UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JANSSEN PHARMACEUTICALS, INC. and JANSSEN PHARMACEUTICA NV, Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC., Defendant.	Civil Action No.: 18-734 **OPINION**

CECCHI, District Judge.

This patent case was brought by Plaintiffs Janssen Pharmaceuticals, Inc. and Janssen Pharmaceutica NV (collectively, "Plaintiffs" or "Janssen") against Defendant Teva Pharmaceuticals USA, Inc. ("Defendant" or "Teva"). This action specifically concerns the validity of Claims 1–21 of U.S. Patent No. 9,439,906 (the "'906 Patent" or the "Patent-in-Suit"). ECF No. 133 ("Final Pretrial Order") at 2. The '906 Patent covers "a dosing regimen for administering paliperidone palmitate to a psychiatric patient in need of treatment for schizophrenia, schizoaffective disorder, schizophreniform disorder, or other psychotic disorders." *Id.*

The Court held a two-week bench trial in this matter that began on October 13, 2020, and concluded on October 30, 2020. ECF Nos. 135–37, 140–41, 145–49, 151. The parties submitted post-trial briefing and proposed findings of fact and conclusions of law in December 2020. ECF Nos. 164 ("Pls. Br."), 165 ("PFOF"), 167 ("Def. Br."), 167-1 (*corrected at* 168-1 ("DFOF")). On January 8, 2021, the parties submitted responsive briefs. ECF Nos. 188 ("Pls. Reply Br."), 189 ("Def. Reply Br."). Closing arguments were held on March 5, 2021. ECF No. 199.

In a letter dated December 5, 2017, Teva notified Janssen that it had submitted Abbreviated

New Drug Application ("ANDA") No. 211149 to the United States Food and Drug Administration ("FDA") "seeking FDA approval to engage in the commercial manufacture, use, sale, offer for sale in, and/or importation into the United States of generic paliperidone palmitate extended-release injectable suspension products . . . prior to the expiration of the 906 Patent." Final Pretrial Order at 2. Defendant does not contest infringement of the '906 Patent. *Id.* Therefore, the only the issue for this Court to decide is whether the Patent-in-Suit is invalid based on the following legal principles: (1) obviousness; (2) lack of written description; and (3) indefiniteness.[1] *Id.* at 2–3.

This Opinion constitutes the Court's findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a). The findings of fact are based on the Court's observations and credibility determinations of the witnesses who testified at trial, and a thorough review of all the evidence admitted at trial. While the Court has reviewed all of the evidence presented, given the length of the trial record, the Court includes references only to the evidence most pertinent to its analysis.[2] For the reasons set forth below, the Court finds that the Patent-in-Suit is not invalid.

I. BACKGROUND

A. Parties

Plaintiff Janssen Pharmaceuticals, Inc. is a corporation organized and existing under the laws of the Commonwealth of Pennsylvania, and has its principal place of business at 1125 Trenton-Harbourton Road, Titusville, New Jersey 08560. *Id.* at 4. Plaintiff Janssen Pharmaceutica

[1] Post-trial, in July 2021, Teva filed a motion to amend pursuant to Federal Rule of Civil Procedure 15(b)(2), asking the Court to deem its pleadings amended with a count for patent invalidity due to incorrect inventorship under 35 U.S.C. § 102(f). ECF No. 244. The Court will discuss this motion and the potential additional invalidity challenge later in this Opinion.

[2] At the request of the Court, the parties submitted motions shortly after trial presenting their arguments on certain evidentiary issues. ECF Nos. 152–153. All relevant evidentiary issues raised in that briefing, any *in limine* motions, and elsewhere (*e.g.*, ECF No. 98), are resolved in this Opinion.

NV is a corporation organized and existing under the laws of Belgium, and has its principal place of business at Turnhoutseweg, 30, B-2340 Beerse, Belgium. *Id.* Janssen Pharmaceutica NV "is the owner of the entire right, title, and interest in and to the '906 Patent." *Id.* at 5. Defendant Teva is a corporation organized and existing under the laws of Delaware, and has its principal place of business at 1090 Horsham Road, North Wales, Pennsylvania 19454. *Id.* at 4.

B. Background of the Invention

The dosing regimens at issue in this case provide detailed information concerning the use of paliperidone palmitate to treat schizophrenia and other psychotic disorders. To this end, the '906 Patent discloses unique combinations of dose amounts, dosing schedules, injection sites, and formulation properties. PFOF ¶ 7.[3] The main dosing regimen contained in Claim 2 consists of a 150 mg-eq.[4] first loading dose of paliperidone palmitate in the deltoid muscle on the first day of treatment, a second loading dose of 100 mg-eq. in the deltoid muscle during the sixth to tenth day of treatment, and successive monthly (± 7 days) maintenance doses of 25 mg-eq. to about 150 mg-eq. in either the deltoid or gluteal muscle. '906 Patent (DTX-1/PTX-1) col. 32:11–36. The main dosing regimen for patients with renal impairment contained in Claim 10 consists of a loading dose from about 75 mg-eq. in the deltoid muscle on the first day of treatment, a second loading dose from about 75 mg-eq. in the deltoid muscle on the sixth to tenth day of treatment, and successive monthly (± 7 days) maintenance doses of 25 mg-eq. to about 75 mg-eq. in either the deltoid or gluteal muscle. *Id.* col. 33:3–27.

[3] The parties have agreed to a representative set of claims for purposes of this matter. Final Pretrial Order at 9. Claim 2 of the '906 Patent represents Claims 1, 3–7, and 15; Claim 10 represents Claims 8–9; Claim 13 represents Claims 11–12, 14, and 16; Claim 20 (as it depends from Claims 1 or 8) represents no other claims; and Claim 21 (as it depends from Claims 1 or 8) represents Claims 17–19. *Id.* These Claims will be collectively referred to as the "Representative Claims."

[4] Doses of paliperidone palmitate are typically expressed in terms of their equivalent amount of paliperidone (expressed as "milligram-equivalent" or "mg-eq.") rather than their actual weight. PFOF ¶ 6.

This section will first provide the scientific background of the claimed invention. Next, the Court will provide the relevant research and patent history for the Patent-in-Suit.

1. Scientific Background

Schizophrenia is a chronic psychotic disorder that affects approximately one percent of the world's population. DFOF ¶ 52; PFOF ¶ 11. The disorder is most commonly characterized by "disorganized behavior and speech, delusions, and hallucinations." PFOF ¶ 11. Schizophrenia often manifests "in young people between the ages of 15 and 30," and is typically diagnosed after an individual suffers an acute psychotic episode. *Id.* ¶ 12; Trial Tr. (Kohler) at 1883:4–12. Antipsychotic medication is the main form of treatment for schizophrenia, and its aim is to achieve remission such that a person with schizophrenia can manage their symptoms and function independently. DFOF ¶¶ 53, 55; PFOF ¶ 12. There is currently no cure for schizophrenia, and each psychotic episode inflicts permanent damage upon the brain and reduces the chances of achieving remission. PFOF ¶¶ 12–13.

Schizophrenia is generally treated with antipsychotic drugs which have been available since the 1950s. DFOF ¶ 54; PFOF ¶ 15. These drugs are typically administered orally or as long-acting injectable formulations ("LAI"), sometimes referred to as a "depot." DFOF ¶¶ 56–57; PFOF ¶¶ 14–15. Schizophrenia is challenging to treat because the symptoms of the disease make it difficult for patients to comply with their prescribed treatment, particularly when it comes to daily oral antipsychotics. DFOF ¶ 57; PFOF ¶ 14. When patients stop taking their medicine or miss a dose, they often have a relapse in the form of an acute psychotic episode, which can set off a cycle of worsening symptoms, additional missed treatment, and possibly institutionalization. *Id.*

"First-Generation" LAIs developed in the 1950s include "Prolixin (fluphenazine) decanoate, Prolixin (fluphenazine) enanthate, and Haldol (haloperidol) decanoate." PFOF ¶ 15. These LAIs were accompanied by serious mental side effects such as dullness and cognitive

impairment. *Id.* ¶ 16; *see also* DFOF ¶ 497. They were also associated with extrapyramidal symptoms ("EPS") consisting of serious motor impairments, painful muscle contractions, tremors, and stiffness. PFOF ¶ 16; *see also* DFOF ¶¶ 497–498. Due to the severe mental and physical side effects associated with First-Generation LAIs, they were generally restricted to institutionalized patients who could not function in society. PFOF ¶ 17.

"Second-Generation" antipsychotics, developed in the 1980s and 1990s, were viewed as a major improvement from First-Generation antipsychotics because they had less frequent and less severe side effects (including EPS). *Id.* ¶ 19. Most of the Second-Generation antipsychotic drugs were administered orally, with Janssen's Risperdal Consta serving as the only Second-Generation LAI on the market for some period of time. *Id.* Risperdal Consta, however, requires oral supplementation for the first three weeks of treatment and provides only two weeks of therapeutic benefits, making biweekly injections necessary. *Id.* ¶ 20.

Janssen sought to improve upon these limitations, and eventually received FDA approval for Invega Sustenna in 2009. *Id.* ¶ 60. Invega Sustenna is seen as a vastly superior product to Risperdal Consta due to its unique dosing regimen consisting of high loading dose injections to initiate treatment and monthly maintenance injections thereafter. *Id.* ¶ 175–76. The dosing regimen does not require oral supplementation, is initiated in a uniform manner, and has led to important benefits such as improved treatment adherence and reduced risk of relapse. *Id.* ¶¶ 176, 190. Invega Sustenna is a "blockbuster" drug, and since 2013, it has accounted for the largest revenue share in the LAI antipsychotic market, with net sales of $1.7 billion in 2019 alone. *Id.* ¶¶ 187–88. When dosed according to its label, Invega Sustenna practices the claims of the '906 Patent. *Id.* ¶ 171.

2. Research and Patent History

Invega Sustenna was developed over the course of more than a decade, in a process

involving multiple stages of research, numerous clinical trials, and various unexpected setbacks. *Id.* ¶¶ 26, 36. The initial preclinical stage of the process consisted of formulation development and animal research. *Id.* Following the preclinical stage, Janssen began Phase I clinical trials. During Phase I, Janssen studied the formulation of paliperidone palmitate to be used in the drug, eventually choosing formulation F13. *Id.* ¶ 27. Janssen also studied single versus multiple-dose regimens, and deltoid versus gluteal injection sites in Phase I. *Id.* ¶¶ 27–29. In the BEL-7 Phase I clinical trial,[5] Janssen observed better results with a loading dose regimen of double doses on day 1 followed by monthly maintenance doses, and chose this regimen for further development. *Id.* ¶ 28. In the USA-3 Phase I clinical trial, Janssen observed that injections in the deltoid led to "higher peak plasma concentrations compared to gluteal injections." *Id.* ¶ 29. Based on these findings, Janssen used the gluteal muscle for all injections in Phase II clinical trials because higher plasma concentrations present a greater risk of severe side effects. *Id.*

After seven years of Phase I clinical trials, Janssen began Phase II clinical trials in October 2003. *Id.* ¶ 30. These clinical trials were designed to measure efficacy, and Janssen was excited by the results of its SCH-201 Phase II clinical trial that indicated rapid efficacy compared to placebo by day 8 of treatment. *Id.* ¶¶ 30–31. As Dr. An Vermeulen, a named inventor of the '906 Patent, testified at trial, this was the "first study to demonstrate efficacy of" paliperidone, it "confirmed safety and tolerability," and "efficacy was achieved quickly within the first week." Trial Tr. (Vermeulen) at 776:8–12; '906 Patent (DTX-1/PTX-1). The Court credits Dr. Vermeulen's trial testimony, and notes that she is currently an internal consultant in the Quantitative Sciences Consulting Group at Janssen. Trial Tr. (Vermeulen) at 744:3–6.

[5] The Court notes that this Research and Patent History section only discusses a subset of the most relevant studies that were conducted during the development of Invega Sustenna.

In Phase III, Janssen developed three different trials to build on the SCH-201 trial. PFOF ¶ 32. The PSY-3004 and PSY-3003 trials compared equal doses of paliperidone palmitate in the F11 and F13 formulations, with all injections given in the gluteal muscle on days 1/8/36/64, and efficacy measured by assessing changes in PANSS scores. *Id.* ¶ 32. PANSS refers to the Positive and Negative Syndrome Scale, a questionnaire administered to a patient asking about the symptoms of schizophrenia. *Id.* ¶ 30. PSY-3002 was a non-inferiority study which tested the F11 and F13 formulations of paliperidone palmitate against Risperdal Consta in 749 patients. *Id.* ¶ 33. Subjects in this study received 50 mg-eq. of paliperidone palmitate in the gluteal muscle on days 1 and 8, followed by either 25, 50, 75, or 100 mg-eq. doses monthly. *Id.*

All three trials were unexpected failures. *Id.* ¶¶ 36, 52. The results of PSY-3004 came in May 2006 and were a major disappointment to Janssen as they showed no effectiveness in subjects in the United States. *Id.* ¶ 34. Next, the PSY-3003 results arrived in August 2006 and brought additional bad news as that study failed to demonstrate superiority of any dose of paliperidone palmitate in the United States when compared to placebo. *Id.* ¶ 35. The results of PSY-3002, which were also disappointing to Janssen, did not arrive until later and are discussed below.

In response to the disappointing results of PSY-3004 and PSY-3003, Janssen assembled a task force of clinical, pharmaceutical, preclinical, bioanalytical, clinical pharmacology, and pharmacometric[6] specialists to understand the results from these studies and formulate a path forward. *Id.* ¶ 38. The task force, relying in large part on population pharmacokinetic modeling

[6] Pharmacometrics is a discipline that applies advanced modeling techniques to make sense of data across entire populations concerning pharmacokinetics (how the body handles a drug), taking into account the patient-specific characteristics that lead to variability in individual exposure profiles. PFOF ¶ 25. This work requires patient data and patient-specific characteristics to build a mathematical model with both explanatory and predictive power. *Id.* The goal of this modeling is to identify dosing regimens that are effective for the majority of subjects. *Id.*

done by Dr. Vermeulen, found that body mass index had an impact on the levels of paliperidone palmitate in the blood and found that choice of injection site had a significant effect as well. *Id.* ¶ 42. In order to overcome these issues, the task force recommended a dosing regimen of 150 mg-eq. in the deltoid muscle on day 1, followed by a dose of 25, 50, 100, or 150 mg-eq. in the deltoid or gluteal muscle on day 8, and monthly maintenance doses. *Id.* ¶ 43.

This new dosing regimen was tested in the PSY-3007 and PSY-3006 Phase III clinical trials. *Id.* ¶ 44. Dr. Srihari Gopal, a senior director in the Psychiatry Department at Janssen Research and Development, LLC, led the design of these new trials. *Id.* ¶ 44; Final Pretrial Order at 29. PSY-3007, which began in March 2007, compared a dosing regimen of 150 mg-eq. in the deltoid muscle on day 1 followed by equal doses of either 25, 100, or 150 mg-eq. in the gluteal or deltoid muscle against a placebo. PFOF ¶ 44. PSY-3006, which began the same month, was a non-inferiority study comparing the F13 formulation of paliperidone palmitate to Risperdal Consta. *Id.* ¶ 45. Patients in this study received 150 mg-eq. in the deltoid muscle on day 1 and 50 mg-eq. on day 8 in the gluteal or deltoid muscle, followed by monthly maintenance doses. *Id.* After the results of PSY-3002 finally came back in May 2007 and failed to demonstrate non-inferiority to Risperdal Consta, Janssen decided to modify the PSY-3006 study to change the day 8 dose from 50 mg-eq. in the gluteal or deltoid muscle to 100 mg-eq. in the deltoid muscle. *Id.* ¶¶ 52–53. Around the same time, Dr. Mahesh Samtani, currently a senior scientific director at Janssen,[7] took over for Dr. Vermeulen (Dr. Vermeulen had been promoted) and further developed the population pharmacokinetic model. *Id.* ¶ 48; Trial Tr. (Samtani) at 1342:6–7. Dr. Samtani's new model ran simulations of different dosing regimens by varying sequencing, dose amount, and

[7] As discussed later in this Opinion, Janssen asserts that Dr. Samtani and Dr. Gopal should be added as named inventors of the '906 Patent.

administration site, to determine if Janssen's preferred dosing regimen could achieve rapid efficacy without oral supplementation in as many individuals as possible without risking severe side effects. PFOF ¶ 50.

While awaiting the results of PSY-3007 and PSY-3006, Janssen began the FDA approval process based in large part on Dr. Samtani's modeling. *Id.* ¶¶ 56–57. In October 2007, Janssen submitted a New Drug Application seeking approval for a 100/100 mg-eq., day 1/day 8 deltoid muscle dosing regimen because it had Phase III safety data available for this regimen. *Id.* ¶ 57. The FDA responded in August 2008 and suggested that Janssen consider a lower dosing regimen of 75 or 100 mg-eq. on day 1, followed by 75 or 100 mg-eq. on day 8. *Id.* ¶ 58. Janssen countered the FDA's recommendation, using Dr. Samtani's models, as well as the PSY-3007 results received in the spring of 2008 and the PSY-3006 results received around July 2009, to show that the 150 mg-eq. day 1 and 100 mg-eq. day 8 dosing regimen (eventually claimed in the '906 Patent) resulted in more patients obtaining therapeutic levels of paliperidone by day 8. *Id.* ¶ 59–60. With this showing, the FDA approved Janssen's higher dosing regimen that Invega Sustenna practices in 2009. *Id.* ¶ 60. Janssen contends that this was a novel approach that went against the traditional dosing philosophy generally used for LAI antipsychotics at the time. *Id.* ¶ 58. [8]

C. Patent-in-Suit and Relevant Prosecution History

The '906 Patent, entitled "Dosing Regimen Associated With Long Acting Injectable Paliperidone Esters," issued on September 13, 2016, and expires on January 26, 2031. '906 Patent (DTX-1/PTX-1). The asserted claims generally relate to:

[8] The Court notes that the parties have different views regarding the development process of Invega Sustenna, as Janssen claims that "the extraordinary skill of Janssen's scientists" led to the project's success in spite of unexpected setbacks (Pls. Br. at 12), while Teva argues that "the alleged difficulties Janssen faced during development were avoidable" (Def. Br. at 55). Given these positions, further details on the drug development process will be discussed below.

> a dosing regimen for administering paliperidone esters to a psychiatric patient in need of treatment comprising administering intramuscularly in the deltoid a first loading dose from about 100 mg-eq. to about 150 mg-eq. of paliperidone as a paliperidone palmitate formulated in a sustained release formulation on the first day of treatment; administering intramuscularly a second loading dose from about 100 mg to about 150 mg-eq. of paliperidone as a paliperidone palmitate formulated in a sustained release formulation between about the 6th to 10th day of treatment; and administering intramuscularly in the gluteal a maintenance dose of about 25 to about 150 mg-eq. of paliperidone as a paliperidone ester in a sustained release formulation on between about the 34th and about the 38th day of treatment.

Id. col. 2:12–25. More specifically, the various claims of the '906 Patent provide details about the injection site, injection timing, and dosage amounts of paliperidone palmitate that should be used (Claim 2), alternative dosing regimens for renally impaired patients whose kidneys do not clear paliperidone as effectively as non-renally impaired patients (Claims 10 and 13), and precise characteristics of the paliperidone palmitate formulation that must be used (Claims 20 and 21). PFOF ¶¶ 7–9; *see also* '906 Patent (DTX-1/PTX-1).

On December 19, 2007, Janssen filed U.S. Provisional Application No. 61/014,918 (the "'918 Provisional"). PFOF ¶ 66. The '906 Patent claims the benefit of both the '918 Provisional and U.S. Provisional Application 61/120,276 filed on December 5, 2008. '906 Patent (DTX-1/PTX-1) col. 1:8–10. Janssen subsequently filed application number 12/337,144 on December 17, 2009, which eventually matured into the '906 Patent. Final Pretrial Order at 5. The '906 Patent then issued on September 13, 2016. '906 Patent (DTX-1/PTX-1).

II. ISSUES TO BE DECIDED

By Stipulation and Order dated June 8, 2020, Teva has agreed that for purposes of this lawsuit, it "will not contest that the making, using, offering to sell, or sale of Teva's Proposed Generic Products within the United States . . . would infringe and/or induce infringement of any valid Asserted Claim." ECF No. 88 at 2. Accordingly, the question before this Court is whether

the '906 Patent is invalid based upon Teva's asserted challenges.

III. DISCUSSION

Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut this presumption, Defendant bears the burden of proving invalidity by clear and convincing evidence. *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1376 (Fed. Cir. 2009) ("Because of this presumption, an alleged infringer who raises invalidity as an affirmative defense has the ultimate burden of persuasion to prove invalidity by clear and convincing evidence, as well as the initial burden of going forward with evidence to support its invalidity allegation.").

