. 91:13–92:14, 93:8–10, 95:4–13, 98:14–23).
7. Defendant's ANDA Product meets all of the elements of claim 1 of the '111 patent.

2. Conclusions of Law

As discussed above, I hold that Defendant failed to prove by clear and convincing evidence that claim 1 of the '111 patent is invalid as obvious. Defendant has made no other non-infringement arguments. Since Plaintiff has shown by a preponderance of evidence that Defendant's ANDA product meets all limitation of this claim, I hold that Defendant infringes claim 1 of the '111 patent.

D. Infringement of the '195 Patent

Plaintiff asserts that Defendant indirectly infringes claim 11 of the '195 patent. Prior to trial, the non-infringement arguments raised by Defendant as to the '195 patent were limited to (1) invalidity, (2) that Defendant did not administer any compounds, (3) no single entity performed all of the steps of the method, and (4) Defendant's product does not meet the claimed dissolution profile. (D.I. 129 at 4). By order dated May 19, 2017, I held that Defendant would not be allowed to raise new non-infringement arguments for the first time at trial and that Defendant had waived the right to contest the "sustained release" limitation of claim 11. (*Id.* at 3, 5).

1. Findings of Fact

1. As construed by the Court, the term "administering" as used in claim 11 of the '195 patent means "delivering into the body." (D.I. 62).
2. As construed by the Court, the preamble "having reduced adverse effects" in claim 11 of the '195 patent is not limiting. (D.I. 62).
3. Actavis had knowledge of the '195 patent prior to filing Actavis's ANDA. (D.I. 131, Ex. 1 at ¶ 18).
4. Claim 11 recites only one step – "administering" naltrexone or a pharmaceutically acceptable

salt thereof and bupropion or a pharmaceutically acceptable salt thereof. (Tr. 159:15–160:1).

5. Claim 11 does not require a separate diagnosing step. (Tr. 160:2–160:14).
6. Because the patient will administer bupropion or a pharmaceutically acceptable salt thereof and naltrexone or a pharmaceutically acceptable salt thereof to himself or herself, a single actor performs all of the steps of the method recited in claim 11 of the '195 patent. (*See* Tr. 158:10–12, 159:15–160:14).
7. The proposed labeling for Defendant's ANDA Product states that it is "indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of: 30 kg/m^2 or greater (obese) or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (*e.g.*, hypertension, type 2 diabetes mellitus, or dyslipidemia)." (PTX-022.0001; D.I. 131, Ex. 1 at ¶ 59; Tr. 223:24–224:24).
8. The proposed labeling for Defendant's ANDA Product states that "Naltrexone hydrochloride and bupropion hydrochloride extended-release tablets should be taken by mouth in the morning and in the evening." (PTX-022.0006; Tr. 223:24–224:24).
9. The "Dosage and Administration" section of the proposed labeling for Defendant's ANDA Product sets forth the following titration schedule:

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

Naltrexone hydrochloride and bupropion hydrochloride extended-release tablets dosing should be escalated according to the following schedule:

	Morning Dose	Evening Dose
Week 1	1 tablet	None
Week 2	1 tablet	1 tablet
Week 3	2 tablets	1 tablet
Week 4 – Onward	2 tablets	2 tablets

A total daily dosage of two naltrexone hydrochloride and bupropion hydrochloride extended-release tablets 8 mg/90 mg tablets twice daily (32 mg/360 mg) is reached at the start of Week 4

(PTX-022.0006; D.I. 131, Ex. 1 at ¶ 62; Tr. 223:24–224:24).

