IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
TYLER DIVISION

POZEN INC.	§	
	§	
Plaintiff,	§	
	§	**CASE NO. 6:08 CV 437**
vs.	§	**PATENT CASE**
	§	
PAR PHARMACEUTICAL, INC.,	§	**CONSOLIDATED WITH**
ALPHAPHARM PTY LTD.,	§	**CASE NO. 6:09 CV 3 AND**
TEVA PHARMACEUTICALS	§	**CASE NO. 6:09 CV 182**
USA INC.,	§	
PAR PHARMACEUTICAL, INC.	§	
	§	
Defendants.	§	

MEMORANDUM OPINION AND ORDER

Having considered the parties' written submissions and the evidence of record,[1] the Court **GRANTS** Pozen Inc.'s Motion for Preliminary Injunction of Par Pharmaceutical, Inc. (Docket No. 408).

BACKGROUND

This case involves a dispute over obtaining approval to market and sell a generic drug under the Hatch-Waxman Act. The Act requires that the United States Food and Drug Administration ("FDA") approve all drugs before they are marketed and sold. 21 U.S.C. § 355 (a). To obtain approval for a new drug, an applicant may file a New Drug Application ("NDA"). The NDA must include examples of the proposed label for the drug and clinical data demonstrating that the drug is safe and effective for use. *Id.* § 355 (b)(1)(A), (b)(1)(F). The NDA must also identify any patent that claims either the drug or a method of using the drug if "a claim of patent infringement could reasonably be asserted." *Id.* § 355 (b)(1); *see AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1045-

[1] The case has been tried to the bench, and the Court has not yet entered its Findings of Fact and Conclusions of Law and final judgment.

46 (Fed. Cir. 2010). The FDA publishes the names of approved drugs and associated patents in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly referred to as the "Orange Book").

An applicant seeking approval to market a generic version of a drug may file an Abbreviated New Drug Application ("ANDA") or a "505(b)(2) application." *Id.* § 355 (b)(2), (j). An ANDA has three requirements:

> First, the applicant must demonstrate that "the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug". . . . Second, subject to changes required by FDA regulations or a successful suitability petition, the applicant must also show that "the labeling proposed for the new drug is the same as the labeling approved for the listed drug." Third, for each patent listed in the Orange Book that claims either the listed drug or a use of the listed drug for which the applicant is requesting approval, an ANDA must include either one of four certifications or a "section viii statement."

AstraZeneca, 633 F.3d at 1045-46 (quoting 21 U.S.C. § 355 (j)(2)(A)(iii), (j)(2)(C), (j)(2)(A)(v)). If the ANDA applicant chooses to include a certification, it must provide "(I) that . . . patent information has not been filed, (II) that such patent has expired, (III) . . . the date on which such patent will expire, or (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug." *Id.* at 1046 (quoting 21 U.S.C. § 355 (j)(2)(A)(vii)(I)-(IV)). These certifications are referred to as Paragraph I, II, III, and IV certifications, respectively.

Pozen Inc. ("Pozen"), a pharmaceutical company, developed a migraine therapy that is marketed as Treximet.[2] Pozen is the assignee of U.S. Patent Nos. 6,060,499 ("the '499 patent"), 6,586,458 ("the '458 patent"), and 7,332,183 ("the '183 patent") (collectively "the patents-in-suit"). The patents-in-suit are listed in the Orange Book as covering Treximet. Treximet is a combination drug product that was approved by the FDA on April 15, 2008 for the acute treatment of migraine

[2] GlaxoSmithKline ("GSK") is Pozen's marketing partner, licensee, and the exclusive distributor of Treximet in the United States.

attacks. The FDA granted Pozen three years of exclusivity to market and sell Treximet, and this exclusivity expires on April 15, 2011.

On October 8, 2008, Par Pharmaceutical Inc. ("Par") notified Pozen that it submitted ANDA No. 90-753 ("Par's ANDA"), seeking FDA approval to sell a generic copy of Treximet before the expiration of Pozen's '499, '458, and '183 patents.[3] Par's ANDA included a Paragraph IV certification that, in Par's opinion, the '499, '458 and '183 patents are invalid and/or will not be infringed by the manufacture, use, or sale of Par's ANDA product. *See* Docket Nos. 1, 11. In filing its ANDA application, Par seeks to sell generic versions of Treximet before the patents-in-suit expire, and as the first generic ANDA applicant, Par will receive 180 days of marketing exclusivity. 21 U.S.C. § 355(j)(5)(B)(iv).