A. Obviousness (35 U.S.C. § 103)

To prove that an asserted claim of a patent is invalid as obvious under 35 U.S.C. § 103, a patent challenger bears the burden of establishing by clear and convincing evidence that 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." 35 U.S.C. § 103;[9] *see also Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1360–61 (Fed. Cir. 2007). A person of ordinary skill in the art will hereinafter be referred to as a "POSA." Obviousness is a question of law that is predicated on several factual inquiries. *See Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966). Specifically, there are four basic factual inquiries that concern: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art;[10] (3) the differences between the claimed subject matter and the prior art;

[9] The parties assert that the pre-America Invents Act version of 35 U.S.C. applies to the Patent-in-Suit. Final Pretrial Order at 2.

[10] Although the parties presented slightly different definitions of a POSA, they agree that any differences are immaterial. *See* Trial Tr. (Closing Argument) at 122:9–123:10. Plaintiffs offer that a POSA would have "an M.D., Ph.D., PharmD, or equivalent work experience in drug formulation, pharmacy, pharmacokinetics, or medicine." PFOF ¶ 77 n.7. Defendant proposes that "[a] POSA is a person who would have an advanced degree such as an M.D., Ph.D., PharmD, master's degree, or other advanced degree in an area related to chemistry, pharmaceutics, medicine or biology, with

and (4) objective indicia (secondary considerations) of nonobviousness, including commercial success, long-felt but unsolved need, failure of others, and other indicia. *See id.*

Defendant asserts that the Patent-in-Suit is invalid because it is obvious in view of prior art that would have motivated a POSA to arrive at the claimed dosing regimens with a reasonable expectation of success. Def. Br. at 18. Defendant further argues that secondary considerations do not overcome the prima facie case of obviousness. *Id*. at 44. Defendant also argues that a presumption of obviousness applies to the Patent-in-Suit, stating that the Representative Claims merely recite dosing and particle size ranges that overlap with ranges disclosed in the prior art. *Id.* at 9–12. The Court will address these arguments in turn.

To establish obviousness, Defendant primarily relied on three prior art references at trial: (1) a summary protocol for Janssen's PSY-3003 clinical study titled "A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (50 Mg eq., 100 Mg eq., and 150 Mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia" (the "'548 Protocol"); (2) U.S. Patent No. 6,555,544 (the "'544 Patent"), a patent assigned to Plaintiff Janssen Pharmaceutica, N.V. titled "Aqueous Suspensions of Submicron 9-Hydroxyrisperidone Fatty Acid Esters"; and (3) International Patent Publication Number WO 2006/114384 (the "WO'384 Publication"), an international patent publication filed on behalf of Plaintiff Janssen Pharmaceutica, N.V. *See* PFOF ¶¶ 89, 93, 101; DFOF ¶¶ 138–39, 141, 178–80, 214; *see also* PTX-54, -55, -66; DTX-54, -55, -72.[11] Defendant also relies upon

several years of experience in the pertinent field and be capable of working in a team comprising others in the field or related fields." DFOF ¶ 136 (internal quotation marks omitted).

[11] The Court notes that the United States Patent and Trademark Office ("USPTO") considered a number of the prior art references at issue in this case and concluded that the Patent-in-Suit was not obvious in light of these references.

various other prior art references, which the Court will address throughout this Opinion where applicable.

In support of its obviousness arguments, Defendant proffered the following experts at trial: (1) Dr. Daniel Paul H. Wermeling, Pharm.D., FCCP, FASHP, Emeritus Professor at the University of Kentucky, College of Pharmacy,[12] and (2) Ivan T. Hofmann, Vice President and Managing Director of Gleason IP.[13] DFOF ¶¶ 14–16, 26–28; Final Pretrial Order at 41, 43–45.[14]

Plaintiffs contend that Defendant's obviousness arguments fail because a POSA would not have been motivated to create the claimed dosing regimens based on the prior art with a reasonable expectation of success. *See* Pls. Br. at 25–41. Plaintiffs further assert that secondary considerations support a finding of nonobviousness. *Id.* at 41–53. Plaintiffs also argue that no presumption of obviousness applies here, and that even if a presumption is applied, it has been rebutted. Pls. Br. at 54. In support of their arguments, Plaintiffs rely on the following experts: (1) Dr. Patrick J. Sinko, Ph.D., R.Ph, Distinguished Professor of Pharmaceutics in the Ernest Mario School of

[12] Dr. Wermeling is a named author on over 35 peer-reviewed publications related to pharmacokinetics, pharmacodynamics, and bioavailability. Final Pretrial Order at 42. He has also worked as a clinical investigator on studies related to pharmacokinetics and pharmacodynamics, and has received over 60 grants for such studies and is a named inventor on six U.S. patents, including two related to pharmaceutical compositions and methods of treatment using the pharmaceutical composition. *Id.*

[13] Mr. Hofmann's work experience includes litigation support and consulting engagements with a variety of pharmaceutical and biologics companies. Final Pretrial Order at 44. In his work in the pharmaceutical and life sciences industry, Mr. Hofmann has performed financial and economic analysis for hundreds of prescription pharmaceutical and biologic products, including virtually every major therapeutic class of drugs. *Id.*

[14] The Court will also consider the testimony of Dr. René S. Kahn, M.D., Ph.D., an expert who "testified . . . in the fields of psychiatry, psychotic disorders, and schizophrenia," to the extent he also opined on obviousness at trial. DFOF ¶ 9 (internal quotation marks omitted). Dr. Kahn is the Esther and Joseph Klingenstein Professor and System Chair of Psychiatry at the Icahn School of Medicine at Mount Sinai. Final Pretrial Order at 40. Dr. Kahn has conducted extensive research on schizophrenia and its treatment, has published over 900 research papers, and has been awarded multiple honors for his work in the field of psychiatry, including a Fulbright Scholarship. *Id.* at 40.

Pharmacy at Rutgers, The State University of New Jersey[15] (Trial Tr. at 1469:1–8; DFOF ¶ 42; Final Pretrial Order at 36–37); (2) Dr. Christian G. Kohler, M.D., Clinical Director of Neuropsychiatry in the Neuropsychiatry Division of the Department of Psychiatry at the Perelman School of Medicine of the University of Pennsylvania[16] (Trial Tr. at 1874:23–1875:6; DFOF ¶ 46; Final Pretrial Order at 37–38); and (3) Carla S. Mulhern, Managing Principal at Analysis Group[17] (Trial Tr. at 2576:24–2577:5; DFOF ¶ 49; Final Pretrial Order at 38–39). Plaintiffs also rely on the following fact witnesses: Dr. An Vermeulen, Dr. Srihari Gopal, and Dr. Mahesh Samtani. Final Pretrial Order at 29–31.

The Court has examined all asserted prior art references, both alone and in combination, as well as all expert testimony and secondary considerations to determine whether it would have been obvious to a POSA to arrive at the claimed dosing regimens. For the reasons discussed below, the Court finds that Defendant has failed to prove by clear and convincing evidence that the Patent-in-Suit is invalid based on obviousness pursuant to 35 U.S.C. § 103.

1. Scope of the Prior Art and Differences Between the Prior Art and the Claimed Invention

The Patent-in-Suit generally provides for a dosing regimen comprised of administering a 150 mg-eq. first loading dose of a sustained-release paliperidone palmitate formulation in the

[15] Dr. Sinko has over thirty years of research experience in drug formulation, drug delivery technology, and drug targeting. Final Pretrial Order at 36. Dr. Sinko has given approximately 169 lectures and published 175 articles, and serves as a grant reviewer for the National Institute of Health. *Id.* at 37.

[16] Dr. Kohler is the author of more than 80 peer reviewed research publications concerning neuropsychiatric disorders and their treatment, has over twenty years of teaching experience, and serves as a reviewer for a number of neuropsychiatry journals. Final Pretrial Order at 38.

[17] Ms. Mulhern has offered analyses of economic matters across a variety of industries, including pharmaceuticals, medical devices, automotive, computer hardware and software, consumer products, entertainment, semiconductors, and telecommunications over the course of her 25 years at Analysis Group. Final Pretrial Order at 39. Ms. Mulhern has been designated as a testifying expert in several forums, including federal and state courts, the International Trade Commission, the Patent Trial and Appeal Board, and various private arbitration tribunals. *Id.*

deltoid muscle on the first day of treatment, followed by a second loading dose of 100 mg-eq. in the deltoid muscle sometime during the sixth to tenth day of treatment, and then successive monthly (± 7 days) maintenance doses of 25 mg-eq. to about 150 mg-eq. in either the deltoid or gluteal muscle. *See generally* '906 Patent (DTX-1/PTX-1). The '906 Patent further provides for reduced loading and maintenance doses for renally impaired patients. *See id.* Therefore, to prove obviousness, Defendant must show by clear and convincing evidence that the claimed invention – which consists of a precise combination of dose amounts, dose timing, sites of administration, and particle size, designed for a patient in need of treatment for schizophrenia and other psychiatric disorders – would have been obvious to a POSA.

Defendant points to various scientific and patent publications that it contends render the claimed invention obvious.[18] The main prior art references focused on by the parties relate to the initiation of treatment with loading doses (the '548 Protocol), a specific formulation of paliperidone palmitate (the WO'384 Publication),[19] and monthly administration of aqueous

[18] In Teva's Proposed Findings of Fact and Conclusions of Law, it offers the following combinations of prior art references: (1) "Claim 2 is obvious in view of the '544 Patent and/or WO '384 in combination with the '548 Regimen, in view of Gibaldi, Goodman, Ereshefsky 1990, Ereshefsky 1993, Karagianis, Revill, and/or Janicak"; (2) "Claims 20 and 21 are obvious in view of the '544 Patent, WO'384, and '548 Regimen, in view of Gibaldi, Goodman, Ereshefsky 1990, Ereshefsky 1993, Karagianis, Revill, and/or Janicak"; (3) "Claims 10 and 13 are obvious in view of the '544 Patent, WO'384, and '548 Regimen, in view of Gibaldi, Goodman, Ereshefsky 1990, Ereshefsky 1993, Karagianis, Revill, Janicak, the '591 Application, Cleton 2007, and/or the 2006 Invega ER Label." DFOF ¶¶ 64–66. The Court has considered all of these prior art references, individually and in combination, insofar as they were presented at trial and in the parties' written submissions.

[19] The WO'384 Publication is an international patent publication filed by Janssen with the World Intellectual Property Organization describing a new process for creating raw paliperidone palmitate crystals, as opposed to a final paliperidone palmitate formulation such as the one utilized in the '906 Patent. DFOF ¶¶ 178, 203; PTX-66. The new method uses a "sterilization process replacing radiation with aseptic filters." Def. Br. at 22; *see also* DFOF ¶ 198. With respect to particle size, the WO'384 Publication states that the particles should have a "specific surface area>4m^2/g," meaning "that at least 90% of the particles have a diameter of less than 2,000 nm."

nanoparticle suspensions of paliperidone palmitate formulations to treat schizophrenia (the '544 Patent).[20] *See* Def. Br. at 18–26. Defendant asserts that, when considering these references and the other prior art in the record individually and in combination, a POSA would have been motivated to arrive at the claimed dosing regimens with a reasonable expectation of success. *See id.* at 18–43. Plaintiffs counter that the references on which Teva relies would not have motivated a POSA to create the claimed dosing regimens, that Teva's obviousness defense is based on impermissible hindsight, and that at least some of the references actually taught away from the claimed invention. *See* Pls. Br. at 25–41. Furthermore, Plaintiffs contend that any motivation to modify the prior art can only be found now with the benefit of non-public information, including Janssen's proprietary scientific data and the unpublished failures of Janssen's clinical trials. *See id.* at 29.

The Court will first address the '548 Protocol individually given that Teva's prior art combinations all involve modifying this prior art which discusses a dosing regimen for initiating treatment of paliperidone palmitate. *See* Pls. Br. at 29; Def. Br. at 23. The Court will then discuss all of the prior art in connection with a POSA's motivation to arrive at the specific claims. As explained below, Teva has failed to show that a POSA would have been motivated to arrive at the

DFOF ¶ 200; PTX-66 cols. 5:23–25, 7:25–26. The publication also instructs that particle size can be altered through a milling process. DFOF ¶¶ 201–202.

[20] The '544 Patent teaches how to make a sustained-release paliperidone palmitate formulation that is therapeutically effective for at least three weeks, but does not teach the use of loading doses or other key features of the '906 Patent such as uniform dosing or particularized injection sites. DFOF ¶ 145; PFOF ¶¶ 94–97; PTX-55. The '544 Patent describes four different formulations of paliperidone palmitate with varying particle sizes and pertinent characteristics, and teaches intramuscular injection of the formulation every three weeks at a dosage range from about 2 to 4 mg/kg of body weight. DFOF ¶¶ 156, 167, 174; PTX-55.

claimed dosing regimens with a reasonable expectation of success based on any of the prior art, considered alone or in combination, discussed at trial.[21]

2. The Prior Art Would Not Have Motivated a POSA to Arrive at the Dosing Regimens Claimed in the '906 Patent

a) The '548 Protocol

The '548 Protocol is a published two-page summary protocol of Janssen's unsuccessful PSY-3003 clinical trial aimed at measuring the safety and efficacy of administering "fixed doses" of either 50, 100, or 150 mg-eq. of paliperidone palmitate "in the gluteal muscle" for "treating subjects with schizophrenia." DTX-55 at 1; *see also* DFOF ¶ 557.[22] In the study, equal doses were to be administered on "Days 1, 8, 36, and 64." DTX-55 at 1; *see also* DFOF ¶ 557. The "hypothesis" of the study was "that the 3 fixed doses of paliperidone are each more efficacious than placebo in treating subjects with schizophrenia." DTX-55 at 1; *see also* PFOF ¶ 91.[23] Janssen received the PSY-3003 results in August 2006. PFOF ¶ 35. The results indicated that PSY-3003 "failed to demonstrate superiority of any dose of [paliperidone palmitate] as compared to placebo

[21] The Court notes that the parties presented very little testimony and evidence on the Janicak and Revill prior art references at trial and only refer to these references in passing in their briefing. Nonetheless, the Court has considered these references in its obviousness analysis and finds that they do not render the claimed invention obvious based on their discussion of oral paliperidone and other meaningful differences. *See* PFOF ¶¶ 118–19; DFOF ¶¶ 232–33, 264–67.

[22] Plaintiffs argue that Defendant failed to establish that the '548 Protocol qualifies as prior art because it was printed on March 8, 2018, from a frequently-updated Internet database and does not indicate which portions were publicly available in 2007. *See* PFOF ¶ 90. This argument is unpersuasive. A cursory review of the versions of the '548 Protocol in the record indicate that the document was "[u]pdated" on September 20, 2005, and show the "[v]iew . . . on" September 20, 2005. PTX-54 at 1; DTX-55 at 1. The Court will therefore consider the '548 Protocol in its entirety.

[23] Over the course of the PSY-3003 study, a "medical kit allocation error" caused some subjects assigned to the placebo treatment group to receive 150 mg-eq. doses and some subjects assigned to the 150 mg-eq. treatment group to receive the placebo. DFOF ¶ 559. As a result, only thirty subjects consistently received the four intended 150 mg-eq. doses during the study. *Id.*; *see also* Trial Tr. (Gopal) at 1063:23–1064:8. At trial, however, Dr. Vermeulen acknowledged that the error "had nothing to do with the 150-milligram dose regimen itself" and "was just an error in the way the study was conducted[.]" DFOF ¶ 560 (internal citations and quotation marks omitted).

in the United States," "failed to show superiority of the 50 and 150 mg-eq. doses world-wide," and showed that the 100 mg-eq. dose—the only dose to establish statistical efficacy—was not fast-acting, first demonstrating superiority on Day 36. *Id.* ¶ 35; *see also* DFOF ¶ 558.

The parties agree that the '548 Protocol does not contain clinical results or safety data, and that a POSA would have to look beyond this reference in order to understand how the '548 Protocol worked in subjects. Pls. Br. at 30–31; Def. Br. at 25. At trial, Dr. Wermeling, Defendant's obviousness expert, explicitly acknowledged that the '548 Protocol "is a protocol without any results" and "does not provide any safety or efficacy data." Trial Tr. (Wermeling) at 423:20–21, 471:10–14.

The '548 Protocol and the '906 Patent differ in several material respects. The '548 Protocol discloses **equal** doses of paliperidone palmitate administered in the **gluteal** muscle on fixed treatment days, while the '906 Patent contains regimens comprised of **unequal** doses (Claim 2), two of which must be administered in the **deltoid** muscle (Claims 2 and 10), and a broader dosing window for the second and monthly maintenance doses (Claims 2 and 10). Defendant asserts that the '548 Protocol provides a proper starting point for arriving at the claimed dosing regimens because it "provided guidance on using loading doses followed by monthly administration of paliperidone palmitate." Def. Br. at 23, 26. But Defendant fails to adequately explain why a POSA would modify the '548 Protocol's teachings in the precise ways required to achieve the dosing regimens claimed in the '906 Patent, and the mere fact that the '548 Protocol and the '906 Patent contain some similar features is not enough to show obviousness. *See Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (noting that "obviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention"); *Heidelberger Druckmaschinen AG*

v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

One issue with starting from the '548 Protocol is that it contains no information about the safety of the dosing regimen or its efficacy (the study was actually ineffective as discussed above), and Defendant has failed to persuasively argue, among other things, how a POSA would know to alter the equal doses in the gluteal muscle described in the '548 Protocol to arrive at the unequal loading doses in the deltoid claimed by the '906 Patent without knowing the results of the trial. As Dr. Sinko credibly testified, without such safety and efficacy information, a POSA would have had no reason to alter the regimen disclosed in the reference. *See* Trial Tr. (Sinko) at 1580:2–16 ("[T]here's no safety data available or efficacy data available that would give the motivation to make any changes. . . . And so there would be no motivation for a person of skill to consider [adopting unequal loading doses to initiate treatment] because once again, there's no data to support that change.").[24] In fact, the only way to know how to modify the '548 Protocol to match the '906 Patent would be to look back at the protocol later with its results in hand, but that type of hindsight analysis is impermissible here.[25]

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[24] Janssen also asserts that Teva presents an internally inconsistent argument by claiming "that a person skilled in the art would have selected the dosing regimens of the 548 Protocol in order to avoid oral supplementation, reach therapeutic plasma levels faster, and reduce the risk of relapse," and simultaneously contending "that these same motivations would have led one to modify the 548 Protocol dosing regimens to arrive at the claimed inventions." Pls. Reply Br. at 17 (internal citations and quotation marks omitted). While the Court acknowledges that there may be some inconsistency in Teva's argument, it nevertheless examines the substance of Teva's arguments on this matter.

[25] Dr. Wermeling also appeared to rely on impermissible hindsight in forming his obviousness opinion. As the Federal Circuit has made clear, "[o]bviousness 'cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention.'" *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013) (quoting *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998)).

At trial, Dr. Wermeling asserted that motivation to modify the '548 Protocol to align with the dosing regimen of the '906 Patent can be derived from Ereshefsky's teachings about high loading doses and a desire to use LAIs to treat "acute life-threatening circumstances." Trial Tr. (Wermeling) at 321:13–14, 372:15–24, 475:10–17. As discussed in more depth below, Ereshefsky did not discuss paliperidone palmitate, uniform dosing, or unequal loading doses, all of which are present in and integral to the '906 Patent. Moreover, Dr. Wermeling's assertion about the use of LAIs in acute life-threating circumstances was contradicted by the testimony of Dr. Kahn, Defendant's other technical expert. According to Dr. Kahn, "long-acting injectables are not designed to be used in emergency situations" because "[t]hey don't work fast enough." Trial Tr. (Kahn) at 90:12–19. This inconsistency between the experts' testimony belies Defendant's theory of motivation, and Defendant has not carried its burden to establish motivation to modify the '548 Protocol by clear and convincing evidence. *See Heidelberger Druckmaschinen*, 21 F.3d at 1072.[26]

During his deposition, Dr. Wermeling conceded that he "formed [his] opinions on obviousness" by "look[ing] at the '906 Patent claims first" and then "went back to see if [he] could find the elements that are in the '906 Patent claims in these other references next." Trial Tr. (Wermeling) at 359:21–360:15. Although he attempted to disavow this testimony at trial on the basis that it was "not particularly accurate" and did not "fully accurately describe" his "process," he elsewhere admitted that his "memory from a year ago is going to be better than a year later." *Id.* at 357:12–25, 358:14–359:5, 359:21–360:15. Dr. Wermeling's testimony also contained inconsistencies regarding his views on "routine optimization." *See, e.g.*, Trial Tr. (Wermeling) at 361:25–364:24. Thus, considering Dr. Wermeling's testimony in its entirety, the Court finds that Dr. Wermeling's deposition admissions undermine his obviousness opinion and that Dr. Wermeling's testimony has credibility issues.