10. At the end of the titration schedule, Defendant's proposed label instructs patients to take a total of 32 mg naltrexone hydrochloride and 360 mg bupropion hydrochloride per day. (*Id.*).
11. At the end of the titration schedule, Defendant's proposed label instructs patients to take two tablets of Defendant's ANDA Product per day in a "Morning Dose" and two tablets of Defendant's ANDA Product per day in an "Evening Dose," *i.e.* 16 mg naltrexone hydrochloride and 180 mg bupropion hydrochloride twice daily. (*Id.*).
12. Defendant's ANDA Product is a tablet containing sustained-release bupropion hydrochloride and sustained-release naltrexone hydrochloride. (Tr. 223:24–224:24, 226:13–18; D.I. 131, Ex. 1 at ¶ 60).
13. Defendant conducted dissolution testing on Lot # 2284R0007 of its ANDA Product, an exhibit batch used for its ANDA submission. (PTX-019.0010; PTX-016.0179; D.I. 131, Ex. 1 at ¶ 61; Tr. 230:24–231:20).
14. Lot # 2284R0007 is representative of Defendant's ANDA Product. (*See* Tr. 255:12–19).
15. Defendant conducted dissolution testing using USP Apparatus 2 at 100 rpm in water at 37°C on six tablets from Lot # 2284R0007, the results of which are set forth below:

Table 4. Dissolution Profile (Naltrexone Hydrochloride) of Lot # 2284R0007 at 100 rpm, paddle [Water, USP Apparatus II, 900 mL]

Units	30 min	60 min	120 min	180 min	240 min	360 min	480 min	600 min
1	30	43	64	90	101	101	101	102
2	27	40	58	72	96	103	104	104
3	30	44	65	82	103	106	107	107
4	28	40	58	71	83	102	103	103
5	30	43	62	77	90	103	105	105
6	30	42	61	78	91	102	103	103
Mean	**29**	**42**	**61**	**78**	**94**	**103**	**104**	**104**
Min	27	40	58	71	83	101	101	102
Max	30	44	65	90	103	106	107	107
% RSD	4.2	4.0	5.1	8.7	7.8	1.7	1.8	1.7

(PTX-019.0011; PTX-015.0005; Tr. 232:5–233:13, 262:5–23, 264:7–15).

16. Claim 11 of the '195 patent does not require analysis or interpretation of the dissolution profile testing results as set forth on page 1943 of the United States Pharmacopeia. (Tr. 248:10-16).
17. Defendant's testing showed that its ANDA Product includes tablets that meet the dissolution profile for naltrexone recited in claim 11 of the '195 patent, *i.e.* between 39% and 70% of naltrexone released in one hour, between 62% and 90% of naltrexone released in two hours and at least 99% in 8 hours. (PTX-019.0011; Tr. 228:20–229:13).
18. Through its label (as set forth in D.I. 165 at ¶¶ 100–11), Defendant actively encourages patients to practice each element of the claimed method of claim 11 by administering Defendant's ANDA Product to themselves.
19. Plaintiff established by a preponderance of the evidence that each of the limitations of Claim 11 of the '195 patent are demonstrated by Defendant's ANDA, and that Defendant had the requisite intent to induce infringement, including knowledge of the '195 patent before submitting its ANDA. (PTX-015.0005; PTX-016.0179; PTX-019.0010–.0011; PTX-022.0001, .0006; D.I. 131, Ex. 1 at ¶¶ 18, 59–62; Tr. 158:10–12, 159:15–160:14, 221:22–234:11).

2. Conclusions of Law

Defendant's non-infringement arguments as to claim 11 of the '195 patent all center on whether its proposed ANDA product meets the claimed dissolution profile. For example, Defendant argues that Plaintiff "has adduced no evidence that Actavis knows what the dissolution profile of Actavis's ANDA Product will actually be in any given administration." (D.I. 165 at 70, ¶ 180). Specifically, Defendant argues that the dissolution profiles of some of the tablets it tested fall outside the claimed range of between 62% and 90% at two hours. (*Id.*, ¶ 181). Defendant also argues that a specific analysis or interpretation protocol is implicitly required by the claim as being part of the USP Apparatus 2 method. (*Id.* at 66-67, ¶¶ 159-67).