Subsequently, on November 14, 2008, Pozen filed suit against Par and later amended its Complaint to add Alphapharm and DRL (collectively "Defendants").[4] Pursuant to the Hatch-Waxman Act, the Complaint stayed the FDA's approval of Par's ANDA until April 8, 2010. In its prayer for relief, Pozen requests the Court enter an order determining infringement and the effective date of the approval of Defendants' ANDAs. *See* 35 U.S.C. § 271(e)(4)(A). Specifically, Pozen requests the Court set the effective dates after the patents-in-suit expire and also permanently enjoin Defendants from making, using, selling, offering to sell or importing into the United States its ANDA products until the patents-in-suit expire. *Id*. at § 271(e)(4)(A)-(B).

With the current case still pending, in January 2011, Par received approval from the FDA to

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[3] Likewise, Defendants Alphapharm Pty Ltd. ("Alphapharm") and Dr. Reddy's Laboratories, Inc. ("DRL") also filed ANDAs with the FDA.

[4] Pozen also sued Teva Pharmaceuticals USA, Inc. ("Teva") for infringement of the same patents-in-suit; however, Pozen and Teva entered into a settlement agreement, and Pozen's claims were dismissed without prejudice. Docket No. 258.

market its generic version of Treximet, allowing Par to launch its product "at risk" once Pozen's three years of regulatory exclusivity expires on April 15, 2011. Accordingly, Pozen requested Par disclose whether it will proceed with an "at risk" launch. Par declined to disclose this information. As such, Pozen moved for the Court to preliminarily enjoin Par from making, using, selling, offering to sell or importing into the United States products that are the subject of Par's ANDA until the Court issues a final decision and order in this case. Thus, absent a ruling that Par infringes one or more of the asserted claims of the patents-in-suit and that the patents-in-suit are valid and enforceable, Par can launch "at risk" on or after April 15, 2011.

LEGAL STANDARD

The Court may grant an injunction to "prevent the violation of any right secured by patent." 35 U.S.C. § 283. The decision to grant a preliminary injunction is within the discretion of the district court. *See Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1363 (Fed. Cir. 2001). The Court's decision to grant a preliminary injunction is reviewed for the abuse of discretion. *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1298 (Fed. Cir. 2009); *see also Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001) ("An abuse of discretion may be established by showing that the court made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings.").

Courts apply a four-part test to determine whether to issue a preliminary injunction. "A plaintiff seeking a preliminary injunction must establish that [it] is likely to succeed on the merits, that [it] is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in [its] favor, and that an injunction is in the public interest." *Winter v. Natural Res.*

Def. Council, Inc., 555 U.S. 7, 24-25 (2008); *see also AstraZeneca*, 633 F.3d at 1049.[5]

ANALYSIS

1) Likelihood of Success on the Merits

To establish a likelihood of success, Pozen "must demonstrate that it will likely prove infringement of one or more claims of the patents-in-suit, and that at least one of those same allegedly infringed claims will also likely withstand the validity challenges presented by the accused infringer." *Amazon.com*, 239 F.3d at 1351. However, a preliminary injunction should not issue if Par raises a substantial question regarding either infringement or validity. *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1364 (Fed. Cir. 1997). In other words, Pozen must show that it will likely prove that Par infringes, and these infringement claims will likely withstand Par's challenges to validity and enforceability. *Id.*

Pozen alleges that: 1) Par's ANDA product infringe claims 11, 12 and 24, which depend on claim 3, and claims 26, 27, 29 and 30, of the '458 patent; 2) Par's ANDA product infringe claim 15, which depends on claim 5, of the '499 patent; and 3) Par's ANDA product infringe claim 2 of the '183 patent under the doctrine of equivalents.[6] Because Pozen may succeed on the merits of its case by proving Par's infringement of any one of the three patents-in-suit, the Court focuses its analysis on claims 11 and 12 of the '458 patent for the purpose of evaluating Pozen's request for a preliminary injunction.

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[5] The Court implores the parties to remain aware that any factual findings are subject to change as the Court has not yet issued its final opinion and order in this case. *See Purdue Pharm.*, 237 F.3d at 1363.

[6] Collectively for all Defendants, Pozen alleges that: 1) Defendants' ANDA products infringe claims 11, 12 and 24, which depend on claim 3, and claims 26, 27, 29 and 30, of the '458 patent; 2) Defendants' ANDA products infringe claim 15, which depends on claim 5, of the '499 patent; and 3) Par's and DRL's ANDA products infringe claim 2 of the '183 patent under the doctrine of equivalents.