[26] Plaintiffs further contend that the claimed invention is not obvious because it solved a problem that was not known in the prior art. Pls. Br. at 34–35. Specifically, they argue that because the '548 Protocol study was designed to achieve rapid and sustained efficacy, and because the prior art did not disclose the unexpected failures of the study, a POSA would have had no reason to solve the problems with the '548 Protocol's equal dose regimen. *Id.* "[W]here a problem was not known in the art, the solution to that problem may not be obvious, because ordinary artisans would not have thought to try at all because they would not have recognized the problem." *Forest Lab'ys, LLC v. Sigmapharm Lab'ys, LLC*, 918 F.3d 928, 935 (Fed. Cir. 2019) (internal citation and quotation marks omitted). As Dr. Wermeling conceded, the '548 Protocol does not contain any results or data on safety or efficacy. Trial Tr. (Wermeling) at 423:20–21, 471:10–14. Indeed, as

The '548 Protocol is a failed study conducted by Janssen that examined using paliperidone palmitate to treat schizophrenia. Yet, for the reasons stated above, even starting from this protocol, Teva has failed to show that a POSA would be motivated to modify the '548 Protocol to comport with the '906 Patent without utilizing safety/efficacy information that was unavailable or impermissible hindsight. The Court will next further analyze Teva's motivation to modify the prior art, including the '548 Protocol, with respect to each claim.

b) Claim 2 – Primary Dosing Regimen

Claim 2 provides for a dosing regimen of high, unequal loading doses in the deltoid muscle followed by monthly maintenance doses in the deltoid or gluteal muscle. PFOF ¶ 7. Specifically, the claim instructs administering 150 mg-eq. of a sustained-release paliperidone palmitate formulation in the deltoid muscle on the first day of treatment, followed by administering 100 mg-eq. in the deltoid muscle six to ten days later, and then successive monthly (±7 days) maintenance doses of 25 to 150 mg-eq. in either the gluteal or deltoid muscle. '906 Patent (DTX-1/PTX-1). Defendant argues that a POSA would have been motivated to arrive at Claim 2 in view of the prior art. *See* Def. Br. at 26–28. After careful consideration of the entire record, the Court is not persuaded.

i. Claim 2 – Deltoid Administration

A key component of Claim 2 is the requirement that the first and second loading doses are given in the deltoid muscle. '906 Patent (DTX-1/PTX-1) col. 32:15–24. Contrary to Defendant's assertions, the prior art would not have motivated a POSA to initiate treatment with deltoid injections as is instructed in the '906 Patent. Indeed, as Dr. Wermeling conceded at trial, none of

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discussed above, Janssen only discovered a solution to the study's problems after conducting additional internal studies and reviewing internal data. Therefore, a POSA would not have recognized the problems associated with the '548 Protocol regimen, and this fact further supports a finding of nonobviousness.

the three primary prior art references—the '548 Protocol, the '544 Patent, or the WO'384 Publication (discussed above)—teach deltoid administration of loading doses. *See* Trial Tr. (Wermeling) at 477:16–25 (Dr. Wermeling testified that he "would have [his] own reasoning as a POSA to understand that's an option."), 504:25–505:8, 512:20–24. As explained above, the '548 Protocol involved gluteal injections, not deltoid injections. DTX-55 at 1. Additionally, as Dr. Wermeling admitted, the WO'384 Publication would not "point you in the direction of giving a Day 1 dose and a second dose on Day 6 to 10 in the deltoid specifically." Trial Tr. (Wermeling) at 512:20–24. As to the '544 Patent, the testing described therein involved an "injection . . . given in the biceps femoris of the left hind paw" of "a beagle dog," not deltoid administration in humans. Trial Tr. (Wermeling) at 504:25–505:8; *see also* Trial Tr. (Sinko) at 1533:19–22 (noting that the '544 Patent does not "provide any guidance on a preferred injection site for a human"). While Dr. Wermeling opined that a POSA knew "you could use various [injection] sites" for dosing, such as the deltoid, gluteus, and vastus lateralis, he conceded that selecting the deltoid was only "an option" and that "[o]ther options would have been reasonable too." Trial Tr. (Wermeling) at 323:4–11, 476:19–23. As explained above, however, the obviousness inquiry "concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention." *See Belden Inc.*, 805 F.3d at 1073; *see also InTouch Techs., Inc. v. VGO Commc'ns, Inc.*, 751 F.3d 1327, 1352 (Fed. Cir. 2014).

Defendant also argues that two textbooks—(1) "Goodman & Gilman's The Pharmacological Basis of Therapeutics" ("Goodman"); and (2) "Gibaldi's Drug Delivery Systems in Pharmaceutical Care" ("Gibaldi")—would motivate a POSA to arrive at the claimed regimens because they teach that deltoid injections lead to faster absorption than gluteal injections. Def. Br.

at 20; DFOF ¶¶ 223, 225, 227; PTX-64, -65; DTX-91, -93.[27] A holistic review of these references indicates, however, that neither discloses deltoid administration of LAI loading doses. Indeed, while Dr. Wermeling relied on a passage from Goodman stating that "[g]enerally, the rate of absorption following injection of an aqueous preparation into the deltoid or vastus lateralis is faster than when the injection is made into the gluteus maximus," Goodman goes on to note that "[s]low, constant absorption from the intramuscular site results if the drug is . . . suspended in various other repository (*depot*) vehicles." Trial Tr. (Wermeling) at 323:2–324:23, DDX3-84, DTX-93 at 32; *see also* PTX-65 at 8 (characterizing absorption rate of drug suspended in repository vehicle as "[v]ery slow"). As Dr. Sinko persuasively conveyed through his testimony, Goodman suggests that in the context of drug suspensions, such as the "aqueous particle nanosuspensions" or "depot formulation" claimed in the '906 Patent, "the formulation," rather than the injection site, "would be controlling the rate of absorption." Trial Tr. (Sinko) at 1533:23–1536:21. Thus, the Court finds that Goodman would not motivate a POSA to use deltoid injections for the claimed formulation.

Similarly, the Court finds that the Gibaldi reference would not have motivated a POSA to initiate treatment with deltoid injections as claimed in the '906 Patent. In support of its position, Defendant cites to Gibaldi's teachings that "[t]he [intramuscular] injection site is usually the deltoid muscle . . . or the vastus lateralis muscle," that the absorption rate "of drugs depend[s] on biopharmaceutical factors such as formulation characteristics and the physiology of the injection site," that deltoid injections "are absorbed faster than gluteal injections . . . likely due to the increased blood flow in the deltoid muscle . . .," and that "[intramuscular] injections are available in immediate-release formulations as well as depot formulations for sustained release." DTX-91

[27] As Defendant notes, although the parties presented two different editions of Goodman (*see* PTX-65, DTX-93), "the teachings relied on are the same in both." DFOF ¶ 226.

at 4–5; DFOF ¶¶ 221, 223–25. Defendant's argument fails to adequately address, however, that Gibaldi also teaches that depot injections are not indicated for treatment initiation, as claimed in the '906 Patent. Indeed, as Gibaldi expressly states, "[d]epot injections release the drug slowly" and "are long-acting dosage formulations indicated for maintenance treatment rather than initiation of therapy." DTX-91 at 5; *see also* PTX-64 at 38 (explaining that "[i]n the acute phase of schizophrenia, short-acting injections may be required because of their quick action," while "[i]n the maintenance phase of therapy for schizophrenia, administration of an atypical agent in a long-acting or depot dosage formulation may be desirable"). When Dr. Wermeling was questioned about this teaching on cross-examination, he admitted that Gibaldi "says that [about depot injections], but that's not my usage of Gibaldi." Trial Tr. (Wermeling) at 472:2–9. In other words, Dr. Wermeling's testimony suggests that he selectively relied on only some of Gibaldi's teachings in forming his opinion rather than the reference as a whole. The Federal Circuit has made clear, however, that the prior art "must be considered in its entirety, i.e., as a *whole*, including portions that would lead away from the invention in suit." *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987). Thus, when viewed as a whole, the Court cannot say that Gibaldi would motivate a POSA to initiate treatment using deltoid injections as directed in Claim 2.

Finally, Defendant contends that patient preference would have motivated a POSA to use deltoid administration. *See* Def. Br. at 20–21. This argument is not fully supported by the record. For example, as Dr. Gopal explained, the participants in the PSY-3007 study were divided "about half and half" between choosing deltoid and gluteal injections. Trial Tr. (Gopal) at 1180:20–1181:2 (explaining that "in the United States, the patients tend to prefer getting the injections in the arm because you don't have to pull down your pants and stigmatize yourself; whereas in other countries, like in Asia, they tend to be lighter, so they prefer getting the injection in the gluteal").

In addition, Gibaldi generally suggests administering depots in the gluteal muscle over the deltoid muscle "because [a deltoid injection] causes discomfort and pain at the injection site." DTX-91 at 15. Moreover, as Plaintiffs correctly note, even if some patients prefer deltoid injections, such preferences would suggest at most using deltoid administration on an individualized basis. Pls. Reply at 20. The '906 Patent, however, claims a generalized dosing regimen. In essence, Defendant's argument is that "a POSA would not have been dissuaded from deltoid injections," (Def. Br. at 26), but this assertion does not satisfy Defendant's burden. *See Endo Pharm. Sols., Inc. v. Custopharm Inc.*, 894 F.3d 1374, 1380 (Fed. Cir. 2018) ("To meet its burden, Custopharm needed to do more than merely show that the prior art does not preclude lowering the dose of TU."). Accordingly, the Court finds that Defendant has not established motivation to use deltoid injections by clear and convincing evidence.

ii. *Claim 2 – Unequal Loading Doses*

A second key feature of Claim 2 is the use of unequal loading doses. '906 Patent (DTX-1/PTX-1) col. 32:15–24. The Court also finds that Defendant has not met its burden of showing that a POSA would have been motivated to use unequal loading doses as claimed in the '906 Patent. According to Defendant, two articles by Dr. Larry Ereshefsky et al.—a 1990 article titled "Kinetics and Clinical Evaluation of Haloperidol Decanoate Loading Dose Regimen" ("Ereshefsky 1990") and a 1993 article titled "A Loading-Dose Strategy for Converting From Oral to Depot Haloperidol" ("Ereshefsky 1993")—and a 2001 article by Dr. James L. Karagianis et al. titled "Rapid Tranquilization With Olanzapine in Acute Psychosis: A Case Series" ("Karagianis") render the claimed regimens obvious. *See* Def. Br. at 24–25, 27, 29; DTX-88, -89, -96.

Defendant's argument fails for three reasons.[28] First, as their titles suggest, neither the Ereshefsky nor Karagianis references concern paliperidone palmitate; the Ereshefsky references involve haloperidol decanoate dosing, and Karagianis relates to oral olanzapine. Trial Tr. (Wermeling) at 312:17–313:20; DTX-88, -89, -96. As Dr. Sinko explained, because these references concern "different drugs and different formulations" than paliperidone palmitate, their "pharmacokinetics and how they act are . . . different." Trial Tr. (Sinko) at 1566:18–1567:5. Defendant's expert Dr. Wermeling agreed with this opinion. *See* Trial Tr. (Wermeling) at 513:17–24 (agreeing that "haloperidol decanoate and paliperidone palmitate have different PK or pharmacokinetic profiles"). Thus, a POSA would know that "you really can't correlate" their teachings to "an injectable version of paliperidone palmitate." Trial Tr. (Sinko) at 1566:18–1567:11.

Second, unlike the '906 Patent, the Ereshefsky and Karagianis references teach individualized, rather than generalized, dosing. Indeed, as Dr. Wermeling acknowledged at trial, Ereshefsky 1990 involved dosing patients "on an individual basis" (Trial Tr. (Wermeling) at 517:10–518:6), and Dr. Sinko similarly testified that Ereshefsky taught "patient-specific approaches" (Trial Tr. (Sinko) at 1569:18–1570:1, 1573:19–1574:13). Furthermore, Karagianis states that the patients in the case series were "not dosed according to a protocol-dosing regimen." DTX-96 at 4; *see also* Trial Tr. (Sinko) at 1577:4–12 (noting that patients in Karagianis received "a personalized dose"). This distinction between dosing approaches undercuts Defendant's argument that Ereshefsky and Karagianis would lead a POSA to the claimed dosing regimens.

[28] Defendant also cites Karagianis's teaching on "rapid neuroleptization," which Defendant characterizes as an "older loading dose strategy" involving very high doses of oral or short-acting injectables, to argue that Karagianis suggests using a high-loading dose strategy. DFOF ¶¶ 258–62; Trial Tr. (Kahn) at 2383:18–2384:11. This argument is unavailing. As Defendant's own expert Dr. Kahn explained, rapid neuroleptization "has nothing to do with the use of long-acting injectables" and treatment providers "don't do this anymore." Trial Tr. (Kahn) at 2382:8–2384:11.

Lastly, these references do not disclose unequal loading doses as claimed in the '906 Patent. Specifically, Defendant contends that Ereshefsky 1993 taught initiating therapy with unequal dose amounts. *See* Def. Br. at 27. While Ereshefsky 1993 does note that the loading dose was "administer[ed] . . . in two or more sequential injections" of "consecutive divided doses" for safety reasons, the reference does not teach the use of unequal loading dose amounts. DTX-89 at 4. To the contrary, it provides that patients received initial "consecutive divided doses of 100 to 200 mg every three to seven days until the full amount is given," and the haloperidol decanoate doses were not reduced until "the second and third months." *Id.*; Trial Tr. (Wermeling) at 322:17–323:1. Ereshefsky 1990 contains similar teachings. *See* DTX-88 at 3, 5–7 (citing case studies and disclosing initial "consecutive divided doses . . . until the full amount was administered").[29] Claim 2 of the '906 Patent, by contrast, directs two loading doses of unequal amounts of paliperidone palmitate. '906 Patent (DTX-1/PTX-1). Accordingly, the Court finds that a POSA would not have been motivated to create the Claim 2 dosing regimen in view of the prior art.

c) Claims 10 and 13 – Renal Impairment Claims

Claims 10 and 13 set forth dosing regimens for patients with renal impairment. Under these claims, renally impaired patients receive reduced loading doses of from about 75 mg-eq. of paliperidone palmitate in the deltoid muscle on both the first day of treatment and sixth to about tenth day of treatment, followed by successive monthly maintenance doses (± 7 days) of about 25 mg-eq. to about 75 mg-eq. in either the deltoid or gluteal muscle. *See* '906 Patent (DTX-1/PTX-1). According to Defendant, Claims 10 and 13 are obvious because several prior art references taught reduced doses for renal impairment. *See* Def. Br. at 36–38. The Court disagrees.

[29] Ereshefsky 1990 also notes that certain patients did not actually "receive a true loading dose" because those doses were "not given as a single injection." DTX-88 at 7.

First, the references on which Dr. Wermeling relied would not have motivated a POSA to achieve the claimed regimens. At trial, Dr. Wermeling testified that, in addition to the three primary prior art references (the '548 Protocol, the '544 Patent, and the WO'384 Publication), a combination of three other references teach "a 50 percent dose reduction from the maximum dose for patients with mild renal impairment." Trial Tr. (Wermeling) at 332:25–333:12; *see also* DFOF ¶ 375. The three additional references are a clinical trial abstract titled "PII-46[:] Effects of Renal Impairment on the Pharmacokinetic Profile of Paliperidone Extended-Release Tablets" (referred to by the parties as "Cleton 2007"), the Invega (paliperidone) Extended Release Tablets label (the "Invega ER Label"), and U.S. Patent Application No. 2007/0197591 (the "'591 Application"). Dr. Wermeling opined that based upon these three prior art references, "it would have been reasonable to do the 50 percent reduction for the loading dose strategy." Trial Tr. (Wermeling) at 333:9–12. Dr. Wermeling's conclusions, however, are unsupported by the record.

Cleton 2007 concerned orally administered paliperidone, rather than the LAI paliperidone palmitate at issue here. PTX-56; DTX-84; Trial Tr. (Sinko) at 1586:11–15; Trial Tr. (Wermeling) at 530:15–531:18 (admitting that Cleton 2007 is not "talking about an injectable paliperidone palmitate"). In addition, while Dr. Wermeling testified that Cleton 2007 teaches that "the two measures of exposure . . . the maximum concentration, . . . and the total exposure by AUC, as area under the curve, is basically doubling for patients who have renal impairment" and "would be a strong consideration for reducing the dose" in a renally impaired patient (Trial Tr. (Wermeling) at 330:19–331:9), his conclusion ignored that Cleton 2007 only suggests dose reductions for patients with moderate and severe renal impairment. Indeed, contrary to Dr. Wermeling's assertions, Cleton 2007 did not suggest a reduction in dosing for patients with mild renal impairment. PTX-56; DTX-84; Trial Tr. (Sinko) at 1586:12–1587:8 (explaining that Cleton 2007 suggests "no dose

reduction for mild renal impairment"). In contrast, the '906 Patent "focuses on mild renal impairment." Pls. Br. at 70.

Defendant's reliance on the Invega ER Label is similarly unavailing. Like Cleton 2007, the Invega ER Label concerns oral paliperidone, not injectable paliperidone palmitate. PTX-57; DTX-102; Trial Tr. (Wermeling) at 531:15–18. Additionally, while Defendant argues that the Invega ER Label can be read to suggest a 50 percent reduction from the **maximum** recommended dose for patients with normal renal function to the **maximum** recommended dose for patients with mild renal impairment (with Janssen challenging that suggestion), a POSA developing a dosing regimen would not start from the maximum recommended dose, but instead would start with the general recommended dose for patients with normal renal function. *See* Trial Tr. (Sinko) at 1587:20–22 ("[I]t's actually more appropriate to start with the recommended dose in healthy patients."); PTX-57 at 26; DTX-102 at 26. Furthermore, as Dr. Sinko convincingly testified, the label does not teach "just a straight 50 percent" reduction for dosing patients with renal impairment as it provides a range of maximum recommended doses that are dependent on a patient's level of renal impairment. Trial Tr. (Sinko) at 1587:20–1588:6.

Defendant further argues that the '591 Application teaches that doses must be reduced for patients with renal impairment. *See* Def. Br. at 37. As Defendant concedes, however, the '591 Application "is directed to . . . patients with hepatic (or liver) impairment," not renal impairment. *Id.* at 36; PTX-69; DTX-108. Moreover, while Defendant contends that the '591 Application teaches that paliperidone is excreted through the kidneys, this purported teaching does not, alone or in combination with Cleton 2007 as Defendant suggests, render the claimed regimens obvious. *See* Def. Br. at 36–37; DFOF ¶ 272. As explained above, the dosing regimens address patients with mild renal impairment, and neither the '591 Application nor Cleton 2007 expressly teach LAI

paliperidone palmitate dose reductions for mild renal impairment. *See* PTX-69; DTX-108; Trial Tr. (Sinko) at 1586:12–1587:8. Therefore, the Court finds that Cleton 2007, the Invega ER Label, and the '591 Application, whether considered individually or in combination, would not motivate a POSA to arrive at the claimed dosing regimens for patients with mild renal impairment.

Finally, even if the Court were to find that the prior art teaches a 50 percent dose reduction for patients with mild renal impairment, this teaching would not actually lead to the claimed invention. Indeed, if the 150/100 mg-eq. loading doses of Claim 2 were reduced by half, the regimen would consist of 75/50 mg-eq. loading doses, not 75/75 mg-eq. as claimed in the Patent-in-Suit. Thus, applying a 50 percent reduction would not yield the regimens disclosed in Claims 10 and 13.

d) Claims 20 and 21 – Paliperidone Palmitate Properties

Claims 20 and 21 recite the properties of the paliperidone palmitate formulation used in the claimed dosing regimens. *See* '906 Patent (DTX-1/PTX-1) col. 34:32–51. Specifically, these claims direct, among other things, that the sustained release depot formulation "is an aqueous nanoparticle suspension consist[ing] essentially of . . . paliperidone palmitate having an average particle size (d50) of from about 1600 nm to about 900 nm." *Id.* d50 refers to a distribution of particle size which indicates that 50 percent of the particles are below the reported size. DFOF ¶ 625. Defendant contends that a POSA would have been motivated to select the claimed particle sizes in view of the prior art. The Court is not persuaded.

Both parties' obviousness experts testified that particle size affects dosing strategy. *See, e.g.*, Trial Tr. (Wermeling) at 291:12–19 (noting that "the pharmacokinetic properties of such a formulation are derived from the formulation itself" and "if you wanted to impart changes in the pharmacokinetics, you could change the particle size"); Trial Tr. (Sinko) at 1544:1–6 (explaining

that particle size "controls the rate of dissolution, release and, ultimately, absorption for a formula like this"). Of the three primary prior art references—the '548 Protocol, the '544 Patent, and the WO'384 Publication—only the '548 Protocol discloses a treatment initiation regimen for paliperidone palmitate. *See* DTX-55. This reference, however, neither specifies the characteristics of the formulation used in the study, nor any information about the formulation's particle size. *See id.* Furthermore, while the two other primary art references discuss particle size for paliperidone palmitate formulations, they do not suggest that that these formulations are appropriate for a treatment initiation regimen. *See* DTX-54; DTX-72; Trial Tr. (Sinko) at 1538:2–1539:6, 1543:9–13, 1550:18–24, 2256:12–14; Trial Tr. (Wermeling) at 506:24–507:1, 511:15–512:8.