As an initial matter, I do not think the claim requires performing the separate analysis or interpretation protocol set forth in the United States Pharmacopeia ("USP"). Defendant argues that because the claim requires the dissolution profile to have certain characteristics when measured using USP Apparatus 2, the protocol for interpretation of the data obtained using the method must also be used. (D.I. 165 at 66-69, ¶¶ 158-77; Tr. 243:11-248:20). I am not persuaded. The claim specifies that the dissolution profile must be measured using USP Apparatus 2. There is no mention of interpretation or analysis in the claim language. Plaintiff's expert, Dr. Treacy, credibly testified that a person of ordinary skill would not have read the claim to require the use of the additional analysis or interpretation protocol "specified in general Chapter 711 of the USP." (Tr. 248:10-16). Defendant did not present expert testimony in rebuttal of Dr. Treacy's conclusion. Defendant cannot create a dispute of fact on an issue requiring technical analysis based solely on attorney argument. *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1068 (Fed. Cir. 2005).

While it is certainly true that some of the tablets fall slightly outside of the claimed range for the two hour dissolution data, I disagree that this has any relevance to the question of whether Defendant's product infringes. Defendant does not appear to dispute that some of the tablets it tested fall squarely within the claimed dissolution profile; rather, Defendant suggests that in order to prevail on its infringement claim, Plaintiff must prove that Defendant knows of some particular administration of the ANDA product that will meet the claimed dissolution profile. (*Id.* at 69-70, ¶¶179-182). This is not the law. "[A]an accused product that sometimes, but not always, embodies a claimed method nonetheless infringes." *Bell Commc'ns Research, Inc. v. Vitalink Commc'ns Corp.*, 55 F.3d 615, 622–23 (Fed. Cir. 1995). Plaintiff has adduced sufficient evidence to prove by a preponderance of the evidence that at least some of Defendant's tablets

will meet the claimed dissolution profile. This is all that is required for a finding of infringement.

Defendant also argues that Plaintiff cannot prove that it "specifically intends to encourage infringement" because its "proposed label does not even mention the dissolution profile" of its product. (D.I. 165 at 70, ¶¶ 183-85). I have already concluded that Defendant's proposed ANDA product meets the dissolution profile; I do not think it is necessary for infringement of this method claim to find that Defendant's proposed label includes the dissolution profile. The claimed method requires administering a product with specific properties. Defendant's product meets all limitations in the claim and the label instructs on administering the product in the amount and with the frequency recited in the claim. Whether the patient who performs the method by administering the tablets knows that the tablets meet the dissolution profile is irrelevant for the purposes of infringement. Defendant knows that the tablets meet all of the claim limitations and, through its proposed label, encourages patients to administer the tablets in a manner that infringes the claimed method.

For the foregoing reasons, I hold that Plaintiff has proven by a preponderance of the evidence that Defendant induces infringement of claim 11 of the '195 patent.

E. Infringement of the '626 Patent

Plaintiff asserts that Defendant indirectly infringes claims 2, 15, 26, and 31 of the '626 patent. As discussed above, I think the question of infringement of claims 2 and 15 is moot. Prior to trial, the non-infringement arguments raised by Defendant as to the '626 patent were limited to (1) invalidity, (2) that Defendant did not administer any compounds, (3) no single entity performed all of the steps of the method, and (4) the proposed label did not include instructions to administer naltrexone and bupropion "to increase satiety" or "suppress the

appetite." (D.I. 129 at 3-4). By order dated May 19, 2017, I held that Defendant would not be allowed to raise new non-infringement arguments for the first time at trial and had waived the right to contest the "effective to induce weight loss" and "effective to enhance the weight loss effect" limitations of the asserted claims. (*Id.* at 3, 5).