A. Pozen's Infringement Claims

Claims 11 and 12, which depend on claim 3, of the '458 patent generally require oral unit dose pharmaceutical compositions for treating migraine headaches. This oral unit dosage contains between 25 and 100 mg of the 5-HT agonist sumatriptan and between 200 and 600 mg of the long-acting, non-steroidal, anti-inflammatory drug ("LA-NSAID") naproxen. The LA-NSAID has a pharmacokinetic half-life of at least four hours and a duration of action of at least six hours. The combination of sumatriptan and naproxen is administered simultaneously, thereby reducing migraine relapse or resulting in a longer lasting efficacy compared to either administered alone. To illustrate, claims 11 and 12, which depend on claim 3, require:

> 3. A pharmaceutical composition in unit dosage form, useful in treating a migraine headache patient, which comprises:
>
> (a) a 5-HT agonist, wherein said 5-HT agonist is a triptan; and
>
> (b) a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID), wherein said LA-NSAID has a pharmacokinetic half-life of at least 4 hours and a duration of action of at least 6 hours;
>
> wherein the respective amounts of said 5-HT agonist and said LA-NSAID in said composition are *effective, upon concomitant administration to said patient of one or more of said unit dosage forms of said composition, to produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist*.
>
> 11. The method or composition of any one of claims 1-5, wherein said LA-NSAID is naproxen or a pharmaceutically acceptable salt in an amount of greater than 200 mg.
>
> 12. The method or composition of any one of claims 1-5, wherein said 5-HT agonist is sumatriptan, and said LA-NSAID is naproxen in an oral unit dosage form comprising sumatriptan in an amount of greater than 25 mg and naproxen in an amount of greater than 200 mg.

'458 patent at 12:29-45 (emphasis added); 13:36-43. Pozen alleges that Par's ANDA product literally meets these claim limitations and argues that it set forth evidence proving such infringement at trial.

Par responds it does not infringe the '458 patent and that Pozen is not likely to succeed on the merits of its infringement claims. In support, Par references Defendants' collective post-trial

briefing.[7]

i. Applicable Law—Pozen's Infringement Claims

To prove infringement, the plaintiff bears the burden of proof to show the presence of every element or its equivalent in the accused device. *Lemelson v. United States*, 752 F.2d 1538, 1551 (Fed. Cir. 1985). The underlying infringement issue is a question of fact reviewed for substantial evidence. *Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1332 (Fed. Cir. 2008).

ii. Analysis—Pozen's Infringement Claims

Claims 11 and 12, which depend on claim 3, demonstrate Pozen's likelihood of success in its assertion of the '458 patent against Par. In support of its infringement claims of the '458 patent, Pozen presented the following: Par's ANDA product is a single tablet for oral dosing. 10/12/10 p.m. Trial Transcript at 110:21-111:4; 114:13-114:24 (hereinafter "TT"); 10/13/10 a.m. TT at 84:7-84:12; 86:24-87:1. The tablet contains sumatriptan and naproxen as the active ingredient, and the tablet contains between 200 and 600 mg of naproxen sodium, a pharmaceutically acceptable salt of naproxen. 10/12/10 p.m. TT at 117:7-119:4; 120:17-120:23; 10/13/10 a.m. TT at 85:24-86:13; 87:2-87:5. The naproxen in Par's ANDA product has a half-life of 19 hours, which is at least four hours, and the action of the naproxen is at least six hours. *Id.* The sumatriptan and naproxen in Par's ANDA product is contained in a single tablet, and as a single tablet, the sumatriptan and naproxen are administered simultaneously. 10/12/10 p.m. TT at 110:21-111:4; 114:13-114:24; 10/13/10 a.m. TT at 84:7-84:12; 86:24-87:1. This simultaneous single unit dose of sumatriptan and naproxen produces a longer lasting efficacy and reduce migraine relapse compared to either administered alone. 10/13/10 a.m. TT at 84:13-84:16. Accordingly, Par's ANDA product is useful in treating a migraine.

[7] In its opposition to the preliminary injunction, Par relied on and incorporated by reference its noninfringement, invalidity, and unenforceability arguments from Defendants' collective post-trial briefing. *See* Docket No. 413; *see also* Docket No. 400, 403.

Id.

Defendants' briefing asserts one noninfringement argument for the '458 patent: that Pozen improperly compared the proposed ANDA products to Treximet rather than the claims, and thus failed to show Defendants met the limitation requiring "effective, upon concomitant administration to said patient of one or more of said unit dosage forms of said composition, to produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist." *See* Docket No. 400; '458 patent at 12:29-45; *see also* Docket No. 413. The Court is not persuaded by this argument, as Pozen's presentation on infringement at trial included comparisons of the proposed ANDA products to the patents-in-suit.

Based on the Court's evaluation of the parties' arguments and evidence presented at trial the Court concludes that Pozen has shown that it is likely to succeed against Par on the merits of its infringement claim of the '458 patent. While Pozen asserted additional claims of the '458 patent along with additional asserted claims of '499 and '183 patents, given that Pozen demonstrated the likelihood of Par's literal infringement of the '458 patent, the Court declines to evaluate each and every asserted claim for the purposes of issuing a preliminary injunction.

B. Par's Invalidity Claims

Defendants collectively claim that the'458 patent is invalid due to anticipation and/or obviousness. Par and Alphapharm also claim that the patent is unenforceable due to inequitable conduct.