With respect to the '544 Patent, it describes four different paliperidone palmitate formulations, referred to as Formulations A, B, C, and D. DTX-54 cols. 8–9; Trial Tr. (Wermeling) at 483:3–11. The d50 particle sizes for the formulations reported in the '544 Patent are: (1) "Formulation A," d50 of 6030 nm; (2) "Formulation B," d50 of 1380 nm; (3) "Formulation C," d50 of 740 nm; and (4) "Formulation D," d50 of 520 nm. DTX-54 col. 9:25–31; Trial Tr. (Wermeling) at 486:23–487:11. Thus, only Formulation B has a d50 particle size that falls within the particle size limitations recited in the '906 Patent, which requires "an average particle size (d50) of from about 1600 nm to about 900 nm." '906 Patent (DTX-1/PTX-1) col. 34:32–51; Trial Tr. (Sinko) at 1530:15–1531:1.

A problem with Formulation B—the only formulation with a proper d50 particle size as claimed in the '906 Patent—is that the '544 Patent expressly teaches away from using this formulation based on its effective particle size limitations, which require that the formulation has a d90 particle size of "less than 2000 nanometers." DTX-54 cols. 3:42–44, 5:16–21, 9:25–31, 10:27–29. d90 is another form of measurement and refers to a distribution of particle size which

indicates that 90 percent of the particles are below the reported size. DFOF ¶ 625. Formulation B has a d90 particle size of 6830 nm, which is significantly above 2000 nm. DTX-54 col. 9:25–31. Consequently, as Dr. Sinko credibly opined, a POSA considering the '544 Patent would have been dissuaded from selecting Formulation B. *See* Trial Tr. (Sinko) at 1783:4–1785:1 (testifying that a POSA would "eliminate . . . [Formulation] B" from further consideration based on "the two critical parameters, the particle size and the specific surface area" taught in the '544 Patent).[30] Thus, because the prior art "must be considered in its entirety, i.e., as a *whole*, including portions that would lead away from the invention in suit," the Court finds that the '544 Patent would not motivate a POSA to arrive at the claimed particle size. *Panduit Corp.*, 810 F.2d at 1568.

Defendant argues that Formulation C, having a d50 of 740 nm, would also motivate a POSA to select the claimed particle size ranges. *See* Def. Br. at 34. This argument is unpersuasive. As Plaintiffs correctly note, Dr. Wermeling's opinion that Formulation C's d50 particle size of 740 nm is covered by the '906 Patent is contradicted by Defendant's own assertion in its proposed findings of fact that a "d50 of 600–800 nm" is "outside the claimed range." Pls. Reply Br. at 22; *compare* Trial Tr. (Wermeling) at 494:16–22 (testifying that he "would consider 740 [to be] in the range" of the claimed "about 900 nanometers" d50 particle size), *with* DFOF ¶ 527 (arguing that the [redacted]).

Finally, Defendant's argument that the WO'384 Publication, in combination with the '544 Patent, would motivate a POSA to arrive at Claims 20 and 21 is unavailing. *See* Def. Br. at 34–36.

[30] Formulations C and D were also "the only formulations that were tested for stability." Trial Tr. (Wermeling) at 491:14–22; DTX-54 col. 9:33–35. As Dr. Sinko explained, a POSA would have understood that the selection of Formulations C and D for stability testing suggests that they "had the most promising attributes that you want to study further." Trial Tr. (Sinko) at 1529:24–1530:8.

By Defendant's own concession, the WO'384 Publication "made no new disclosure on particle size," and a POSA would refer back to the '544 Patent's teachings on particle size. *Id.* at 23, 34–36; *see also* DTX-72. Indeed, Dr. Wermeling agreed at trial that the WO'384 Publication discussed measurements of raw materials before milling, and "none of [the 32 measurements for particle size described in the WO'384 Publication] have a d50 of between about 1600 and 900 nanometers." Trial Tr. (Wermeling) at 511:10–14. Dr. Wermeling further agreed that the WO'384 Publication teaches that "what you want is an average particle size d90 of less than 2000 nanometers corresponding to a specific surface area greater than 4 meters squared per gram"—the same teaching as the '544 Patent. *Id.* at 560:24–561:5; DTX-72 at 6. Thus, the WO'384 Publication does not alter the Court's analysis, and Defendant has failed to show that a POSA would have been motivated to select the claimed particle size.

3. A POSA Would Not Have a Reasonable Expectation of Success in Arriving at the Claimed Dosing Regimens

In addition to motivation, "[a]n obviousness determination requires that a skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art." *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1362 (Fed. Cir. 2009); *see also Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) ("A party seeking to invalidate a patent based on obviousness must demonstrate '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.'") (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007). The Federal Circuit has noted that "[t]he presence or absence of a reasonable expectation of success is . . . a question of fact." *Novartis Pharm. Corp. v. W.-Ward*

Pharm. Int'l Ltd., 923 F.3d 1051, 1059 (Fed. Cir. 2019) (internal citation and quotation marks omitted). The Court finds that Defendant has not met its burden for several reasons.

First, the unpredictability of developing treatment initiation regimens using LAIs supports a finding of nonobviousness. The Federal Circuit has noted that "evidence showing unpredictability in the art" suggests "that one of ordinary skill would not have been motivated to combine the references with a reasonable expectation of success." *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. DE C.V.*, 865 F.3d 1348, 1354 (Fed. Cir. 2017). Moreover, "even if it was obvious to experiment with [certain] options," an invention is not obvious where "there is nothing to indicate that a skilled artisan would have had a reasonable expectation that such an experiment would succeed." *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1357 (Fed. Cir. 2013) (internal citation and quotation marks omitted). Here, the record establishes that developing a generalized multi-dose regimen using an LAI to initiate therapy was an unpredictable process. As Dr. Wermeling acknowledged, there were "a large number of possibilities for combining" the dose amounts disclosed in the '548 Protocol with "different injection sites." Trial Tr. (Wermeling) at 473:19–474:19. He further testified that different injection sites, dosing intervals, and dose amounts can affect therapeutic blood levels. *Id.* at 279:3–8; 312:7–16. While Dr. Wermeling opined that the WO'384 Publication disclosed a safe and effective dosing range of 25 to 150 mg-eq., he did not credibly explain how a POSA could expect to develop effective multi-dose treatment regimens, such as those claimed in the '906 Patent, from this range. *Id.* at 321:23–322:13. Indeed, as noted above, Dr. Wermeling clearly stated that the WO'384 Publication itself "does not disclose anything about a dosing regimen," does not discuss deltoid or gluteal administration, and

does not "point you in the direction of giving a Day 1 dose of 150 mg equivalents in the deltoid and a second dose in the deltoid of 100 mg equivalents on Day 6 to 10." *Id.* at 511:15–512:8.

The record further indicates that, in contrast to single doses, multi-dose regimens must account for effects like "accumulation" and "fluctuations [in a patient's blood levels] between administrations." Trial Tr. (Sinko) at 1597:17–1600:10. Therefore, to successfully arrive at a multi-dose regimen based on the prior art, a POSA would need safety, efficacy, and pharmacokinetic data in order to evaluate how a generalized dosing regimen would perform in patients. *See Id.* at 1583:24–1584:16 (noting that without "this triumvirate of pharmacokinetics, efficacy and safety [data], you have no way to understand if some random combination of elements would lead to an effective dosing regimen"). The prior art, however, contained no such data. *Id.* at 1582:19–1583:18. While Dr. Wermeling testified that the '548 Protocol involved a Phase III trial, which is a clinical trial that "use[s] doses that are thought to be safe and effective," he admitted that this reference is "a protocol without any results." Trial Tr. (Wermeling) at 316:4–23, 423:20–21. Moreover, as Dr. Wermeling conceded, "most drugs fail" the drug development process. *Id.* at 543:7–10. On these facts, and given the difficulty the Janssen inventors encountered during the invention process described in detail above, the Court finds that the unpredictability of the art weighs against a reasonable expectation of success. *See Sanofi v. Watson Lab'ys Inc.*, 875 F.3d 636, 641, 646–50 (Fed. Cir. 2017) (affirming finding of no reasonable expectation of success where prior art disclosed large-scale clinical trial's hypothesis but not results); *Endo Pharm. Inc. v. Actavis LLC*, 922 F.3d 1365, 1377 (Fed. Cir. 2019) (noting that finding of no reasonable expectation of success was "further supported by the fact that the inventors of the '779 patent

engaged in extensive experimentation, involving much failure, to ultimately produce the oxymorphone of the Asserted Claims").

In addition, a POSA would not have had a reasonable expectation of successfully initiating treatment with LAI loading doses in view of the prior art. For instance, as discussed above, the Gibaldi reference on which Dr. Wermeling relies expressly teaches that "[d]epot injections are . . . indicated for maintenance treatment rather than initiation of therapy." DTX-91 at 5. Moreover, as set forth in detail below, both parties' experts agreed that the traditional dosing paradigm for treating schizophrenia used lower initial doses followed by slow upward adjustments. *See, e.g.*, Trial Tr. (Kahn) at 168:19–169:5 (for dosing risperidone, it is "recommended" to begin with an "initial dose" and then "work your way up in small increments until you get to your target dose or your effective dose range"); Trial Tr. (Kohler) at 1905:12–17 (explaining that the initial dose of Risperdal Consta "was limited to 25 milligrams or less, which was in many people not the eventual dose required to manage the psychosis," followed by subsequent higher doses weeks later). The Goodman reference also instructed initiating low doses of risperidone and watching for side effects as dose amounts are increased. *See* DTX-93 at 339 ("Low doses of risperidone have been reported to attenuate negative symptoms of schizophrenia with a low incidence of extrapyramidal side effects. Extrapyramidal effects are commonly seen, however, with doses of risperidone in excess of 6 mg/day."). Even the FDA and an external panel of experts suggested that Janssen use lower initial doses. PTX-92 at 1, PFOF ¶¶ 57–58; PTX-94 at 59, 61. Contrary to the prior art teachings and traditional dosing strategy, the '906 Patent claims high-loading dose regimens using

depot injections. Thus, the Court is not persuaded that a POSA would have had a reasonable expectation of successfully achieving the claimed regimens.[31]

4. The Cleton 2008 References Support a Finding of Nonobviousness

Defendant contends that four additional references—two abstracts published in *Clinical Pharmacology & Therapeutics* in March 2008 titled "PI-74" and "PI-75" and two corresponding posters allegedly presented at an April 2008 conference (collectively, "Cleton 2008")—render Claim 2 obvious. Def. Br. at 33–34; DTX-18, -19, -20.[32] Plaintiffs counter that the Cleton 2008 references are not prior art because the claimed invention antedated them and the inventors had possession of the information disclosed in the references prior to their publication. Pls. Br. at 58–64. The Court finds that even if it considers the Cleton 2008 references, they weigh in favor of nonobviousness.[33]

[31] No additional showing has been required of Teva despite its presentation of testimony and argument concerning motivation to alter the prior art in order to achieve rapid and long-term efficacy with paliperidone palmitate. *See, e.g.*, Trial Tr. (Wermeling) at 469:2–470:13 (Dr. Wermeling agreed that the '906 Patent claims dosing regimens that provide both "rapid efficacy" and "long-term efficacy."); 311:18–23 (testifying that a POSA would be motivated to modify the '544 Patent and WO'384 Publication to "accelerate the onset of effect"); 321:1–22 (noting that a POSA "would be motivated to use the maximum effective and safe dose" when initiating treatment of an "acutely agitated" patient). Nonetheless, a party raising an argument at trial places that argument at issue. *See Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1066 (Fed. Cir. 2020), cert. denied, 209 L. Ed. 2d 751 (May 17, 2021) (rejecting post-trial argument due to party's focus on challenged issue during trial).

[32] The Cleton 2008 references all reflect work done by or associated with Janssen. *See* DFOF ¶¶ 287, 298; Pls. Br. at 58–59.

[33] Janssen offers strong arguments in support of its view that Cleton 2008 is not prior art. Pls. Br. at 58–64. Janssen asserts that the claimed invention was conceived and reduced to practice in the Summer of 2007 prior to the publication of Cleton 2008, citing to testimony and evidence from Drs. Gopal and Samtani. *Id.* at 61. As discussed later in this Opinion, Janssen is seeking to add Drs. Gopal and Samtani as inventors of the '906 Patent. Janssen further contends, citing to the '918 Provisional as evidence, that the inventors had possession of the information disclosed in Cleton 2008 before these references were published. *Id.* at 63–64. Regardless, even considering the Cleton 2008 references as prior art does not alter this Court's analysis regarding obviousness.

PI-74 and its corresponding poster do not support Defendant's obviousness arguments because they relate to a single-dose, rather than multi-dose, regimen. *See* DTX-18, -19. As Dr. Wermeling noted, PI-74 "is a single dose [proportionality] study" in which "[e]ach subject received a single injection of paliperidone palmitate" in "either the deltoid or the gluteal muscle." Trial Tr. (Wermeling) at 378:3–12; *see also* DTX-18, -19. Unlike the dosing regimens claimed in the '906 Patent, PI-74 did not involve any loading or maintenance doses. Trial Tr. (Wermeling) at 378:13–21. Moreover, Dr. Wermeling allowed that PI-74 neither contains efficacy data nor "disclose[s] giving a Day 1 loading dose of 150 mg. equivalents in the deltoid and a second loading dose in the deltoid of 100 mg. equivalents on Days 6 to 10." Trial Tr. (Wermeling) at 392:9–18.[34] As discussed above, multi-dose regimens like the claimed invention differ from single doses because they need to account for "accumulation," and "fluctuations [in a patient's blood levels] between administrations." Trial Tr. (Sinko) at 1597:17–1600:10. To develop an effective multi-dose regimen, a POSA would need efficacy data, which these references lack. *See Id.* at 1583:24–1584:16, 1605:17–1606:25. Thus, when viewed as a whole, the Court cannot say that this reference renders the claimed invention obvious.

Similarly, the Court finds that PI-75 and its corresponding poster would not change the obviousness analysis. PI-75 concerns a "fixed-dose" study of four equal doses of 100 mg-eq. of

[34] The Court also notes that Cleton 2008 would not create a reasonable expectation of success. DTX-18, -19, -20. Contrary to Defendant's assertion that "Cleton 2008 provides the confirmatory data that Dr. Sinko desired" (Def. Br. at 33), none of these references contain efficacy data. *See* Trial Tr. (Wermeling) at 392:9–13, 408:23–25; Trial Tr. (Sinko) at 1603:11–20; DTX-18, -19, -20. At most, Cleton 2008 discloses average pharmacokinetic data, not patient-level data. Without efficacy data, a POSA would "have to do . . . controlled clinical studies to prove that those [target blood] levels were actually effective." Trial Tr. (Sinko) at 1540:5–1541:9; *see also id.* at 2134:1–2134:11 (noting that "the correlation between the target range and what a clinical investigator determines is efficacy is not straightforward" and the two "may not be linked"). Thus, the Court finds that Cleton 2008 does not change the above analysis.

paliperidone palmitate administered in either the deltoid or gluteal muscle on days 1, 8, 36, and 64. DTX-18; Trial Tr. (Wermeling) at 394:6–395:4. Similar to PI-74, PI-75 does not contain any efficacy data that would motivate a POSA to modify the reference's equal dose regimen to arrive at the dose regimens claimed in the '906 Patent. Trial Tr. (Sinko) at 1603:11–20, 1604:7–10; *see also* Trial Tr. (Wermeling) at 396:10–16 (conceding that "PI-75 [does not] give any indication as to whether the first dose of 100 mg equivalence was effective or ineffective"). Moreover, PI-75 and its corresponding poster would dissuade a POSA from using deltoid injections. Indeed, as Dr. Wermeling allowed, PI-75 disclosed "more fluctuation in drug content in the blood" and "more variation in drug absorption between different individuals when they were injected in the deltoid as opposed to the gluteal muscle." Trial Tr. (Wermeling) at 397:12–21. The corresponding poster makes similar disclosures. *See* DTX-20 at 6–7 (noting higher incidence of adverse events, "clinically relevant difference" in injection site pain, and greater fluctuation index for deltoid treatment group compared to gluteal treatment group). As Dr. Sinko credibly explained, a POSA would "want to keep . . . fluctuations at a minimum because that means changes in blood levels," which can "correspond[to] . . . toxicity." Trial Tr. (Sinko) at 1601:13–21, 1605:7–14. Accordingly, given the "higher fluctuation index and larger subject variability," a POSA considering PI-75 "would not look at injecting into the deltoid." *Id.* at 1605:7–14. Thus, the Court finds that the Cleton 2008 references support a finding of nonobviousness.[35]

5. Objective Indicia of Nonobviousness

As part of its obviousness analysis, the Court must also consider evidence regarding objective considerations of nonobviousness when present. *In re Cyclobenzaprine Hydrochloride*

[35] Defendant also contends that the claimed regimens are obvious in view of another poster reporting on the results of the SCH-201 Phase II trial ("Kramer"). *See* Def. Br. at 17–18, 30. Plaintiffs assert that the Court should not consider Kramer because: (1) it was not disclosed in Defendant's obviousness contentions, expert reports, or the trial testimony of its experts; and (2) it

Extended-Release Capsule Patent Litig., 676 F.3d 1063, 1075–77 (Fed. Cir. 2012). Such evidence is used to "guard against slipping into use of hindsight, . . . and to resist the temptation to read into the prior art the teachings of the invention in issue." *Graham*, 383 U.S. at 36 (internal citation and quotation marks omitted). Secondary considerations such as unexpected results, commercial success, long felt but unsolved needs, and the failure of others may be relevant indicia of nonobviousness. *See id.* at 17–18; *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1380 (Fed. Cir. 2006). Moreover, evidence of copying, industry praise, and skepticism may also be considered. *See Diamond Rubber Co. v. Consol. Rubber Tire Co.*, 220 U.S. 428, 441 (1911); *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1335 (Fed. Cir. 2016); *Geo. M. Martin Co. v. Alliance Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1304–05 (Fed. Cir. 2010).

Plaintiffs presented evidence of certain objective indicia that they argue support a finding of nonobviousness. A number of witnesses opined on the existence of these objective indicia including, for the Plaintiffs, (1) Dr. Srihari Gopal; (2) Dr. An Vermeulen; (3) Dr. Mahesh Samtani; (4) Dr. Christian Kohler; and (5) Ms. Carla Mulhern (Final Pretrial Order at 29–31, 38); and for the Defendant, (1) Dr. René Kahn; and (2) Mr. Ivan Hofmann (Final Pretrial Order at 39, 43).[36] While both parties offered evidence on the issue of secondary considerations, the burden always remains on Defendant to prove by clear and convincing evidence that the claimed invention is obvious. *In re Cyclobenzaprine Hydrochloride,* 676 F.3d at 1075–79 (concluding that, when considering secondary considerations of nonobviousness, the burden never shifts to the patentee

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was found not to be prior art in a parallel foreign litigation in Canada. Pls. Reply at 14–15, 23–24. While the Court acknowledges Janssen's assertions and fairness concerns, even considering the Kramer reference, the Court's obviousness analysis would be unaltered because, unlike the '906 Patent, Kramer discloses equal doses injected into the gluteal muscle only.

[36] These witnesses' relevant backgrounds and qualifications have been described in earlier sections of this Opinion.

to prove nonobviousness and instead always remains on the party challenging the validity of the patent to prove by clear and convincing evidence that the patent at issue is obvious).

As to the objective indicia, Defendant challenges whether there is a sufficient nexus between the merits of the claimed invention and the objective evidence. Plaintiffs counter that the appropriate nexus between the objective evidence and the claims of the '906 Patent is present. Here, the Court finds that the secondary considerations have a sufficient nexus to the claimed invention because the proffered evidence is linked to the high loading dose deltoid injections and subsequent maintenance injections described in the '906 Patent.[37] *See WBIP, LLC*, 829 F.3d at 1330 (internal citations and quotation marks omitted) ("Where the allegedly obvious patent claim is a combination of prior art elements, we have explained that the patent owner can show that it is the claimed combination as a whole that serves as a nexus for the objective evidence; proof of nexus is not limited to only when objective evidence is tied to the supposedly 'new' feature(s)."); *Tokai Corp. v. Easton Enters., Inc*., 632 F.3d 1358, 1369–70 (Fed. Cir. 2011) (concluding that, to establish a nexus to the merits of a claimed invention, the offered secondary consideration must actually result from what is both claimed and novel in the patent). To the extent more specific arguments concerning nexus were made by the parties, such assertions are addressed in the relevant sections.

a) Unexpected Results

Unexpected or surprising results can support nonobviousness. To demonstrate unexpected results, a party must "show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected." *In*

[37] Because the Court finds that there is a nexus between the claimed invention and the objective indicia, the Court need not address Janssen's argument that a presumption of nexus should apply here (Pls. Br. at 42).

re Soni, 54 F.3d 746, 750 (Fed. Cir. 1995). "The principle applies most often to the less predictable fields, . . . where minor changes in a product or process may yield substantially different results." *Id.* Furthermore, "when unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 970 (Fed. Cir. 2006) (internal citation and quotation marks omitted). Plaintiffs assert that the claimed dosing regimens produced the unexpected outcome of a second-generation LAI that successfully treated schizophrenia and other psychotic disorders without the need for oral supplementation, due to the dosing regimens' use of high initial loading doses to achieve rapid efficacy and monthly maintenance doses to achieve sustained efficacy. Pls. Br. at 45–46. Defendant disagrees that these properties were unexpected. Def. Br. at 54–58.