1. Findings of Fact

1. As construed by the Court, the term "administering" as used in the claims of the '626 patent means "delivering into the body." (D.I. 62).
2. As construed by the Court, the term "a weight loss effective amount of a first and second compound" as used in the claims of the '626 patent means "a weight loss effective amount of a first and second compound, in combination." (D.I. 62).
3. Actavis had knowledge of the '626 patent prior to filing Actavis's ANDA. (D.I. 131, Ex. 1 at ¶ 18)
4. Actavis's ANDA sets forth a method for treating overweight or obesity through the use of Actavis's ANDA Product. (D.I. 131, Ex. 1 at ¶ 19; PTX-022; Tr. 87:11–88:2).
5. Actavis's ANDA instructs physicians (or other healthcare provider) to diagnose an individual as suffering from overweight or obesity by determining that the individual has a body mass index ("BMI") of at least 27 kg/m^2. (PTX-022.0001, 0005–.0007; Tr. 87:20–88:2).
6. Actavis's ANDA (prescribing information) includes a BMI conversion chart for use in diagnosis. (PTX-022.0007; Tr. 87:21–88:2).
7. Actavis's ANDA Product is indicated for the treatment of obese or overweight individuals based on calculating BMI. (PTX-022.0001, 0005–.0007; Tr. 87:11–88:2, 92:15–93:8).
8. Each tablet of Defendant's ANDA Product contains 90 mg of bupropion HCl and 8 mg naltrexone HCl in a single extended-release, oral dosage form. (D.I. 131, Ex. 1 at ¶¶ 33–34; Tr. 91:13–92:14, 93:8–10, 95:4–13, 98:14–23).
9. As Defendant's ANDA Product contains both bupropion and naltrexone in a single tablet, the two active ingredients are administered together when a patient takes the product. (PTX-022.0002, .0006, .0008; Tr. 91:13–23, 95:4–13).
10. As required by claims 26 and 31, the amount of bupropion and naltrexone in combination in Defendant's ANDA Product is effective to cause weight loss for an overweight or obese individual. (PTX-022.0005–.0006, .0039–.0040; Tr. 92:18–93:10, 152:23–153:3).
11. As required by claims 26 and 31, the weight loss activity of the bupropion and naltrexone in Defendant's ANDA Product is enhanced compared to the administration of the same amount of naltrexone or bupropion alone. (PTX-022.0005, .0028, .0039–.0040; Tr. 90:7–91:8, 92:15–93:8, 93:11–19, 94:10–23, 114:11–24, 152:23–153:3).
12. Claim 25 of the '626 patent, from which claims 26 and 31 depend, only contains an administering step. (JTX-002.0024; Tr. 85:1–7, 158:13–159:3).
13. Through its label, Defendant actively encourages patients to practice each element of the claimed method of claim 26 by administering Defendant's ANDA Product to themselves in accordance with the limitations of claim 26.
14. Through its label (as set forth in D.I. 165 at ¶¶ 8–71), Defendant actively encourages patients to practice each element of the claimed method of claim 31 by administering Defendant's

ANDA Product to themselves in accordance with the limitations of claim 31.

15. Plaintiff established by a preponderance of the evidence that each of the limitations of Claims 26 and 31 of the '626 patent is demonstrated by Defendant's ANDA, and that Defendant had the requisite intent to induce infringement, including knowledge of the '626 patent before submitting its ANDA. (D.I. 131, Ex. 1 at ¶¶ 18–19, 33–34; PTX-022.0001–.0003, 0005–.0006, .0028, .0039–.0040; Tr. 77:6–96:14, 152:23–153:3; 157:18–183:8).

2. Conclusions of Law

As summarized in the findings of fact above, at trial, Plaintiff presented evidence that Defendant's proposed label induces infringement by meeting all limitations of claims 26 and 31 of the '626 patent. Divided infringement was the only non-infringement defense Defendant presented at trial. (D.I. 165 at 40, ¶ 83). I have already held that claims 26 and 31 involve the single step of administering and do not require a separate diagnosing step. Therefore, I hold that Plaintiff has shown by a preponderance of evidence that Defendant's ANDA product infringes claims 26 and 31 of the '626 patent.

V. CONCLUSION

Defendants failed to prove by clear and convincing evidence that claims 26 and 31 of the '626 patent, claim 1 of the '111 patent, and claim 11 of the '195 patent are invalid. Plaintiff proved by a preponderance of the evidence that Defendant directly infringes claim 1 of the '111 patent and indirectly infringes claims 26 and 31 of the '626 patent and claim 11 of the '195 patent.

Plaintiffs should submit an agreed upon form of final judgment within two weeks.