In its opposition to the preliminary injunction, Par generally references Defendants' arguments at trial and post-trial briefing. All Defendants claim that references Parma, Catarci, Saadah, the public treatment of four patients at Henry Ford Hospital, and the international Patent Corporation

Treaty ("PCT") application WO 1998/06392, alone or in combination with additional prior art, invalidate the '458 patent.

i. Applicable Law—Par's Invalidity Claims

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." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Although the ultimate determination of obviousness is a question of law, it is based on several underlying factual findings, including: 1) the scope and content of the prior art; 2) the level of ordinary skill in the pertinent art; 3) the differences between the claimed invention and the prior art; and 4) evidence of secondary factors, such as commercial success, long-felt need, and the failure of others. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

A patent is invalid as anticipated if "the invention was patented or described in a printed publication in this or a foreign country . . . more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). Although § 102 refers to "the invention" generally, the anticipation inquiry proceeds on a claim-by-claim basis. *See Hakim v. Cannon Avent Group, PLC*, 479 F.3d 1313, 1319 (Fed. Cir. 2007). The single prior art reference must expressly or inherently disclose each claim limitation to anticipate a claim. *Finisar Corp.*, 523 F.3d at 1334. Additionally, the reference must "enable one of ordinary skill in the art to make the invention without undue experimentation." *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009).

ii. Analysis—Par's Invalidity Claims

Par claims that the '458 patent is obvious to a person of ordinary skill in the art in light of Catarci (DTX 412), Parma (JTX 70), Saadah (DTX 400), or Henry Ford Patient Records 2, 5, 13, and 15 (DTX 378-79, 382-83), or the PCT application WO 1998/06392 (DTX 612), alone or in

combination with additional prior art references. These references, except Catarci and the Henry Ford Patient Records, were before the Patent Office during the prosecution of the '458 patent. JTX 2 at POZ01343987-POZ01343988. Defendants argue that the Parma and Catarci references each teach the concomitant administration of sumatriptan and naproxen and the Saadah and Raskin references together teach the combination of ergotamine and naproxen for the treatment of migraine, with the motivation to substitute sumatriptan for ergotamine. Defendants also contend the Henry Ford Patient Records show that doctors prescribed the combination of sumatriptan and naproxen for migraine patients.

The Catarci reference is a case report entitled "Ergotamine-induced headache can be sustained by sumatriptan daily intake." DTX 412 at ParPharma 009885. Catarci describes a single migraine sufferer who developed ergotamine-induced headaches and subsequently replaced ergotamine with daily administration of sumatriptan. *Id.* Sumatriptan was "effective in alleviating episodic severe headache [sic] but did not relieve her constant, mild head pain," and the patient continued to have daily migraines that were only relieved by sumatriptan. *Id.* Catarci discloses that the patient was subsequently withdrawn from sumatriptan and "[n]on-steroidal anti-inflammatory drugs (NSAIDs) were [then] prescribed both on a daily basis and when required." *Id. "*Four weeks later [the patient] reported three migraine attacks per week, treated either with NSAIDs im [intramuscular] or sumatriptan sc [subcutaneous]." Catarci discloses that "[n]one of these [treatments] produced benefit." *Id.* Catarci further describes that the patient resumed taking daily doses of sumatriptan in addition to receiving acupuncture and the patient's migraine attacks were "promptly aborted by one tablet of sumatriptan." *Id.* Finally, Catachi concludes that "this case illustrates that acupuncture is occasionally of benefit in treating drug-induced daily headache." *Id.* at ParPharma 009886.

Contrary to Par's arguments, the Catarci reference does not teach the combination of

sumatriptan and naproxen provided migraine relief to the patient. Rather, the reference teaches combining sumatriptan and acupuncture to treat migraine patients. *See Ricoh Co., Ltd. v. Quanta Computer Inc.*, 550 F.3d 1325, 1332 (Fed. Cir. 2008) (a reference teaches away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant"); *see also Iron Grip Barbell Co. v. USA Sports, Inc.,* 392 F.3d 1317, 1322 (Fed. Cir. 2004). Moreover, Catarci does not disclose longer lasting efficacy or reduced migraine relapse from the combination of sumatriptan and naproxen. Thus, Par's arguments that the '458 patent would have been obvious to one of ordinary skill in the art in light of Catarci lack substantial merit.

Parma is an Italian language reference entitled "The treatment of migraine: a study in general medicine." JTX 70. The Parma reference, with an English translation, was before the Patent Office during the '458 patent's prosecution. 10/12/10 p.m. TT at 153:12-153:14; JTX 2, 70. Parma is an epidemiological survey of migraine sufferers that assesses various migraine treatments. JTX 70. Parma listed the data collected and analyzed by the study in various tables. *Id.* A table labeled "Table VI. Combinations: 2 drugs" lists "FANS + sumatriptan"[8] and provides that "[t]he cornerstone of treatment is now still represented by FANS, both in monotherapy and in combination therapy." Parma also discloses "Table VIII. 'Unsatisfactory' treatments," which lists treatments using monotherapies, including the monotherapy of sumatriptan, and provides the percentage of "unsatisfactory" treatments received by the patients using monotherapies.