The Court finds that the Representative Claims led to unexpected results. Prior to the invention of Invega Sustenna, the conventional wisdom for both first-generation and second-generation antipsychotics was to "start low and go slow." PFOF ¶ 163 (internal citation and quotation marks omitted). Indeed, experts for both Plaintiffs and Defendant agreed that the traditional dosing paradigm for treating schizophrenia involved beginning with lower doses and slowly making upward adjustments. *See* Trial Tr. (Kahn) at 168:19–169:5 (for dosing risperidone, it is "recommended" to begin with an "initial dose" and then "work your way up in small increments until you get to your target dose or your effective dose range"), 2392:23–2393:1 (according to label, "the preferred approach" for dosing haloperidol decanoate "is to begin with lower initial doses and to adjust the dose upward as needed"); Trial Tr. (Kohler) at 1905:12–17 (explaining that initial dose of Risperdal Consta "was limited to 25 milligrams or less, which in many people was not the eventual dose required to manage the psychosis," followed by subsequent higher doses weeks later). Moreover, as the Gibaldi prior art reference indicated, "[d]epot

injections are long-acting dosage formulations indicated for maintenance treatment rather than initiation of therapy." PTX-64 at 5. The claimed dosing regimens run contrary to these prior art teachings because they use depot injections of high, rather than low, loading doses to initiate treatment.

In addition, as explained above, the claimed invention also led to unexpected results in view of the '548 Protocol prior art reference. In multi-dose regimens, such as those covered by the Representative Claims, there are many possible combinations of dose amounts, schedule, and sites of administration. PFOF ¶ 248. The '548 Protocol, which Defendant identifies as one of the closest prior art references, tested three different combinations of equal doses of paliperidone palmitate administered in the gluteal muscle and failed to properly initiate treatment in a rapid manner to aid with treatment adherence. *Id.* ¶ 249. By contrast, the '906 Patent regimens, which are comprised of high loading doses that must be administered in the deltoid muscles for the first two doses, succeeded. *Id.* ¶ 60. Therefore, the Court finds that in view of the prior art, the claimed invention led to unexpected results.

Defendant's primary argument against a finding of unexpected results is that "the alleged difficulties Janssen faced during development were avoidable." Def. Br. at 55. This argument is unpersuasive. As set forth above, Plaintiffs' inventors expected the Phase III clinical trials to be a success, especially because they built on the promising results of the SCH-201 study, which showed rapid efficacy. PFOF ¶ 36. Contrary to their expectations, however, the inventors encountered several clinical failures during Phase III, including a "high dropout rate" of patients discontinuing treatment because of "lack of efficacy." Trial Tr. (Vermeulen) at 784:3–10, 793:12–794:5; *see also* PTX-284 at 66–67. The evidence at trial showed that Invega Sustenna improved patient treatment adherence through its use of high initial loading doses that rapidly achieved

therapeutic concentrations of paliperidone palmitate and monthly loading doses which maintained these concentrations. Trial Tr. (Kohler) at 1910:9–1912:13 (Dr. Kohler providing a detailed and persuasive analysis of the benefits of Invega Sustenna); *see also* PTX-627 at 51. Such a "difference between an effective and safe drug and one with significant side effects that caused many patients to discontinue treatment" has been found to "constitute an unexpected difference in kind." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1307 (Fed. Cir. 2015). Thus, the unexpected results indicator weighs in favor of nonobviousness.

b) Skepticism

"Evidence of industry skepticism" is relevant to the obviousness inquiry. *WBIP, LLC*, 829 F.3d at 1335. "If industry participants or skilled artisans are skeptical about whether or how a problem could be solved or the workability of the claimed solution, it favors non-obviousness." *Id.* The Federal Circuit has "recognize[d] a range of third-party opinion that can constitute skepticism," including "testimony that third parties were 'worried' or 'surprised'" as "sufficient to establish skepticism." *Neptune Generics, LLC v. Eli Lilly & Co.*, 921 F.3d 1372, 1378 (Fed. Cir. 2019) (citing *Circuit Check Inc. v. QXQ Inc.*, 795 F.3d 1331, 1337 (Fed. Cir. 2015)).

Here, Plaintiffs have proffered evidence of skepticism that supports a finding of nonobviousness. The trial record indicates that on February 28, 2007, in response to Janssen scientists' proposal of the dosing regimen of 150 mg-eq. on the first day of treatment and 100 or 50 mg-eq. on the eighth day, a panel of external advisors "expressed their opinion" that a lower dosing regimen with "lesser risk" should be considered. PTX-92 at 1.

These external advisors were not the only industry participants to express doubt regarding aspects of the claimed invention. Indeed, after Janssen initially applied for regulatory approval of a dosing regimen of "100/100 mg-eq., day 1/8, deltoid dosing regimen" in October 2007, the FDA suggested that Janssen use even lower initiation doses starting at 75 mg-eq. up to 100 mg-eq. on

the first and eighth days of treatment. PFOF ¶¶ 57–58; PTX-94 at 59, 61. Although the FDA's recommendation comported with the "start low, go slow" conventional wisdom of the time (*see* PTX-808 at 3 (internal quotation marks omitted)), it also evidenced skepticism toward the high-loading dose strategy later claimed in the '906 Patent.

Moreover, even after Invega Sustenna received FDA approval, treating psychiatrists had reservations about the claimed dosing regimens. *See* Trial Tr. (Kohler) at 1907:2–1908:4 (credibly explaining that when Invega Sustenna first became available, psychiatrists found the treatment initiation guidelines "unusual," "very different from what we had been familiar and, to some extent, comfortable with," and thought it might "lead to side effects that would prevent the person from continuing with treatment"). Such concerns weigh in favor of nonobviousness. *See Neptune Generics, LLC*, 921 F.3d at 1378 (affirming finding of skepticism based on FDA concerns); *Cir. Check Inc.*, 795 F.3d at 1337 (testimony that customers were "worried" about using claimed invention supported finding of skepticism).

Defendant's arguments against a finding of skepticism are unpersuasive. Defendant contends that Plaintiffs have failed to establish skepticism because: (1) they rely on inadmissible hearsay from fact witness testimony; and (2) the FDA's statements were merely advice in keeping with its regulatory duties, rather than skepticism. *See* Def. Br. at 52–54. With respect to Defendant's first argument, the Court finds that even if it were to exclude the testimony cited by Plaintiffs regarding the outside experts' concerns as inadmissible hearsay,[38] Plaintiffs nevertheless proffered sufficient evidence of the panel's skepticism in the form of meeting minutes. *See* PTX-

[38] Dr. Gopal testified, for example, that in regard to the 150 mg-eq. day 1 and 100 mg-eq. day 8 dosing regimen, outside experts "didn't think it was necessary. They thought it actually was risky. They thought that the dose was too high and that we should go for a lower dose." Trial Tr. (Gopal) at 1075:14–16.

92. These minutes, which relate to the February 28, 2007, "Clinical Pharmacokinetic and Dosing Advisory Board Meeting," documented the outside experts' skepticism of a high-dosing regimen, rather than, as Defendant argues, merely the probability of receiving regulatory approval. They are an admissible business record under Federal Rule of Evidence 803(6). *See* Fed. R. Evid. 803(6) (recognizing exception to rule against hearsay for records of regularly conducted activities);[39] PTX-92 at 1 (noting that compared with the "[p]roposed dosing regimen," "[a] more acceptable regimen from a regulatory viewpoint would be 100 mg eq. (Day 1) followed by either 100 or 50 mg eq. on Day 8" because it "provides therapeutic concentrations early and in a safe range").

Defendant's contention regarding the FDA's statements is similarly unavailing. According to Defendant, the FDA's suggestion of a 75 mg-eq. dose is not probative of skepticism, but instead "'reflect[ed] attention to the FDA's normal duties ensuring the safety and efficacy of new drugs.'" Def. Br. at 53 (quoting *Bayer Healthcare Pharm., Inc. v. Watson Pharm., Inc.*, 713 F.3d 1369, 1377 (Fed. Cir. 2013)). Defendant's reliance on *Bayer*, however, is misplaced. In *Bayer*, the Federal Circuit found an FDA request for efficacy and safety data regarding an element of the proposed dosing regimen insufficient to establish skepticism. *Bayer Healthcare Pharm., Inc.*, 713 F.3d at 1377. The *Bayer* court concluded that the FDA's request was in keeping with the agency's

[39] "The business records exception allows admission of records of regularly conducted activity through the testimony of a custodian or other qualified witness," if the records meet the other requirements of Federal Rule of Evidence 803(6). *Crash Dummy Movie, LLC v. Mattel, Inc.*, 601 F.3d 1387, 1392 (Fed. Cir. 2010) (citing Fed. R. Evid. 803(6)). At trial, Dr. Samtani confirmed that PTX-92 contains the minutes of Janssen's February 28, 2007, meeting with the external advisors, which he attended, and the Court finds that Plaintiffs have laid a sufficient foundation for the admission of the minutes as a business record. *See* Trial Tr. (Samtani) at 1346:16–1347:2. Furthermore, the Court finds that Defendant has not met its burden of showing that the meeting minutes "indicate a lack of trustworthiness," as required for exclusion under Rule 803(6). Fed. R. Evid. 803(6). Finally, and in any event, both parties agree that PTX-92 may be admitted to show its effect on the listener, rather than for its truth. *See* Trial Tr. (Gopal) at 1074:16–1076:3; Fed. R. Evid. 801(c)(2) (excluding only out-of-court statements offered "to prove the truth of the matter asserted in the statement"). Therefore, the Court will consider the minutes in its analysis.

regulatory duties "requiring actual data to corroborate statements in a new drug application" and "in no way indicates that FDA experts would have been surprised to receive such data." *Id.* Here, by contrast, the FDA's statement is not a simple request for data, but rather a recommendation to move away from the high-loading dose strategy proposed by Janssen. *See* PTX-94 at 59, 61. As the FDA's suggestion concerned aspects of the invention at issue, the Court finds that it is evidence of industry skepticism and weighs in favor of nonobviousness. *See Neptune Generics, LLC*, 921 F.3d at 1378 (affirming skepticism finding based on FDA's disagreement with patentee's proposed course of action during clinical trial).

c) Praise

"Evidence that the industry praised a claimed invention or a product which embodies the patent claims weighs against an assertion that the same claim would have been obvious. Industry participants, especially competitors, are not likely to praise an obvious advance over the known art." *WBIP, LLC*, 829 F.3d at 1334; *see also Institut Pasteur & Universite Pierre Et Marie Curie*, 738 at 1347 (noting that "industry praise . . . provides probative and cogent evidence that one of ordinary skill in the art would not have reasonably expected [the invention at issue]"). Plaintiffs identify several sources of industry praise in support of their position, including Dr. Kohler's testimony that Invega Sustenna is his "first choice" LAI, trade publication articles, an FDA employee's remarks at a 2013 industry conference, and Invega Sustenna's nomination for the Prix Galien award. Pls. Br. at 49–50; PFOF ¶ 208. The Court finds that certain of the cited trade publications are the most probative evidence of praise, while affording lesser weight to others.

At trial, Plaintiffs introduced articles touting the benefits of Invega Sustenna. One such article is titled "New Label for LAI Paliperidone Breaks FDA Ground by Including Real-World Data" from the trade publication *Psychiatric News*. This article noted that the results of the Paliperidone Palmitate Research In Demonstrating Effectiveness study indicated that "the average

time before any treatment failure was about six months longer in the LAI group compared with the oral antipsychotic group." PTX-131 at 1, 3. According to the article, "[t]he improvements seen were due in part to better adherence rates of the medication, which is an advantage of LAIs as the medication is administered at clinics." *Id.*; *see also* PFOF ¶ 206. Another article, published by Thomas R. Einarson et al. in the *Journal of Medical Economics*, stated that "[s]ince [paliperidone palmitate]-LAI is the drug with the lowest cost per patient treated and the highest number of [quality adjusted life years], it dominates the other two atypical antipsychotic depots" and "should be considered the drug of choice in many situations." PTX-134 at 5. While Defendant asserts that the results discussed in Einarson were limited to the Czech Republic (*see* Def. Br. at 50–51), the Court finds that the article nevertheless amounts to praise of the claimed invention.

Plaintiffs point to two other articles as evidence of industry praise. Pls. Reply Br. at 41. The first article, "Efficacy and Safety Profile of Paliperidone Palmitate Injections in the Management of Patients with Schizophrenia: An Evidence-Based Review" (PTX-133), reported on clinical trials confirming the importance of Invega Sustenna's high initial loading doses. *See* Trial Tr. (Kahn) at 2412:9–20. The second article, "Paliperidone palmitate: a new long-acting injection for schizophrenia" (PTX-506), noted advantages to using Invega Sustenna over Risperdal Consta. *See* Trial Tr. (Kahn) at 2422:1–4. Defendant notes that both articles were funded or reviewed by Janssen. *See* Def. Br. at 51. Nevertheless, the Court acknowledges Plaintiffs' contention that these articles were peer-reviewed and data driven (*see* Pls. Reply Br. at 41) and finds that Defendant has not provided persuasive evidence of bias or improper influence by Janssen sufficient to reject these articles entirely.

Similarly, Janssen argues that the selection of Invega Sustenna as a finalist for the Prix Galien award is evidence of industry praise. Pls. Br. at 49. The Court acknowledges the Prix

Galien is an important award that has been compared to the Nobel Prize in the pharmaceutical world. PFOF ¶¶ 188, 208. While Teva raised issues regarding who nominated Invega Sustenna for this award, the Court gives some weight to this item given Janssen was a finalist.[40] *See, e.g.*, *Genzyme Corp. v. Dr. Reddy's Lab'ys, Ltd.*, No. 13-1506, 2016 WL 2757689, at *15 (D. Del. May 11, 2016), aff'd, 716 F. App'x 1006 (Fed. Cir. 2017).

d) Copying

It is well settled that the copying of an invention can be indicative of nonobviousness. *Diamond Rubber*, 220 U.S. at 440–41 (finding "imitation" of a certain tire as a "concession to its advance beyond the prior art and of its novelty and utility"). Generally, copying is not considered evidence of nonobviousness in the ANDA context "because a showing of bioequivalence is required for FDA approval." *Bayer Healthcare Pharm., Inc.*, 713 F.3d at 1377 (citing *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 377 F. App'x 978, 983 (Fed. Cir. 2010)). Copying may, however, be probative of nonobviousness where the generic manufacturer "rel[ies] on the accused process." *Merck Sharp & Dohme Corp. v. Hospira, Inc.*, 874 F.3d 724, 728, 731 (Fed. Cir. 2017) (finding evidence of copying where defendant "tried five alternative formulations in an attempt to avoid copying" before relying on patent owner's process because the "[Hatch-Waxman] Act does not . . . require the generic manufacturer to copy the NDA holder's process of *manufacturing* the drug"); *see also Dey, L.P. v. Teva Parenteral Meds., Inc.*, 6 F. Supp. 3d 651, 681 (N.D.W. Va. 2014), *aff'd sub nom. DEY LP v. Teva Parenteral Meds., Inc.*, 600 F. App'x 773 (Fed. Cir. 2015) (Copying was established where "Teva could have developed its own solution using different excipients, but instead chose to reverse engineer Dey's formulation based on Dey's patents. This

[40] To the extent that Invega Sustenna's market share is also presented as evidence corroborating industry praise of the drug as a "first choice" LAI (Pls. Br. at 49), the Court discusses this factor in its commercial success analysis.

provides a strong indication that the prior art provided Teva with no obvious alternative to Dey's invention.").

Here, Plaintiffs have proffered evidence of copying and the Court affords some limited weight to this factor to support the nonobviousness conclusion the Court independently reaches. In its ANDA submission, Defendant stated that the [redacted] PTX-26 at 176; PFOF ¶ 209. While Defendant contends that it [redacted] (DFOF ¶ 528), [redacted] *See* Trial Tr. (Sinko) at 1625:1–6 [redacted]; *see also* PFOF ¶ 209. Absent such a requirement, [redacted] the claimed invention. *See Merck Sharp & Dohme Corp.*, 874 F.3d at 728, 731; *Dey, L.P.*, 6 F. Supp. 3d at 681.

In addition, Defendant argues that there is no evidence of copying because before it filed its ANDA, "Janssen submitted a Citizen's Petition to the FDA seeking a heightened bioequivalence standard that, if granted, would serve to implicitly regulate the particle size of Teva's ANDA product." Def. Br. at 46. This argument is similarly unavailing. The record contains no evidence that the FDA responded to the petition, and, as of the date of this decision, the petition appears to remain pending. Thus, because the petition has not imposed particle size regulations on generic manufacturers, it does not weaken the evidence of copying.[41]

[41] Defendant cites *Liqwd, Inc. v. L'Oreal USA, Inc.*, 941 F.3d 1133, 1138 (Fed. Cir. 2019) to argue that the similarities between the particle sizes of its generic product and Invega Sustenna and the '906 Patent are not probative of copying. Def. Br. at 47. While the court in *Liqwd, Inc.* did note

e) Long-Felt Need and Failure of Others

"The existence of a long-felt but unsolved need that is met by the claimed invention is . . . objective evidence of non-obviousness." *Millennium Pharm., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1369 (Fed. Cir. 2017); *see also WBIP, LLC*, 829 F.3d at 1332 ("Evidence of a long felt but unresolved need tends to show non-obviousness because it is reasonable to infer that the need would have not persisted had the solution been obvious."). In order to show satisfaction of long-felt need, one must establish that (1) a POSA recognized a problem that existed for a long period of time without a solution; (2) the long-felt need had not been satisfied by another before the claimed invention; and (3) the invention in fact satisfied the long-felt need. *See Newell Cos., Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988); *In re Cavanagh*, 436 F.2d 491, 495–96 (C.C.P.A. 1971); *In re Gershon*, 372 F.2d 535, 538–39 (C.C.P.A. 1967).

The trial evidence showed that the claimed invention satisfied the long-felt need for an LAI that could successfully initiate and maintain treatment without oral supplementation. Prior to the invention of Invega Sustenna, all antipsychotics on the market had significant limitations. For example, first-generation antipsychotics had unfavorable side effect profiles and required oral pretreatment and individualized dosing. PFOF ¶¶ 15–18. Similarly, Risperdal Consta, the only second-generation LAI to predate Invega Sustenna, provided only two weeks of therapeutic benefits and required oral supplementation for the first three weeks of treatment. *Id.* ¶¶ 19–20. These limitations contributed to patient non-adherence, a significant barrier to treatment. *Id.* ¶¶ 14,

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that "more is needed than merely showing that similarity exists between the patent and the competitor's accused product," it nevertheless went on to explain that "access to an *issued patent* coupled with circumstantial evidence regarding changes to a competitor's design is sufficient to support copying." *Ligwd, Inc.*, 941 F.3d at 1137–38 (internal citation omitted) [redacted] PTX-26 at 176. Thus, the record here discloses more than mere similarities between the parties' products.

17–20. Thus, as Drs. Kahn and Kohler testified, prior to Invega Sustenna, none of the second-generation treatments on the market were able to provide monthly dosing without the need for oral supplementation. *See* Trial Tr. (Kahn) at 2410:8–17 (agreeing that "there [were] no second-generation antipsychotics that were dosed monthly without the need for oral supplementation"); Trial Tr. (Kohler) at 1910:6–1912:19 (describing clinical benefits of Invega Sustenna and noting that "none of the previous long-acting injectables were able to provide all these benefits").

Contemporaneous documentary evidence confirmed the need for an LAI that could achieve the benefits that Invega Sustenna provides. Indeed, in an email dated September 22, 2006, a Janssen clinician noted that the then-used dosing regimens were "not getting sufficient numbers of subjects into a therapeutic range early enough" and that "[i]t is not sufficient to say that they get there by day 22 or 36 - that is too late for subjects with schizophrenia and will not lead to the efficacy that this product needs to have in the market place." PTX-812 at 1; PFOF ¶ 174. During the paliperidone palmitate project development process, Janssen made it its goal to overcome these treatment limitations. *See* PFOF ¶ 21; Trial Tr. (Vermeulen) at 751:13–23 (explaining that the "target protocol" for the project was "to have a better product that started releasing quickly after injection and then not need supplementation"); PTX-166 at 19.