At trial, Pozen presented a declaration from one of the authors of the Parma reference, Dr. Tognoni. PTX 254. Dr. Tognoni is a medical doctor and clinical researcher at the Mario Negri

[8] FANS is the Italian abbreviation for non-steroidal anti-inflammatory drugs ("NSAIDs"). 10/12/10 p.m. TT at 154:7-154:9.

Institute in Milan, Italy. *Id*. at 1. Mr. Tognoni was not retained as a consultant by Pozen, nor did he receive compensation for his declaration. *Id*. Dr. Tognoni provides that his publication does not suggest taking sumatriptan at the same time as another medicine, such as LA-NSAID. *Id.* at 1-2. Dr. Tognoni further provides that "[w]hile my article speaks of the 'associazone' [translated one way as combination therapy] of many pairs of drugs, including NSAIDs and sumatriptan, this is not meant as a reference to administering those two drugs at the same time, such as in a unit dose form, or together. Instead, when my article refers to the 'associazone' of drugs, it refers to the common practice of that time of migraine patients taking drugs separately in sequence, with a required gap in time between the administration of the drugs to determine the efficacy of the first drug before trying additional drugs." *Id.* at 3. Likewise, Pozen's expert, Dr. Blumenfeld, testified consistently with Dr. Tognoni's declaration. Dr. Blumenfeld testified that at the time of the invention, a person of ordinary skill in the art would have interpreted these statements in Parma as disclosing the sequential administration of the various drug combinations. 10/12/10 p.m. TT at 154:2-154:17. Accordingly, Dr. Blumenfeld noted that "Table VI. Combinations: 2 drugs" refers to many drugs that would not have been administered simultaneously, such as two NSAIDs. *Id*. at 154:20-155:11.

On the other hand, Defendants' expert, Dr. Ramadan, offered a contrary opinion. Dr. Ramadan asserted that the reference teaches simultaneous administration and dismissed Dr. Blumenfeld's reasoning that Parma's inclusion of two NSAIDs in the Table VI shows that the administration was not concomitant. 10/14/10 a.m. TT at 104:15-105:4. JTX 70. To justify his position, Dr. Ramadan testified that "FANS and FANS [or NSAIDS and NSAIDs] are used in acute treatment of migraine as evidenced by clinical practice and the literature." 10/14/10 a.m. TT at 104:15-105:4. In addition, Dr. Ramadan testified that "Table VIII. 'Unsatisfactory' treatments" of the Parma reference indicated that the dissatisfaction would motivate a person of ordinary skill in the

art to "[e]ither [administer] another agent or to [administer] combination therapy." 10/14/10 a.m. TT at 105:5-105:24.

Considering the parties' arguments and the evidence of record, Parma, in combination with what was known to a person of ordinary skill in the art before 1996, does not render the '458 patent obvious. While Parma lists "FANS + sumatriptan" in "Table VI. Combinations: 2 drugs," taking the entire article in context, and as viewed by a person of ordinary skill in the art at the time of the invention, the reference does not teach simultaneous administration of naproxen and sumatriptan. Nor does Parma teach the combination of sumatriptan and naproxen produces longer lasting efficacy or reduces migraine relapse compared to the administration of sumatriptan or naproxen alone. Likewise, Dr. Ramadan's testimony fails the show these claim elements, which are not expressly disclosed, were otherwise present in the prior art or would have been obvious to one of ordinary skill in the art. Nor is the Court persuaded by Defendants' arguments that a person of ordinary skill in the art would become motivated to use the combination of sumatriptan and naproxen due to the dissatisfaction rate of patients using sumatriptan monotherapy listed in Table VIII of the Parma reference. In light of Pozen's evidence and assertions regarding the Parma reference, supported with credible testimony from the reference's author and Pozen's expert, Pozen demonstrated that Defendants' invalidity claims regarding the '458 patent lack substantial merit.

The Saadah reference, entitled "Abortive Migraine Therapy With Oral Naproxen Sodium Plus Metoclopramide Plus Ergotamine Tartrate With Caffeine" discloses the simultaneous delivery of a formulation of ergotamine (a 5-HT agonist), naproxen, metoclopramide, and caffeine. DTX 400. The Saadah reference discloses the purposes for the inclusion of each of these components: ergotamine as a pain agent, metoclopramide and caffeine as anti-emetics to reduce nausea that is typically exacerbated by ergotamine, and naproxen as an additional analgesic. DTX 400; 10/15/10 TT at

91:25-93:16.

Defendants argue that because sumatriptan was known to be more effective and better tolerated than ergotamine, a person of ordinary skill in the art would have been motivated to substitute sumatriptan for ergotamine as disclosed in Saadah.[9] DTX 400, 364; 10/15/10 TT at 92:9-93:21; 10/14/10 TT at 116:3-11. As such, Defendants reason that the substitution of sumatriptan would also eliminate the need to co-administer anti-emetics, likewise eliminating the inclusion of caffeine and metoclopramide included by Saadah. *Id.* Finally, Defendants argue the remaining claim elements not expressly disclosed by Saadah would have been obvious to one of ordinary skill in the art.

Pozen acknowledges a person of ordinary skill in the art may have been motivated to substitute sumatriptan for ergotamine; however, Pozen argues that the substitution would also eliminate the need for naproxen as well. In support, Pozen cites a contemporaneous letter, written to the editor of the journal that published Saadah, recommending the removal of naproxen and caffeine due to the side effects noted in the Saadah reference. 10/15/10 TT at 95:1-20; JTX 152.

The Court is not persuaded that a person of ordinary skill in the art would find it obvious, after reading Saadah, to substitute sumatriptan for ergotamine, metoclopramide, and caffeine. This would require the replacement of three out of the four components disclosed in Saadah's formulation, and Saadah disclosed each as having a specific purpose. Nor is the Court persuaded that a person of ordinary skill in the art would find the remaining claim elements, such as the simultaneous administration of naproxen and sumatriptan for the purpose of prolonged efficacy, obvious in light of Saadah. Even considering the Saadah and Raskin references together, the references do not teach the combination of ergotamine and naproxen for the treatment of migraine, with the motivation to

[9] Defendants cite Raskin, entitled "Acute and prophylactic treatment of migraine: Practical approaches and pharmacologic rationale" with Saadah to support its claim that it was known that sumatriptan was more effective and better tolerated than ergotamine. DTX364 at MS_001889 (left col.).

substitute sumatriptan for ergotamine. Defendants' arguments that the Saadah reference renders the '458 patent obvious fail to raise a substantial question regarding the validity of the '458 patent.

Defendants also argue that four patient records from the Henry Ford Clinic in Detroit, where Dr. Ramadan was employed, render the '458 patent invalid. 10/14/10 p.m. TT at 107:9-15; DTX383 (Patient 15); DTX378 (Patient 2); DTX379 (Patient 5); DTX382 (Patient 13). The records disclose that patients were treated for migraines with a combination of sumatriptan and naproxen. *Id.* However, the records do not indicate simultaneous administration of naproxen and sumatriptan, and Ramadan testified he did not recall ever prescribing or giving to a patient sumatriptan and naproxen simultaneously. 10/14/10 p.m. TT at 59:2-5; 10/15/10 TT at 91:5-15. Nor is there any indication that one of ordinary skill in the art would view the patient records to teach or suggest the administration of sumatriptan and naproxen simultaneously. 10/15/10 TT at 91:14-91:24. Accordingly, Defendants' arguments that the patient records render the '458 patent obvious fail to raise a substantial question regarding the validity of the '458 patent.

Finally, Defendants argue that WO1998/06392, an international patent application published on February 19, 1998 under the PCT, anticipates the '458 patent. DTX 612. Defendants argue that the '458 patent is not entitled to claim priority to any of the prior applications because the '458 patent defines "concomitant" or "concomitantly" differently than the prior applications. Defendants' support for its position is the Court's different claim constructions regarding "concomitant" in the '458 patent and "concomitantly" in the '499 patent. Docket No. 257 at 10-14.[10]

[10] The Court construed "concomitantly administering" and its permutations in the '499 patent as "simultaneous administration," or "administration of a second drug for migraine relief while a first drug for migraine relief is present in a therapeutically effective amount," or "administration of a 5-HT agonist and NSAID such that the effective plasma levels of the NSAID will be present in a subject from about one hour to about 12–24 hours after the onset of migraine or onset of precursor symptoms of a migraine." *Id.* at 10-13. The Court construed "concomitantly" and its permutations in the '458 patent as "given in close enough temporal proximity to allow their individual therapeutic effects to overlap." *Id.* at 13-14.

The '458 patent claims a unit dosage form of sumatriptan and naproxen that is simultaneously administered to patient for the treatment of migraines. The '458 patent claims priority to the originally filed claims and specification of application No. 60/024,129 (the "'129 application"). JTX 131. The '129 application discloses the simultaneous administration of a composition with therapeutically effective amounts of sumatriptan and naproxen to treat a migraine. Moreover, Example 1 of the '129 application discloses each element of the asserted claims of the '458 patent. JTX 131 at POZ01276682. Accordingly, the effective filing date of the '458 patent is August 16, 1996, thereby rendering WO1998/06392 inapplicable as prior art.