The '906 Patent fulfilled this long-felt need. As Drs. Sinko and Kohler agreed, Invega Sustenna is an LAI that initiates and maintains therapeutic levels of paliperidone palmitate without oral supplementation. *See* Trial Tr. (Sinko) at 1473:3–5; Trial Tr. (Kohler) at 1911:9–22. Unlike earlier treatment options, Invega Sustenna is a well-tolerated medication that uses a uniform initiation regimen. *See* Trial Tr. (Kohler) at 1910:6–1912:19. Moreover, it has "improved adherence" among patients. *Id.* at 1912:8–9; *see also* PTX-627 at 51. While Defendant relies on Dr. Kahn's testimony to argue that the claimed invention did not resolve any long-felt need (*see*

Def. Br. at 61), Dr. Kahn's testimony is unsupported by the record. According to Dr. Kahn, "the major change" in schizophrenia treatment "occurred in the mid-1950s," when chlorpromazine, the first antipsychotic, was introduced. Trial Tr. (Kahn) at 2296:15–17. Since that time, Dr. Kahn asserted, "even though many antipsychotics ha[ve] been introduced, it hasn't materially changed the outcome in schizophrenia." Trial Tr. (Kahn) at 2296:22–24. These contentions, however, are contradicted by a reference relied on by Defendant's other expert Dr. Wermeling and the prescription frequency data for various medications. *See* DTX-104 at 5 (explaining that "Chlorpromazine and other first-generation antipsychotics . . . do not improve and may even exacerbate the negative symptoms of schizophrenia and are associated with dose-limiting extrapyramidal symptoms (EPS)"); PTX806B at 66–73 (chart showing total days of treatment for various schizophrenia medication from 2015 through 2018); *see also* PFOF ¶¶ 178–79. Thus, in view of the trial record as a whole, and the fact that Defendant did not credibly rebut Dr. Sinko's assertion that Invega Sustenna practices Representative Claims 2, 19, 20, and 21 when dosed in accordance with its label, the Court finds that the objective indicator of long-felt need weighs in favor of nonobviousness. *See* Trial Tr. (Sinko) at 1610:8–1614:19; Trial Tr. (Kahn) at 2337:1–2338:16, 2344:2–18; *Eli Lilly & Co.*, 471 F.3d at 1380 (finding of "need for a safer, less toxic, and more effective" alternative to existing treatment options provided a basis for unmet need); *WBIP, LLC*, 829 F.3d at 1331 (holding that a nexus can be presumed when the asserted objective indicia is tied to a specific product and the product is the invention claimed in the patent).

f) Commercial Success

"The commercial response to an invention is significant to determinations of obviousness. . . ." *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1391 (Fed. Cir. 1988). For evidence of commercial success to be accorded significant weight, there must be "a nexus between the claimed invention and the commercial success." *Ormco Corp. v. Align Tech., Inc.*,

463 F.3d 1299, 1312 (Fed. Cir. 2006). The claimed invention need not, however, be "solely responsible for the commercial success, in order for this factor to be given weight appropriate to the evidence." *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991).

Here, Plaintiffs demonstrated that the claimed dosing regimens contributed to Invega Sustenna's commercial success. The record indicates that, when adjusted for rebates and discounts, Invega Sustenna's net sales in the United States have grown annually since its launch in 2009 and have exceeded $1 billion from 2015 through 2019. PTX-8, -9, -806B at 3; Trial Tr. (Mulhern) at 2579:11–2580:1; Trial Tr. (Hofmann) at 2741:24–2742:7, 2833:18–2834:21. Furthermore, Invega Sustenna has accounted for over 50 percent of all revenue generated by sales of LAI antipsychotics in the United States annually from 2013 through 2019. PTX-806B at 91–92.[42] In the fourth quarter of 2019 alone, Invega Sustenna had 30.9 percent of the market share based on days of treatment among second-generation long-acting treatments—more than twice the share of its closest competitor. *Id.* at 37 (noting next closest competitor Abilify Maintena had 12.6 percent fourth quarter 2019 market share based on days of treatment). Defendant's economic expert did not dispute the underlying market data relied on by Plaintiffs (*see* Trial Tr. (Hofmann) at 2741:22–2742:7, 2833:18–2835:8, 2836:18–22), and Plaintiffs' economic expert opined that "[b]ased on [her] review of the economic evidence, it's quite clear that Invega Sustenna has achieved substantial success in the marketplace no matter how you look at it, sales or market penetration" (Trial Tr. (Mulhern) at 2586:2–5). *See also* Trial Tr. (Hofmann) at 2838:10–21 (agreeing that none of the competing LAIs introduced after Invega Sustenna's launch "has

[42] The LAI antipsychotic market consists of two first-generation and eight second-generation products. PTX-806B at 91–92; PFOF ¶ 188.

managed to displace Invega Sustenna from its position as the best-selling second-generation antipsychotic[] in the United States").

The record further establishes that the benefits of the patented dosing regimens contributed to Invega Sustenna's success on the market. At trial, Defendant's economic expert did not refute Janssen's assertion that Invega Sustenna's dosing regimen consisting of a monthly injectable without oral supplementation "is a factor contributing to [its] marketplace performance." Trial Tr. (Hofmann) at 2852:17–2853:7. Janssen highlighted these features in its marketing materials, which, as Plaintiffs' expert, Carla Mulhern, credibly opined, suggests that they were viewed as "the key differentiators that distinguish their product from the competition." Trial Tr. (Mulhern) at 2594:12–21. Indeed, Janssen's "[c]ore [m]essage" for Invega Sustenna emphasized that "patients can receive two starting doses . . . in 7 days with rapid & sustained plasma-levels for up to one month and no need for oral supplementation." PTX-416 at 33; *see also, e.g.*, PTX-395 at 6, -417 at 76, -456 at 111. Furthermore, market research indicated that the claimed benefits "are differentiators for healthcare providers." Trial Tr. (Mulhern) at 2597:8–2598:6; PTX-410, -412, -415, -417, -421.

In addition, LAI market data demonstrates that the patented benefits helped contribute to Invega Sustenna's commercial success. The record establishes that paliperidone palmitate is the only second-generation antipsychotic whose market share is greater for its long-acting form than for its short-acting oral form. Trial Tr. (Mulhern) at 2599:8–18 ("Invega Sustenna has substantially outperformed the performance of the paliperidone molecule in the short-acting segment, and this stands apart from the other molecules in the long-acting space. We can see – for most of them, we see the opposite relationship."). Indeed, it holds approximately 31 percent of the long-acting market share compared to about 1 percent of the short-acting market share. Trial Tr. (Mulhern) at

2600:5–7; PTX-454, -806B at 74–81. The difference in paliperidone palmitate's short- and long-acting market shares indicates "that there is something besides the molecule that is explaining or contributing to the success of Invega Sustenna." Trial Tr. (Mulhern) at 2599:19–21.

Defendant asserts that Invega Sustenna's commercial success can be attributed to factors other than the claimed dosing regimens, such as Janssen's marketing efforts, its industry reputation, its rebates and sampling program, and off-label usage of the product.[43] Def. Br. at 66–67; Def. Reply Br. at 29–30. This argument is unpersuasive. With respect to marketing, the trial evidence established that Janssen's promotional expenditures for Invega Sustenna were lower than that of its competitors (*see* PTX-806B at 124, Trial Tr. (Mulhern) at 2665:21–2666:4), and the marketing intensity for the product was lower than the industry average. *See* Trial Tr. (Mulhern) at 2615:16–24, PTX-806B at 9, 122–24. Moreover, Defendant's economic expert testified that he did not have any alternative data comparing the marketing activities of Janssen and its competitors. Trial Tr. (Hofmann) at 2846:5–8, 2848:13–22. While Defendant contends that Janssen's discount and rebate offers drove prescriptions of Invega Sustenna (*see* Def. Br. at 67), its economic expert conceded that he did not have data on rebates and discounts offered by Janssen's competitors (Trial Tr. (Hofmann) at 2848:17–22), and Plaintiffs' economic expert found that, based on publicly-available information, the "discounts and rebates for Invega Sustenna are in line with the pharmaceutical industry as a whole." Trial Tr. (Mulhern) at 2615:25–2616:20. Furthermore, Janssen's sampling program does not weaken the commercial success evidence because Janssen's competitors also maintain sampling programs and Defendant's economic expert did not have any data to show that Janssen's sampling efforts were stronger than its competitors' efforts. Trial Tr.

[43] Defendant's argument that blocking patents undermine the evidence of Invega Sustenna's commercial success is discussed below. Def. Br. at 60–65.

(Mulhern) at 2616:7–13; Trial Tr. (Hofmann) at 2848:9–16. Thus, the Court finds that Plaintiffs' marketing efforts did not meaningfully distinguish Invega Sustenna from its competitors. Trial Tr. (Mulhern) at 2615:25–2616:20.

Defendant's argument regarding the impact of Janssen's reputation on sales is similarly unavailing. As Plaintiffs correctly point out, Invega Sustenna has substantially outperformed other Janssen products on the market, belying Defendant's assertion that the Janssen brand is responsible for Invega Sustenna's success. Trial Tr. (Mulhern) at 2616:24–2618:1; *see also* PTX-806B at 10. Furthermore, Defendant's contentions regarding off-label usage do not overcome Plaintiffs' evidentiary showing. [redacted], which was repeatedly objected to by Janssen, the trial record as a whole indicates that Janssen's core marketing message emphasized the claimed dosing regimens (*see* PTX-416 at 33), and Plaintiffs' economic expert explained that her analysis was not based on any "explicit assumptions about whether every sale used the dosing regimen." Trial Tr. (Mulhern) at 2642:4–6. Thus, the Court finds that the off-label usage evidence does not change the above analysis or refute evidence of nexus, and the commercial success indicator as a whole supports a finding of nonobviousness.

i. *The Alleged "Blocking Patents" Do Not Undermine Evidence of Long-Felt Need or Commercial Success*

Defendant argues that evidence of Invega Sustenna's commercial success, or any long-felt need resolved by the product, is not probative of nonobviousness because three alleged blocking patents owned by Plaintiffs precluded competitors from arriving at or practicing the claimed dosing

regimens.[44] *See* Def. Br. at 60–65; DFOF ¶ 416. On the facts of this case, the Court finds Defendant's contentions unpersuasive.

A patent is considered "a 'blocking patent' where practice of a later invention would infringe the earlier patent." *Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1337 (Fed. Cir. 2018). "Where 'market entry by others was precluded [due to blocking patents], the inference of non-obviousness of [the asserted claims], from evidence of commercial success, is weak.'" *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 740 (Fed. Cir. 2013) (quoting *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1377 (Fed. Cir. 2005)) (alterations in original). The Federal Circuit has explained, however, that "the mere existence or sheer number of blocking patents does not, without more, 'necessarily detract from evidence of commercial success of a product or process.'" *Acorda Therapeutics, Inc.*, 903 F.3d at 1338 (quoting *Merck Sharp & Dohme Corp.*, 874 F.3d at 731). Rather, whether commercial success evidence should be discounted because of a blocking patent is "a fact-specific inquiry." *Merck Sharp & Dohme Corp.*, 874 F.3d at 731.

As an initial matter, Plaintiffs correctly note that Defendant did not proffer any technical expert opinion on the scope of the alleged blocking patents. *See* Pls. Br. at 50–51. Indeed, at trial, Defendant originally indicated that it intended to recall Dr. Wermeling, its obviousness expert, for rebuttal on the issue of secondary considerations. *See* Trial Tr. at 412:17–19. After Dr. Wermeling completed his initial testimony, however, Defendant advised the Court that it would not recall him

[44] The three alleged blocking patents are the '544 Patent, U.S. Patent No. 5,254,556 (the "'556 Patent"), and U.S. Patent No. 6,077,843 (the "'843 Patent"). All three patents are directed towards paliperidone palmitate. *See* DTX-157, -159, -160. Although Defendant identified U.S. Patent No. 5,352,459 (the "'459 Patent") as a fourth alleged blocking patent in a pretrial submission (*see* Final Pretrial Order at 28), it did not discuss the '459 Patent in its post-trial briefing. The Court therefore will not specifically address the '459 Patent, but notes that it would be subject to the analysis of blocking patents below.

(*id.* at 2456:23–2457:2), and instead solely relied on the opinion of Mr. Hofmann, its economic expert, on the subject of blocking patents. Mr. Hofmann admitted, however, that he was not qualified to assess the scope of the prior patents himself, that prior to trial he had considered Dr. Wermeling's reply expert report in forming his opinion, that he knew that Dr. Wermeling had not read the '556 Patent, and that he did not know whether Dr. Wermeling had analyzed the scope of the '843 Patent. Trial Tr. (Hofmann) at 2786:24–2787:2, 2788:11–14, 2798:2–6, 2812:18–22; 2813:11–16. The Court finds that these admissions considerably weaken the probative value of Mr. Hofmann's testimony.

Defendant does not dispute that Mr. Hofmann made these admissions, but instead urges the Court to find a technical foundation for his testimony from other evidence in the record, such as the '544, '556, and '843 Patents themselves, Dr. Sinko's opinions, and Janssen's representations to the FDA and USPTO. Def Br. at 63 n.14. Defendant's contentions are unavailing. Even if the Court were to assume that Mr. Hofmann had an adequate foundation for his opinions, Defendant's blocking patent arguments are nevertheless unpersuasive in light of the countervailing evidence proffered by Plaintiffs. As Plaintiffs properly note, Mr. Hofmann testified that he understood it was possible to practice Claim 2 of the '906 Patent—which, as explained above, includes the dosing regimen of Claim 1 on which Claims 20 and 21 depend—without infringing the claims of the '544 and '843 Patents. Trial Tr. (Hofmann) at 2820:23–2821:10; 2823:16–21. In other words, neither the '544 nor '843 Patent would have blocked a competitor from commercializing the claimed dosing regimens at any time.

Moreover, and in any event, even if the Court assumes that the '544, '556, and '843 Patents are blocking patents, the record demonstrates that they did not in fact deter competition in this case. Indeed, as Mr. Hofmann conceded, the governing patent infringement statute contains "a

safe harbor [provision] that allows companies to develop a drug in research and development using patented technology without infringing the patent." *Id.* at 2824:3–8; *see also* 35 U.S.C. § 271(e)(1) ("It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products."). Both parties' economic experts further agreed that the drug development process can take many years, even up to a decade or longer. Trial Tr. (Hofmann) at 2823:22–2824:2; Trial Tr. (Mulhern) at 2628:21–2629:10. Given this drug development timeline and the fact that the last alleged blocking patent expired in November 2018,[45] the Court finds that these patents created little, if any, disincentives to innovate as of the claimed December 19, 2007, priority date or the December 5, 2008, application date.

Finally, the evidence presented at trial establishes that competitors in fact had incentives to develop competing products during the allegedly blocked periods, and did so. Indeed, contrary to Mr. Hofmann's testimony that "[n]o one would have an economic motivation to try and research and discover [] the alleged novelties of the '906 patent" because of Janssen's "patent fortress around paliperidone palmitate for the treatment of schizophrenia," Defendant itself filed a provisional patent application involving the purification and preparation of paliperidone palmitate on January 10, 2008. Trial Tr. (Hofmann) at 2752:15–24; PTX-813 at 1. The application noted that paliperidone is "[m]arketed under the trade name Invega" and "is an anti-psychotropic agent approved in the United States for the treatment of schizophrenia." PTX-813 at 9. Furthermore, Mr. Hofmann conceded that there was an incentive to research and develop paliperidone palmitate

[45] The '556 Patent expired on October 27, 2012, the '843 Patent expired on May 12, 2017, and the '544 Patent expired on November 10, 2018. DTX-157, -159, -160.

as of December 2007, that entities other than Janssen in fact conducted such clinical trials, and that a competitor began seeking FDA approval for an alternative risperidone LAI in 2009—ten years prior to the expiration of the patents covering Janssen's Risperdal Consta product, belying Defendant's argument that Janssen maintained a monopoly over the market. Trial Tr. (Hofmann) at 2826:19–2828:6, 2829:4–10. On these facts, the Court finds that the alleged blocking patents did not discourage innovation in this case. Therefore, Plaintiffs' evidence of commercial success and long-felt unmet need should not be discounted.

6. Presumption of Obviousness

Defendant argues that the Representative Claims should be presumed obvious because they merely recite limitations from ranges disclosed in the prior art. Def. Br. at 5–12. Janssen argues that no presumption of obviousness applies here because "the unique combinations of dose amounts, dosing schedule, injection sites and particle size range claimed in the 906 Patent go far beyond simply picking a dose amount within a range." Pls. Br. at 54. Janssen cites to *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1320 (Fed. Cir. 2004) to argue that where "an invention is contended to be obvious based upon a combination of elements across different references, there is no presumption, and the patent challenger must prove that there was motivation to combine." Pls. Br. at 54 (internal citations and quotation marks omitted). Plaintiffs make convincing arguments that cause the Court to question the applicability of the "range" cases here, where the claimed invention at issue is composed of a unique combination of elements that are not all easily defined with numerical values that can be found in the prior art (such as injection site, unequal loading doses, and characteristics of the paliperidone formulation). *See* Pls. Reply Br. at Moreover, the differences between the prior art and the claimed invention go beyond numerical ranges, and the invention took place in an unpredictable field of art. *See* Pls. Reply Br. at 3–8.

Regardless, even if the Court were to apply a presumption of obviousness here, Plaintiffs have proffered sufficient evidence to rebut any such presumption.

The Federal Circuit has recognized that "where there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness." *Iron Grip Barbell Co.*, 392 F.3d at 1322. This presumption may be rebutted, however, "with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations." *Allergan, Inc.*, 796 F.3d at 1305 (quoting *Galderma Lab'ys, L.P.*, 737 F.3d at 738).

Here, Plaintiffs have demonstrated that, at a minimum, the prior art taught away from the invention, the claimed dosing regimens led to unexpected results, certain elements of the dosing regimen were not known to be result-effective, there were a large number of possible combinations of the relevant claim parameters, and there are other pertinent secondary considerations that support a finding of nonobviousness. *See* Pls. Reply Br. at 9–16. As both parties' experts agreed, the traditional dosing paradigm for schizophrenia treatment involved low initiation doses followed by gradual dose increases. *See* Trial Tr. (Kahn) at 168:19–169:5, 2392:23–2393:1; Trial Tr. (Kohler) at 1905:12–17. Furthermore, the Gibaldi reference taught the use of depot injections for treatment maintenance rather than initiation. DTX-91 at 5. When Janssen inventors deviated from these teachings during Phase III, including by initiating therapy with two high-loading doses administered in the deltoid muscle, they were able to overcome the failures of the earlier clinical trials, including the '548 Protocol/PSY-3003 study, and develop successful dosing regimens. *See* PFOF ¶ 60.

Similarly, as explained above, compared to the prior art, the claimed regimens unexpectedly achieved successful initiation and maintenance treatment goals. Where the '548

Protocol taught the use of equal doses administered in the gluteal muscle and failed (*see* PFOF ¶ 249), the '906 Patent dosing regimens, comprised of high initial loading doses administered in the deltoid muscle followed by maintenance doses in either the deltoid or gluteal muscle, succeeded. Additionally, it was not known in the prior art that using a LAI in the deltoid to initiate treatment would have such a major impact on blood levels of paliperidone palmitate (Trial Tr. (Vermeulen) at 770:23–771:14) and there were so many potential combinations of the claimed dosing regimen that Janssen relied on complex modeling and simulations to make their discovery (*id.* at 756:6–23). These considerations further rebut a presumption of obviousness from applying here. *See E.I. du Pont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018); *Allergan, Inc.*, 796 F.3d at 1305.

Other secondary considerations, discussed at length above, further rebut any alleged presumption of obviousness. Plaintiffs have proffered evidence of commercial success, industry praise and skepticism, copying, and long-felt need related to the claimed dosing regimens sufficient to support a conclusion of nonobviousness. Thus, even if the Court were to assume *arguendo* a presumption of obviousness applied here, it would not alter the Court's obviousness analysis because Plaintiffs have clearly rebutted the presumption. Having found that Teva has failed to meet its burden of showing that the '906 Patent is invalid as obvious, the Court next considers Teva's written description challenge.

B. Written Description (35 U.S.C. § 112)

A patent specification "shall contain a written description of the invention." 35 U.S.C. § 112. The specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). The test for written description "requires an objective inquiry into the four corners of the specification from the perspective of a [POSA]." *Id.* "[W]hether

a patent complies with the written description requirement will necessarily vary depending on the context. Specifically, the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Id.* (internal citation omitted). When reviewing a patent according to these principles, "[w]ritten description is a question of fact, judged from the perspective of [a POSA] as of the relevant filing date." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006) (citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563–64 (Fed. Cir. 1991)).

Defendant argues that the Patent-in-Suit is invalid because the specification does not provide sufficient written description of the invention described in Claims 10, 13, 20, and 21. Def. Br. at. 67–70. In response, Plaintiffs contend that the specification is sufficiently detailed and that Defendant failed to prove these Claims lack adequate written description by clear and convincing evidence. Pls. Br. at 68–71.