In light of the record and the parties' arguments, the Court does not find that Par raises a substantial question that the prior art references invalidate the '458 patent.[11] The prior art references, separate or in combination, do not teach or suggest the simultaneous administration of sumatriptan and naproxen. Nor do the references teach or otherwise disclose to one of ordinary skill in the art that the combination of sumatriptan and naproxen produces a longer lasting efficacy reducing migraine relapse compared to administration of naproxen or sumatriptan alone. Moreover, Pozen's evidence and assertions addressing the prior art references, bolstered by credible testimony and arguments, effectively demonstrated that it is likely to succeed against Defendants' invalidity claims.

C. Par's Inequitable Conduct Claims

Defendants also claim that during the '458 patent's prosecution , the inventors made material misrepresentations regarding clinical data with the intent deceive the Patent Office, thus rendering the patent unenforceable due to inequitable conduct.

i. Applicable Law—Par's Inequitable Conduct Claims

[11] Because Par did not raise a substantial question regarding the '458 patent's validity, for the purposes of the preliminary injunction, the Court need not additionally evaluate Pozen's evidence of secondary considerations related to non-obviousness.

"Inequitable conduct resides in failure to disclose material information, or submission of false material information, with an intent to deceive, and those two elements, materiality and intent, must be proven by clear and convincing evidence." *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988); *see also Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1313 (Fed. Cir. 2008). Because an actual "intent to deceive" is required, "[m]istake or negligence, even gross negligence, does not support a ruling of inequitable conduct." *Abbott Labs.*, 544 F.3d at 1353. A court only has discretion to invalidate a patent for inequitable conduct after a showing of both materiality and intent to deceive. *Id.* When examining intent, the alleged conduct must be "viewed in light of all the evidence, including evidence indicative of good faith." *Kingsdown*, 863 F.2d at 876. However, when a "failure to disclose" is alleged, intent to deceive may be inferred when: 1) highly material information is withheld; 2) the applicant knew of the information and knew or should have known of the materiality of the information; and 3) the applicant has not provided a credible explanation for the withholding. *Praxair*, 543 F.3d at 1313-1314.

ii. Analysis—Par's Inequitable Conduct Claims

Defendants argue that the applicants presented misleading data to the Patent Office during the prosecution of the '458 patent. In response to a rejection from the Patent Office, the applicants submitted an Amendment and Response and a Declaration of Dr. Plachetka. The applicants also submitted a two studies, a Pilot Study and a Naproxen Study, arguing the study data supported "a surprising, synergistic effect" of the combination of sumatriptan and naproxen. JTX6 at POZ01353110-16, POZ01353730-33.

The Pilot Study compared sumatriptan alone against the combination of sumatriptan and naproxen. JTX4 at POZ01341841. No patients in the Pilot Study took just naproxen; thus the Pilot Study permitted a comparison only of the combination against sumatriptan alone. JTX4 at

POZ01341842. The applicants told the Patent Office they had data from a separate clinical study, the Naproxen Study, that included a naproxen-only treatment group. The applicants combined the data from the two studies to compare the 24-hour sustained response rates for all three treatments (i.e., sumatriptan alone, naproxen alone, and the combination of sumatriptan and naproxen). Defendants argue that the applicants made improper "adjustments" to the studies that resulted in an exaggeration of the "effectiveness" of the combination therapy the applicants sought to patent. Defendants contend that the percentage of patients who responded to the combination was 3% less than the sum of the percentage of patients who responded to each active agent alone, thus showing that the combination was not synergistic as stated by the applicants. Defendants further argue these adjustments were highly material since the applicants argued the'458 patent was patentable over the prior art because of the advantageous combination of sumatriptan and naproxen and that applicants' deceptive intent can be inferred.

Pozen offered testimony from the applicants that contradicts Defendants' claims. The applicants explained the testing data and that the representations made to the Patent Office of the analysis were accurate. 10/12/10 p.m. TT at 33:2-37:9; 94:13-103:1; 10/13/10 a.m. TT at 104:1-112:12;10/13/10 p.m. TT at 28:3-39:3. Dr. Plachetka, the named inventor on the '458 patent and Pozen's President, Chief Executive Officer, and Chief Scientific Officer, testified that multiple analyses of the pilot study data were presented to the Patent Office to provide as much information as possible about the studies. 10/12/10 p.m. TT at 34:15-36:5. Likewise, Mr. McNamara, Pozen's Vice President of Business Development, also testified that Pozen explained to the Patent Office the differences between the two studies, including how and why the comparison was made. 10/13/10 a.m. TT at 105:20-107:7; 10/13/10 p.m. at 29:1-34:10. The Court deems this testimony credible, and the evidence does not indicate that the applicants intentionally mislead the Patent Office. Weighing

the materiality of the statements with the lack of intent, the Court does not find that Defendants' arguments raise a substantial question regarding the enforceability of the '458 patent.