In support of their arguments, the parties rely on the testimony of Defendant's expert Dr. Kahn and Plaintiffs' expert Dr. Kohler, whose qualifications were discussed previously in this Opinion. For the reasons set forth below, the Court finds that Defendant has failed to prove invalidity based on the written description requirement by clear and convincing evidence, and therefore the Patent-in-Suit is not invalid under 35 U.S.C. § 112.

1. Overview of the Parties' Positions

Defendant argues that Claims 10, 13, 20, and 21 (together, the "Renal Impairment Claims"), which claim a dosing regimen for administering paliperidone palmitate to a renally impaired psychiatric patient, lack written description because these Claims do not specify the severity of renal impairment addressed by the dosing regimens, with only renal impairment and mild renal impairment discussed in the '906 Patent. Def. Br. at 67–68. Defendant notes that there are only two passages in the '906 Patent specification that discuss patients with renal impairment.

One passage instructs administering loading doses of about 100/75 or 75/75 mg-eq. to patients with renal impairment. *Id.* at 68. A second passage instructs adjusting loading doses for renally impaired patients to account for increased exposure levels to paliperidone, clarifying that for patients "with ***mild*** renal impairment the loading doses should be reduced to 75 mg-eq. for the first two loading doses." *Id.* (internal citations and quotation marks omitted). In Teva's view, the '906 Patent fails the written description requirement because it does not advise how patients with moderate or severe renal impairment would be dosed. *Id.* Teva also contends that the claims are invalid because they do not provide an upper limit "in terms of degree of renal impairment or maximum dose." *Id.* at 69.

Plaintiffs' first response is procedural as they argue that Teva presented a "brand-new written description challenge at trial" that was not identified in the Final Pretrial Order and is therefore waived. Pls. Br. at 69. Janssen argues that Defendant's expert, Dr. Kahn, initially asserted that the dosing regimen in the Renal Impairment Claims contained no upper limit, but later abandoned that theory to now argue that the Claims failed to properly specify the type of renally impaired patient that can be treated with the claimed dosing regimen. *Id.* at 69; PFOF ¶¶ 225–26. While the Court acknowledges Plaintiffs' argument regarding Teva's evolving positions on this issue, this Opinion addresses the issue regardless.

Turning to the merits of Teva's written description challenge, Plaintiffs assert that the '906 Patent contemplates loading doses for patients with renal impairment that allow a physician to use medical judgment when dosing. Pls. Br. at 70. Plaintiffs further argue that a POSA would recognize the '906 Patent's focus on mild renal impairment (specifically highlighted in the specification), and would not treat a patient with moderate or severe renal impairment using Invega

Sustenna.[46] Pls. Reply Br. at 48. In addition, Plaintiffs contend that the experts agreed at trial that the renal impairment doses range from about 75 mg-eq. to an upper limit of 150 mg-eq., and that the '906 Patent contains several representative embodiments of dosing regimens for renally impaired patients. Pls. Br. at 70.

2. The Claims Relevant to the Written Description Challenge

Claim 10 of the '906 Patent covers the "dosing regimen of claim 8 wherein the sustained release formulation is an aqueous nanoparticle suspension." '906 Patent (DTX-1/PTX-1) col. 33:26–27. The dosing regimen of Claim 8 is "for administering paliperidone palmitate to a renally impaired psychiatric patient in need of treatment for schizophrenia, schizoaffective disorder, or schizophreniform disorder" and consists of (1) a loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone" on day 1; (2) a second loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone . . . on the 6th to about 10th day of treatment"; and (3) a maintenance dose in the deltoid or gluteal muscle "of about 25 mg-eq. to about 75 mg-eq. of paliperidone" a month (± 7 days) after the second loading dose. *Id.* cols. 32:66–33:20.

Claim 13 of the '906 Patent covers the "dosing regimen of claim 11 wherein the psychiatric patient is in need of treatment for of a psychotic disorder wherein the psychotic disorder is schizophrenia." *Id.* col. 33:50–52. The dosing regimen of Claim 11 is "for administering paliperidone palmitate to a renally impaired psychiatric patient in need of treatment for psychotic disorder" and consists of (1) a loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone" on day 1; (2) a second loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone . . . on the eighth day of treatment"; and (3) a maintenance dose in the deltoid or gluteal muscle "of about 25 mg-eq. to about 50 mg-eq. of paliperidone" one month (± 7 days) after

[46] The Invega Sustenna label states that Invega Sustenna "is not recommended in patients with moderate or severe renal impairment." PTX-105 at 6.

the second loading dose. *Id.* col. 33:28–47.[47]

The '906 Patent contains additional discussion of renal impairment beyond its claims. In the "Detailed Description" section, for instance, the Patent-in-Suit directs that "patients with renal impairment will have a higher total exposure to paliperidone after i.m. injections of paliperidone palmitate. For patients with renal impairment it would [be] desirable to adjust the loading doses to account for the increased exposure levels of patients with renal impairment." *Id.* col. 5:54–58. This section also instructs that "[f]or patients with mild renal impairment the loading doses should be reduced to 75 mg-eq. for the first two loading doses" and that "[f]or the purpose of this patent application renal function is estimated by glomerular filtration rate (GFR) usually measured by the creatinine clearance (best calculated from a 24-hour urine collection) . . . . Patients with mild renal impairment have a creatinine clearance of 50 to <80 mL/minute." *Id.* cols. 5:59–6:15.

3. Analysis

The Court finds that the '906 Patent sufficiently describes the claimed loading doses for renally impaired patients. A patent must include sufficient details such that a POSA could understand the subject invention and recognize that the inventor possessed it. *Ariad Pharm. Inc.*, 598 F.3d at 1351. However, this requirement does not necessarily mean that the specification of the patent must include every nuanced detail as "a patent need not teach, and preferably omits, what is well known in the art." *Falko-Gunter Falkner*, 448 F.3d at 1365 (quoting *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987)). Here, Teva has failed to show by clear and convincing evidence that the Renal Impairment Claims lack adequate written description. *See Ariad Pharms., Inc.*, 598 F.3d at 1351 ("[T]he test for sufficiency is whether the disclosure of

[47] While Claims 20 and 21 (which generally describe the characteristics of the paliperidone palmitate formulation) are included in Teva's written description challenge as they refer back to the dosing regimens for patients with renal impairment, they are not independently analyzed by the parties.

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.").

a) Relevant Testimony

Based on the testimony and evidence presented at trial, the Court finds that a POSA would have understood that the inventors of the '906 Patent had possession of the invention embodied in the Renal Impairment Claims as of the filing date of the '906 Patent. Experts for both parties in fact agreed that the '906 Patent instructs that paliperidone palmitate doses must be lowered when given to patients with renal impairment because paliperidone is cleared through the kidneys and renally impaired patients have reduced kidney function. *See* Trial Tr. (Kahn) at 116:1–3 ("It specifies to mild renal impairment, which wasn't in the other two, and that the loading dose should be reduced to 75 milligrams."); Trial Tr. (Kohler) at 1997:8–13 (agreeing that the '906 Patent states that "for patients with mild renal impairment, the loading doses should be reduced to 75-milligrams equivalent for the first two loading doses").

Further, both experts agreed that Invega Sustenna is not designed to be given to patients with moderate or severe renal impairment. *See* Trial Tr. (Kahn) at 105:12–15 ("**Q.** And then you may have said this, but for moderate and severe renal impairment, would a psychiatrist give Invega Sustenna to those patients? **A.** Well, it's not recommended, so I doubt it."); Trial Tr. (Kohler) at 1998:6–8 ("The way I read these specifications and the patent claims is that you do not administer paliperidone palmitate to people with moderate or severe renal impairment.").

Finally, the experts further agreed that the highest dose listed in the '906 Patent, 150 mg-eq., would be the upper limit for dosing any patient with renal impairment. *See* Trial Tr. (Kahn)[48]

[48] In Dr. Kahn's opening expert report, he wrote that "nothing in the '906 Patent indicates to a skilled artisan that the inventors were in possession of dosing regimens for administering paliperidone palmitate in schizophrenia patients with renal impairment in doses ranging from 75 mg eq. to infinity." Kahn Opening Expert Report at 14–15. The Court notes that Dr. Kahn's

at 145:12–14 ("I said, you know, the upper limit -- I am willing to accept that the upper limit is 150 milligrams."); Trial Tr. (Kohler) at 1935:7 (agreeing with Dr. Kahn that "the upper limit for the initiation doses for any patient is 150-milligram equivalents"). In addition, both experts testified that, at the time of the filing of the '906 Patent, it would have been well known to a POSA how to measure a patient's level of renal impairment. *See* Trial Tr. (Kahn) at 146:9–10 ("I mean, in general it can be done with a GFR. By assessing the GFR, yes."); Trial Tr. (Kohler) at 1936:17–19 ("Renal function is estimated by the glomerular filtration rate, or GFR, and which we can use the creatinine clearance as a proxy.").

Based on this testimony and the text of the '906 Patent, the Court finds that the Renal Impairment Claims are adequately described. The '906 Patent clearly conveys a dosing regimen for patients with renal impairment, supported by the specification which specifically discusses dosing for patients suffering from mild renal impairment. It would have been reasonably conveyed to a POSA that the maximum dose listed in the '906 Patent is 150 mg-eq. and that Invega Sustenna is not recommended for patients with moderate to severe renal impairment. As the written description requirement does not mandate that a patent expressly state all information currently known in the art, the Court finds the '906 Patent is not invalid.

b) Relevant Caselaw

The law is clear that written description must focus on whether a patent reasonably conveys possession of the claimed subject matter to those skilled in the art. *Ariad Pharms., Inc.*, 598 F.3d at 1351. The written description requirement is highly contextual and fact-dependent, taking into account the nature and scope of the claims, what is already known in the art, and the complexity of the invention. *See id*. ("[T]he level of detail required to satisfy the written description

written description testimony evolved to acknowledge that the '906 Patent contains an upper limit for dosing, as indicated above.

requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology."). The following cases are instructive.

The Court in *In re Wertheim*, 541 F.2d 257 (C.C.P.A. 1976), held that a patent's specification and what is well-known in the art must be read together when conducting a written description analysis. *Id.* at 265. Applying this holding, the court rejected a written description challenge over the claimed invention, finding that the patent sufficiently described the invention in light of its specific embodiments and what was known in the prior art. *Id.* at 264–65. Here, the Renal Impairment Claims set out a dosing regimen containing specific dosing instructions which are sufficiently described when combined with the information contained in the '906 Patent and known in the art that: the maximum dosage listed in the '906 Patent for any patient is 150 mg-eq., levels of renal impairment can be measured using standardized methods, and Invega Sustenna is not suitable for patients with moderate to severe renal impairment. As such, the Renal Impairment Claims are supported by adequate written description because "[i]t is not necessary that the application describe the claim limitations exactly . . . but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations." *Id.* at 262.

Further, in *Nalpropion Pharmaceuticals, Inc. v. Actavis Laboratories FL, Inc.*, 934 F.3d 1344 (Fed. Cir. 2019), the Federal Circuit held that "[i]t is not necessary that the exact terms of a claim be used in *haec verba* in the specification." *Id.* at 1350. On this basis, the court rejected a written description challenge wherein the claim and the specification used different terms and methods to describe a process, finding the different language did not create a written description issue. *Id.* at 1351. As with the patent at issue in *Nalpropion*, the Court finds that the specification and the Renal Impairment Claims of the '906 Patent can be read and understood together despite

not using the exact same language. Accordingly, a "flexible, sensible interpretation" of the Patent-in-Suit shows that the inventors of the '906 Patent had possession of the invention embodied in the Renal Impairment Claims as of the filing date. *Nalpropion Pharms., Inc.*, 934 F. 3d at 1351; *see also Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1371 (Fed. Cir. 2009) ("[A] patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed.").

The cases on which Defendant relies do not alter the Court's analysis. Each of these cases is factually distinguishable from this matter, or in fact supports the Court's finding and reaffirms that the proper written description inquiry is whether the '906 Patent reasonably conveys possession of the claimed subject matter to those skilled in the art.

Synthes USA, LLC v. Spinal Kinetics, Inc., 734 F.3d 1332 (Fed. Cir. 2013), essentially hinged on the meaning of a single word and how it was understood within a given field based on extensive evidence and testimony presented at trial. *Id.* at 1342. Here, as in *Synthes*, the Court makes its written description decision based upon evidence and testimony presented at trial. The evidence presented to the Court was clear that Invega Sustenna should not be used to treat patients with moderate or severe renal impairment (*see* Trial Tr. (Kahn) at 105:12–15; Trial Tr. (Kohler) at 1999:6–14) and confirmed that the Renal Impairment Claims convey possession of a dosing regimen for patients with mild renal impairment.

In *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F. Supp. 3d 566 (D. Del. 2018), the district court found the patents at issue invalid because "the invention is a method of treating pain that consists of administering a particular formulation to patients," but the patents failed to identify the class of formulations that will work and were drafted in functional terms. *Id.* at 625–26. Accordingly, the Court found that the patents "merely describe[] the problem to be

solved and claim[] all solutions to it." *Id*. Unlike in *Pernix*, the Renal Impairment Claims are not written in functional terms, but rather recite specific dose amounts to be used in a specific manner at specific times when treating a renally impaired psychiatric patient in need of treatment for schizophrenia or psychotic order. '906 Patent (DTX-1/PTX-1) cols. 32:67–34:47. Additionally, as noted above, Invega Sustenna is not recommended for patients with moderate or severe renal impairment, and the '906 Patent makes no reference to these types of renal impairment. In this factual context the dosing regimens for patients with renal impairment contained within the Renal Impairment Claims are a stark contrast to the claims at issue in *Pernix*.

Eli Lilly & Co. v. Perrigo Co., 202 F. Supp. 3d 918 (S.D. Ind. 2016) is also distinguishable from the present matter as the patent at issue in *Eli Lilly* contained a claim calling for a "at least one dermal penetration enhancer present in an amount of from 10 to 10,000[%] based on the weight of the testosterone," and there was inadequate guidance from the patent specification or examples that could help narrow the entire expansive range of 10–10,000%. *Id.* at 929, 996–97. Here, the specification of the '906 Patent contains multiple embodiments and discussions of the renal impairment claims, specifically discussing how to utilize the dosing regimen (which recites specific dose amounts, sites of injection, and dose timing) for patients with mild renal impairment and how to calculate mild renal impairment. *Id.* col. 3:27–56, col. 5:53–6:14.

Thus, the Court finds that the Renal Impairment Claims, when read in context of what is described in the specification, and what is detailed in the embodiments, reasonably convey to those skilled in the art possession of the claimed invention. Based on the testimony and evidence presented at trial, as well as the arguments presented to the Court at closing arguments and in the parties' papers, the Court finds that Teva has failed to show by clear and convincing evidence that the Renal Impairment Claims fail based on a lack of written description. Next, the Court addresses

Teva's indefiniteness challenge.

C. Indefiniteness (35 U.S.C. § 112)

"[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). Indefiniteness is a question of law, which may rely on subsidiary determinations of underlying facts. *Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1343 (Fed. Cir. 2016). A patent is presumed to be valid; the challenger bears the burden of establishing invalidity by clear and convincing evidence. 35 U.S.C. § 282(a); *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011).

Defendant argues that the Patent-in-Suit is invalid as indefinite for two reasons. First, Defendant argues that Claims 20 and 21 fail to properly characterize the claimed d50 range given that d50 can be measured and expressed in a number of different ways. Def. Br. at 70. Second, Defendant contends that Claims 10, 20, and 21 fail to properly characterize the term "aqueous nanoparticle suspension" which lacks a typical meaning in the art. *Id.* at 74. Plaintiffs argue that Claims 20 and 21 are not indefinite because Teva failed to show that different methods or expressions of measurement lead to meaningfully different results. Pls. Br. at 65. Plaintiffs further contend that Claims 10, 20, and 21 are not indefinite because the '906 Patent defines the term aqueous nanoparticle suspension and makes clear the d50 ranges that encompass a nanoparticle. *Id.* at 68. In support of their arguments, the parties rely on the testimony of the following witnesses: Defendant's expert Lawrence Block, Ph.D.,[49] and Plaintiffs' expert Dr. Sinko

[49] Defendant's expert Lawrence Block, Ph.D., is a Professor Emeritus of Pharmaceutics at the School of Pharmacy and Graduate School of Pharmaceutical Sciences at Duquesne University. Final Pretrial Order at 42. Dr. Block is recognized as a leader in the field of pharmaceutics and is a Fellow of both the American Association of Pharmaceutical Scientists and the American

(introduced above). For the reasons set forth below, the Court finds that Defendant has failed to prove invalidity based on indefiniteness by clear and convincing evidence, and therefore the Patent-in-Suit is not invalid under 35 U.S.C. § 112.

1. Overview of the Parties' Positions

a) d50 Indefiniteness

Defendant argues that Claims 20 and 21 are indefinite because although they require "an average particle size (d50) of from about 1600 nm to about 900 nm," this requirement fails to properly limit the claims due to numerous variations that affect particle size measurements. Def. Br. at 70. Defendant notes that the paliperidone palmitate particles described in the '906 Patent are asymmetrical and their size is reported as the diameter of a hypothetical equivalent sphere which can be measured using different techniques and expressed in different ways. *Id.* at 70–71. Defendant also notes that the type of instrument used to make measurements, and the conditions under which particles are measured, can influence measurements. *Id.* at 71.

Plaintiffs respond that "a claim term is not indefinite for failure to specify which method should be used to measure a quantity unless different methods lead to significantly different results, and there is no evidence of that here." Pls. Br. at 65. Plaintiffs further argue that different measurements of particle size taken at different times are equally correct, that instrument error accounts for the only meaningful discrepancy in particle size measurement discussed at trial, and that no ordinary scientist would have difficulty measuring the particle size of paliperidone palmitate suspensions, also noting that scientists at the FDA and USPTO did not have any difficulty taking particle size measurements during the relevant agency proceedings. *Id.* at 66–68.

Pharmacists Association - Academy for Pharmaceutical Research and Science. *Id.* Dr. Block has authored or co-authored over 120 publications and his research interests include excipient technology, rheology, drug and cosmetic delivery systems, pharmaceutical engineering, biopharmaceutics, and pharmacokinetics. *Id.* at 42–43.

b) Aqueous Nanoparticle Suspension Indefiniteness

Defendant argues that Claims 10, 20, and 21 are "invalid for failing to define the bounds of the term aqueous nanoparticle suspension." Def. Br. at 74 (internal quotation marks omitted). Defendant maintains that this term has no typical meaning in the art, that no definite bounds of particle size are provided, and that the '906 Patent incorporates "suitable aqueous depot formulations" from the '843 Patent that exceed the particle sizes listed in the '906 Patent, making it impossible for a POSA to determine with reasonable certainty whether a formulation is a nanoparticle suspension or not. *Id.* at 74–75.[50]

Plaintiffs argue that the '906 Patent adequately defines the term aqueous nanoparticle suspension and "makes clear that suspensions having an average particle size d50 within the ranges disclosed in the patent's specification and claims qualify as nanoparticle suspensions." Pls. Br. at 68 (internal quotation marks omitted). Plaintiffs also stress that "[e]ven if an ordinarily skilled person might be interested in further information about particle size distribution for other purposes, they would have no difficulty determining the 'scope of the invention' with reasonable certainty," which is all that is required to render a claim definite. *Id.* (citing *Nautilus, Inc.*, 572 U.S. at 901).

2. The Claims Relevant to Indefiniteness

Claim 10 of the '906 Patent covers the "dosing regimen of claim 8 wherein the sustained release formulation is an aqueous nanoparticle suspension." '906 Patent (DTX-1/PTX-1) col. 33:26–27. The dosing regimen of Claim 8 is "for administering paliperidone palmitate to a renally impaired psychiatric patient in need of treatment for schizophrenia, schizoaffective disorder, or

[50] To the extent Teva also argues that the term aqueous nanoparticle suspension is indefinite because the '906 Patent incorporates the '843 Patent and '544 Patent into its disclosure, Teva has not supported this argument with persuasive testimony or evidence presented at trial. The Court also notes that "nanoparticle" does not appear in the '843 Patent and finds that the incorporation by reference of these patents does not render the term aqueous nanoparticle suspension indefinite for the reasons discussed below.

schizophreniform disorder" and consists of (1) a loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone" on day 1; (2) a second loading dose in the deltoid muscle "of from about 75 mg-eq. of paliperidone . . . on the 6th to about 10th day of treatment"; and (3) a maintenance dose in the deltoid or gluteal muscle "of about 25 mg-eq. to about 75 mg-eq. of paliperidone" a month (± 7 days) after the second loading dose. *Id.* cols. 32:66–33:20.