D. Conclusion

Defendants' invalidity and unenforceability claims fail to cast enough doubt on the '458 patent to avoid the grant of a preliminary injunction. Based on the Court's evaluation of the parties' arguments, supporting evidence, and for the reasons stated above, the Court concludes that Pozen has demonstrated its infringement claims will likely withstand Par's challenges to validity and enforceability as Par has failed to raise a substantial question regarding either enforceability or validity. Accordingly, the first prong of the test weighs in favor of granting a preliminary injunction. Pozen has demonstrated that "it will likely prove infringement of one or more claims of the patents-in-suit, and that at least one of those same allegedly infringed claims will also likely withstand the validity challenges presented by the accused infringer." *Amazon.com*, 239 F.3d at 1351.

2) Likelihood of Irreparable Harm in the Absence of Preliminary Relief

Pozen argues it will suffer irreparable harm if Par is not enjoined because: 1) Pozen will lose vital revenue; 2) irreversible market share and price erosion will occur; and 3) a temporary entry of Par's ANDA product would irreparably damage Pozen's goodwill.

First, relying on a declaration from Dr. Plachetka, Pozen submits that the loss of revenue stream from the launch of Par's ANDA product would devastate Pozen. Under the Pozen-GSK agreement, once a generic copy of Treximet enters the market, the royalty rate on Treximet will decrease by 70% (from its current rate of 18% to 5%). Pozen argues that it relies on this revenue from Treximet to develop and commercialize products and the loss of this revenue could force Pozen out of business. Pozen further argues the revenue loss would disrupt its primary business objective of developing innovative therapies. Second, Pozen contends that the entry of Par's ANDA product

would cause Pozen to lose sales and market share to the lower priced generic product. Pozen also agues entry of Par's ANDA product could force Pozen to lower the price of Treximet to maintain its market share. Third, Pozen contends that if the Court ultimately issues a permanent injunction, denial of a preliminary injunction would harm Pozen's goodwill because the temporary availability of Par's lower priced ANDA product could frustrate or confuse Pozen's customers and cause ill-will.

As demonstrated by Pozen's agreement with GSK, the launch of a generic product would significantly affect Pozen's revenue stream. Such a reduction of revenue would subsequently impact Pozen's ability to allocate its resources to product development. Likewise, Pozen would be harmed from the introduction of Par's ANDA product, which at a lower coset, would undoubtedly affect Pozen's market share. Taken together, Pozen has demonstrated that without a preliminary injunction, it would suffer irreparable harm. *See, e.g., Abbot Labs.*, 544 F.3d at 1361-62 (affirming the district courts' conclusion that price erosion from current generic competition did not negate irreparable harm from the market share and revenue loss upon the entry of another generic competitor); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382-83 (Fed. Cir. 2006) (affirming the district courts' finding of irreparable harm based, in part, on price erosion); *Purdue Pharma*, 237 F.3d at 1368 (likelihood of price erosion and loss of market position are evidence of irreparable harm).

3) Balance of Equities

The balance of equities tips in favor of Pozen. While Par argues that the delay of bringing its ANDA product to market delays Par's revenue generation, Par's ANDA product has not entered the market.[12] However, if the Court ultimately finds for Pozen and issues a permanent injunction, a temporary entry of Par's ANDA would result in a cascade of consequences that, as provided above,

[12] Par additionally requests the Court to require Pozen to post a bond of $1.4 million per month. The Court **DENIES** Par's request.

cannot be undone. Thus, the balances of equities weighs in favor the preservation of the status quo until the Court issues a final decision.

4) The Public Interest in an Injunction

The public interest in a preliminary injunction does not tip in favor of either party. The importance of the patent system in encouraging innovation, as the "encouragement of investment-based risk is the fundamental purpose of the patent grant, and is based directly on the right to exclude." *See Sanofi-Synthelabo*, 470 F.3d at1383. Nor is the public harmed by a preliminary injunction, as Treximet is readily supplied to patients. On the other hand, as Par contends, the public would benefit from its lower priced ANDA product. However, a reduction of cost to consumers is balanced by the possibility of premature elimination of Pozen's patent rights before the Court can enter a final determination.

CONCLUSION

Based on the Court's analysis of: 1) Pozen's likelihood of success on the merits; 2) a likelihood that Pozen will suffer irreparable harm in the absence of preliminary relief; 3) that the balance of equities tips in Pozen's favor; and 4) the neutral weight of the public's interest, and reviewing the evidence and arguments presented by the parties, the Court **GRANTS** Pozen Inc.'s Motion for Preliminary Injunction of Defendant Par Pharmaceutical, Inc.

The Court **ORDERS** that Defendant Par Pharmaceutical, Inc. is enjoined from making, using, selling, offering to sell, or importing into the United States products that are the subject of Par's Abbreviated New Drug Application No. 90-753 until the issuance of a final decision and order in this case.

So ORDERED and SIGNED this 14th day of April, 2011.

LEONARD DAVIS
UNITED STATES DISTRICT JUDGE