Claim 20 of the '906 Patent covers the "dosage regimen of claim 19 wherein the buffering agents contained in the aqueous nanoparticle suspension are citric acid monohydrate, disodium hydrogen phosphate anhydrous, sodium dihydrogen phosphate monohydrate, sodium hydroxide." *Id.* col. 34:44–48. Claim 19 of the '906 Patent provides details on the aqueous nanoparticle suspension to be used as a sustained release depot formulation in the dosing regimens of Claims 1, 4, 8, or 11. *Id.* col. 34:32–34. Specifically, it instructs that the aqueous nanoparticle suspension should consist of: (1) 156 mg/ml of paliperidone palmitate "having an average particle size (d50) of from about 1600 nm to about 900 nm"; (2) 12 mg/ml of polysorbate 20; (3) one or more buffering agents sufficient to give the composition a pH of 8.5; (4) 30 mg/ml of the suspending agent polyethylene glycol 4000; and (5) "water q.s. ad 100%." *Id.* col. 34:34–43.

Claim 21 of the '906 Patent covers the "dosage regimen of claim 19 wherein the pH of the aqueous nanoparticle suspension is in the range of pH 7 to 7.5." *Id.* col. 34:49–51.

3. Analysis

a) d50 Indefiniteness

The Court finds that Claims 20 and 21[51] are not invalid for indefiniteness as "the mere possibility of different results from different measurement techniques does not render a claim indefinite." *Ball Metal Beverage Container Corp. v. Crown Packaging Tech., Inc.*, 838 F. App'x

[51] Claim 10 will be discussed in connection with the aqueous nanoparticle suspension indefiniteness analysis below.

538, 542 (Fed. Cir. 2020) (internal citations and quotation marks omitted). Teva has failed to provide clear and convincing evidence that possible variations in d50 measurement methodology and procedure would lead to materially different results such that Claims 20 and 21 "fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc.*, 572 U.S. at 901.

i. Relevant Testimony

The testimony of Defendant's expert, Dr. Block, and Plaintiffs' expert, Dr. Sinko, is largely consistent on a number of key issues relevant to this Court's analysis. Both experts agree that a POSA would be able to use different methods to measure a particle size of d50. *See* Trial Tr. (Block) at 589:6–13 (testifying that the specification "tells one to measure [d50] by art-known conventional techniques," and "gives examples of art-known conventional techniques," such as "Sedimentation field flow fractionation, photon correlation spectroscopy and disk centrifugation"); Trial Tr. (Sinko) at 1554:1–3 ("[T]here were several methods for measuring. And this is just some of the machines that were listed in those relevant sections that I discussed. These are a few examples.").

Both experts further agree that that using different methods, tools, or expressions of measuring d50 can lead to the same or materially similar results, and that different d50 measurements of the same particle size can all be "correct" measurements that vary because of the conditions under which the particle was measured. *See* Trial Tr. (Block) at 613:13–16 ("**Q.** So we've talked about a lot of different techniques this morning and this afternoon. Is there one technique that's more correct than others? **A.** No."); *Id.* (Block) 630:18–25 ("**Q.** Sure. Whether or not there are significant differences between number-weighted, volume-weighted and intensity-weighted d50 measurements would depend on various factors, right? **A.** Yes. **Q.** And

the differences may or may not be significant, depending upon those factors, right? **A.** That's true."); Trial Tr. (Sinko) at 2194:16–20 ("**Q.** And if you use all those different methods, you'd come up with a different diameter, potentially, right? **A.** Maybe. **Q.** Maybe you would, right? **A.** And maybe you wouldn't."); *Id.* (Sinko) 2195:19–2196:2 ("**Q.** You agree, Doctor, that the '906 patent does not limit the d50 value expressly to any particular type of diameter measurement, right? **A.** It states a d50, that's true. But as we saw from the data from, you know, from Janssen, from Teva, you know, using multiple methods, you get the same answer. . . . And they use different methods with different diameters, and they get the same answer.").

Finally, both experts agree that throughout the development of Invega Sustenna, the prosecution of the Patent, and the development of Teva's ANDA, there was no apparent confusion over how to measure or express d50 that cannot be explained by artificial error. *See* Trial Tr. (Block) at 650:8–11 ("**Q.** And Teva was able to determine the d50 value for its paliperidone palmitate suspension and report that value to the FDA, right? **A.** Apparently."); Trial Tr. (Sinko) at 1563:7–9 ("**Q.** Was there any suggestion that either the FDA or Teva had any difficulty understanding a d50 particle size distribution? **A.** No, there was not.").

The relevant disagreement here comes almost entirely from counsel, as they disagree over the legal significance of the largely congruent testimony of Dr. Block and Dr. Sinko. A review of the relevant caselaw cited by the parties, however, confirms that any asserted differences in measuring and expressing d50 particle size present in this matter do not render Claims 20 and 21 invalid because a POSA would understand, "with reasonable certainty," the scope of the d50 particle measurement within Claims 20 and 21.

ii. *Relevant Caselaw*

A review of the relevant caselaw demonstrates that the differing methods of measuring and

representing d50 particle size must lead to meaningfully different results in order to render Claims 20 and 21 indefinite. In *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558 (Fed. Cir. 1996), the party challenging patent validity argued that the claims at issue were indefinite because "the inventors failed to state the method they used to measure the ultraviolet transmittance of the invention." *PPG Indus., Inc.*, 75 F.3d at 1562. The Federal Circuit rejected this argument, finding that the evidence presented "established that, setting aside the equipment error that plagued PPG's testing procedures, all of the conventional methods of testing ultraviolet transmittance produce essentially identical results." *Id.* at 1563.[52] Similarly, in *Ethicon Endo-Surgery, Inc. v. Covidien, Inc.*, 796 F.3d 1312 (Fed. Cir. 2015), the Federal Circuit found that slight variations in measurements taken through different methods did not render the claims at issue indefinite because they were "simply due to natural variances in real-world testing conditions." *Id.* at 1319–20, 1322. In *Takeda Pharmaceutical Co., Ltd. v. Zydus Pharmaceuticals USA, Inc.*, 743 F.3d 1359 (Fed. Cir. 2014), the Federal Circuit stressed that "there is no evidence that the differences between these techniques are in fact significant; there was evidence before the trial court that although the results may be different, there is a high degree of correlation for the results between the two techniques, . . . indeed, there was no evidence in this case that different measurement techniques in fact produced significantly different results for the same sample." *Id.* at 1367 (internal citations and

[52] *PPG Industries* is also instructive because in the present case Teva seeks to place great weight on an outlier measurement taken with a defective device. Def. Br. at 72 (noting differences in measurements Janssen obtained using "Coulter counter" and "Mastersizer"). As *PPG Industries* instructs, the Court does not find that this outlier measurement renders the claims at issue indefinite because it has been adequately explained (with no persuasive rebuttal) as an equipment defect. *See* Trial Tr. (Sinko) at 1558:4–9 ("So basically using three different methods they came up with, in essence, the same particle size distribution, and therefore they could conclude that that Coulter and the artifact that they thought existed was definitely an artifact or an artificial result. And so they could rely on their laser diffraction original method, the Malvern Mastersizer."); Trial Tr. (Block) at 662:6–17 (testifying that Janssen found artificial differences between the Coulter and the Malvern device measurements).

quotation marks omitted). Based on this evidence, the Federal Circuit held that "[a]ny theoretical minor differences between the two techniques are therefore insufficient to render the patent invalid." *Id.*

Cases that find patents invalid based upon different methods of measurement crucially contain evidence that the different methods are likely to lead to significantly different results. In *Dow Chemical Co. v. Nova Chemicals Corp. (Canada)*, 803 F.3d 620 (Fed. Cir. 2015), the Federal Circuit found the claims at issue invalid as "[t]here is no question that each of these four methods may produce different results, i.e., a different slope" based on Dow's expert testimony which conceded that "the 10% secant tangent method, the final slope method, the most linear method, and the method he invented could produce different results. In comparison to the three other methods, [the Dow expert]'s method would produce a higher value." *Id.* at 633–635. In *Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335 (Fed. Cir. 2015), the indefiniteness analysis hinged on the term "molecular weight" which can be measured and expressed in multiple forms. *Id.* at 1338. The Federal Circuit found these different forms of molecular weight rendered the patent at issue invalid as "[t]he parties agree that 'molecular weight' could refer to [peak average molecular weight, number average molecular weight, or weight average molecular weight]. And they agree that each of these measures is calculated in a different way and would typically yield a different result for a given polymer sample." *Id.* at 1341, 1345. *Otsuka Pharmaceutical Company, Ltd. v. Torrent Pharmaceuticals, Ltd., Inc.*, 151 F. Supp. 3d 525 (D.N.J. 2015), involved the question of whether the term "mean particle size" was indefinite "because it's amenable to multiple meanings." *Id.* at 544. In finding this term indefinite, the district court first noted that "Otsuka readily acknowledges the susceptibility of 'mean particle size' to multiple measurements, each of which could yield varied results," and found that the record showed a lack

of uniform understanding of the term in the relevant scientific community, and that the patent at issue provided "no information from which to divine, with reasonable certainty, the appropriate measure of the 'mean.'" *Id.* at 546–48.

Here, the '906 Patent does discuss methods of measuring d50 and does contain examples wherein those methods are utilized. *See* Trial Tr. (Block) at 637:2–11 ("**Q.** The patent reports a particle size distribution was measured by laser diffraction, correct? **A.** Yes. **Q.** So you would agree that a person of skill in the art reading the patent would know that they could measure particle size by laser diffraction, right? **A.** Yes. **Q.** And if you measure particle size by laser diffraction, you typically get a volume-weighted measure of d50, right? **A.** That's my understanding."). Additionally, the evidence and testimony admitted during the bench trial showed that the different methods of measuring and expressing d50 were likely to produce substantially similar values. *See* Trial Tr. (Block) at 651:25–652:7 [redacted]; Trial Tr. (Sinko) at 2196:5–10 ("I don't think it needs to be. I mean, that's – everyone uses the methods. And they know that the software that every manufacturer uses for their different methods normalizes for all this because otherwise, no one would be able to rely on it. And everyone does rely on it. Teva relies on it. Janssen relies on it. My lab relies on it."). As the '906 Patent provides examples of how to measure d50 particle size and different methods or expressions of measurement lead to essentially identical values, the differing methods or expressions would have no effect on a POSA's ability to understand the scope of the claims with reasonable certainty. Additionally, the Court notes that both experts testified at trial that throughout the relevant agency proceedings there were no issues with measuring d50,

providing further evidence to support the finding that differing methods or expressions of d50 do not render Claims 20 and 21 indefinite. *See* Trial Tr. (Block) at 650:8–11; Trial Tr. (Sinko) at 1563:7–9.

Based on all of the evidence and testimony presented at trial, the Court finds that Teva has failed to show by clear and convincing evidence that the different methods or expressions of d50 particle size render Claims 20 and 21 invalid.

b) Aqueous Nanoparticle Suspension Indefiniteness

The Court also finds that Claims 10, 20, and 21 are not invalid for indefiniteness based on their utilization of the term "aqueous nanoparticle suspension." That term is defined with reasonable certainty.

i. Relevant Testimony

At trial, Dr. Block, Teva's expert, agreed that the '906 Patent describes "characteristics of the nanoparticle suspension," such as the range of 1600 nanometers to 400 nanometers for particle size d50, but maintained that the term is indefinite because "there could be particles potentially outside that range on the upper end and some particles below that range." Trial Tr. (Block) at 670:10–14; 672:8–18. Dr. Sinko, Janssen's expert, disagreed with Dr. Block and stated that the '906 Patent adequately defines the term because "it says, an aqueous formulation would preferably be a nanoparticle suspension of wherein the nanoparticles would fit in average sizes of less than 2000 nanometers to about 100 nanometers. And then it goes on and on. But basically, you know, it defines what an aqueous nanoparticle suspension is." Trial Tr. (Sinko) at 1560:24–1561:4.

The Court agrees with Dr. Sinko that the term "aqueous nanoparticle suspension" is defined with reasonable certainty in the '906 Patent and rejects the arguments proffered by Teva that this definition is lacking.

ii. Relevant Caselaw

In *Vapor Point LLC v. Moorhead*, No. 11-4639, 2013 WL 11275459 (S.D. Tex. Dec. 18, 2013), the district court found the term "micro-sized particles" not indefinite, noting that "[a]n issued claim is presumed valid." *Vapor Point LLC*, 2013 WL 11275459, at *17 (internal citations and quotation marks omitted). The *Vapor Point* plaintiffs argued that the term micro-sized particles was indefinite because it was used in a manner contrary to its ordinary meaning, but the court rejected that argument as it found that the "specification communicates a deliberate and clear preference for an alternative definition." *Id.* The court also noted that "close questions of indefiniteness" are resolved in favor of the valid patent. *Id.* Finally, the court found "no clear conflict" in the patent's specification that "micro-sized particles may vary in range between 5–500 microns, although smaller and larger particles may also be used with embodiments described herein." *Id.*

These holdings make clear that the '906 Patent is not indefinite based on the term aqueous nanoparticle suspension. As in *Vapor Point*, the '906 Patent provides a clear definition of the term aqueous nanoparticle suspension such that there does not need to be an ordinary meaning of the term. Specifically, the '906 Patent states that the aqueous nanoparticle suspension would preferably have nanoparticles of an average size of less than 2000 nm to about 100 nm, and provides further details on the preferred d50 and d90 measurements for nanoparticles. '906 Patent (DTX-1/PTX-1) col. 7:24–32. In addition, *Vapor Point* instructs that the '906 Patent's failure to define what is not an aqueous nanoparticle suspension does not render it indefinite, as the court in that case found the patent's reference to "smaller and larger particles" did not render the claims at issue indefinite.

For all of the reasons discussed at length above, the Court finds Teva has failed to show by clear and convincing evidence that Claims 10, 20, and 21 fail as indefinite based on the testimony and evidence presented at trial.

D. Rule 52(c) Motions

During the bench trial, both parties made motions for judgment on partial findings pursuant to Federal Rule of Civil Procedure 52(c). ECF Nos. 138, 150. Rule 52(c) reads:

> If a party has been fully heard on an issue during a nonjury trial and the court finds against the party on that issue, the court may enter judgment against the party on a claim or defense that, under the controlling law, can be maintained or defeated only with a favorable finding on that issue. The court may, however, decline to render any judgment until the close of the evidence. A judgment on partial findings must be supported by findings of fact and conclusions of law as required by Rule 52(a).

Fed. R. Civ. P. 52(c). Thus, Rule 52(c) permits a judge to enter judgment as a matter of law on partial findings once "a party has been fully heard on an issue." *Id.* "To grant a [motion for judgment as a matter of law] under Rule 52(c), a district judge must weigh the evidence and resolve credibility." *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000). "A judgment on partial findings is made after the court has heard all the evidence bearing on the crucial issue of fact." Fed. R. Civ. P. 52(c) advisory committee's note to 1991 amendment.

Consistent with the terms of Rule 52(c), the Court exercised its discretion to reserve judgment on the motions during trial. Fed. R. Civ. P. 52(c) ("The court may, however, decline to render any judgment until the close of the evidence."). The Court now concludes that the best course of action is to render a judgment based on all of the evidence, testimony, and applicable law. Accordingly, the Rule 52(c) motions (ECF Nos. 138, 150) are denied.

E. Motion to Correct Inventorship (35 U.S.C. § 256)

Along with its post-trial submissions, Plaintiffs also filed a renewed motion (in lieu of a

previously withdrawn motion)[53] "for the entry of an Order pursuant to 35 U.S.C. § 256(b) directing the United States Patent and Trademark Office [] to issue a certificate adding Drs. Srihari Gopal and Mahesh Samtani as inventors of U.S. Patent No. 9,439,906." ECF No. 166 at 1.[54] Plaintiffs rely on the trial record as well their post-trial briefs, proposed findings of fact, and proposed conclusions of law in support of this motion. *Id.* at 1–2. Plaintiffs argue that Drs. Gopal and Samtani should be added as inventors of the '906 Patent based on trial testimony describing their substantial contributions to the claimed invention and corroborating contemporaneous evidence introduced and admitted at trial. Pls. Br. at 72–73. Teva did not file a separate brief in opposition to Plaintiffs' renewed motion to correct inventorship, but instead argued against the motion in its post-trial submissions. *See* Def. Br. at 42–43; Def. Reply Br. at 42–47. Teva contends that Janssen has improperly changed its position on inventorship insofar as it asserted that there were four additional inventors of the '906 Patent in the Final Pretrial Order, but now only seeks to add Drs. Gopal and Samtani. Def. Br. at 42–43. Teva also argues that the testimony presented at trial establishes that there were numerous additional individuals who made contributions to the '906 Patent and could be considered inventors, that the entire inventive entity must be correct, and that Janssen failed to provide corroborating evidence confirming that Drs. Gopal and Samtani should be added as inventors. *Id.*; Def. Reply Br. at 43–47.

District courts may order the correction of patent inventorship by the USPTO "on notice

[53] Plaintiffs initially filed a motion to amend/correct inventorship pursuant to 35 U.S.C. § 256(b) on June 17, 2020. ECF No. 91. After full briefing on that motion (ECF Nos. 91-2, 115, 118) and oral argument (ECF No. 127), that motion was withdrawn by Plaintiffs who indicated they would file a renewed motion after trial to conform with the evidence presented to the Court. *See* ECF No. 127. Janssen now renews the motion as to Drs. Gopal and Samtani. ECF No. 166; PFOF ¶ 296.

[54] The Court also notes that in 2017, Janssen directly filed an application with the USPTO asking it to correct inventorship of the '906 Patent, but the USPTO has not taken action with respect to that application. Final Pretrial Order at 12.

and hearing of all parties concerned." 35 U.S.C. § 256(b). The concerned parties are "named inventors, omitted inventors, and assignees." *See Nichols Inst. Diagnostics, Inc. v. Scantibodies Clinical Lab'y, Inc.*, 218 F. Supp. 2d 1243, 1250 (S.D. Cal. 2002). 35 U.S.C. § 116(a) provides the standard for joint inventorship:

> When an invention is made by two or more persons jointly, they shall apply for patent jointly and each make the required oath, except as otherwise provided in this title. Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.

"[A] joint invention is simply the product of a collaboration between two or more persons working together to solve the problem addressed." *Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997) (citing *Burroughs Wellcome Co. v. Barr Lab'ys, Inc.*, 40 F.3d 1223, 1227 (Fed. Cir. 1994)). To be a joint inventor, one must:

> (1) contribute in some significant manner to the conception or reduction to practice of the invention, (2) make a contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention, and (3) do more than merely explain to the real inventors well-known concepts and/or the current state of the art.

Pannu v. Iolab Corp., 155 F.3d 1344, 1351 (Fed. Cir. 1998). "Because the issuance of a patent creates a presumption that the named inventors are the true and only inventors, the burden of showing . . . nonjoinder of inventors is a heavy one and must be proved by clear and convincing evidence." *Falana v. Kent State Univ.*, 669 F.3d 1349, 1356 (Fed. Cir. 2012) (internal citation omitted). To meet the clear and convincing evidence standard, putative joint inventors must provide some corroborating evidence instead of relying solely on their own testimony. *Symantec Corp. v. Comput. Assocs. Int'l, Inc.*, 522 F.3d 1279, 1295 (Fed. Cir. 2008). This requirement for corroboration "addresses the concern that a party claiming inventorship might be tempted to

describe his actions in an unjustifiably self-serving manner in order to obtain a patent." *Chen v. Bouchard*, 347 F.3d 1299, 1309 (Fed. Cir. 2003). As such, the corroboration requirement only applies to a putative joint inventor's testimony; documentary evidence does not need corroboration before a court may consider it. *Price v. Symsek*, 988 F.2d 1187, 1195 (Fed. Cir. 1993).

As an initial matter, there are numerous cases holding that "alleged infringers have no innate right to participate in correction-of-inventorship proceedings, whether before the USPTO or a court on the complaint of a party to a patent." *Cobra Int'l, Inc. v. BCNY Int'l, Inc.*, No. 05-61225, 2014 WL 11321379, at *3 (S.D. Fla. Dec. 10, 2014); *see also Nichols Inst. Diagnostics, Inc.*, 218 F. Supp. 2d at 1250 ("An alleged infringer is not a necessary party to a motion for correction under § 256."). Nonetheless, Teva functionally raises arguments on behalf of other potential omitted inventors and maintains that the Court cannot correct the '906 Patent by only adding two omitted inventors when Janssen previously indicated there were four. Against the backdrop of the caselaw discussed above defining and limiting the interested parties to correction of inventorship proceedings pursuant to 35 U.S.C. § 256, the Court notes that Teva has now separately sought leave to amend its affirmative defenses to assert that the '906 Patent is invalid due to incorrect inventorship.

The Court finds more than adequate support in the record to confirm that Drs. Gopal and Samtani should be added as inventors of the '906 Patent.[55] At trial, Dr. Gopal testified credibly about his contributions to the '906 Patent, describing how he revised the dosing regimens,

[55] Janssen asserts the correction of inventorship is rather straightforward because the named inventors, patent assignee, and proposed inventors to be added all agree that inventorship of the '906 Patent should be corrected to add Drs. Gopal and Samtani. *See* Pls. Br. at 71 n.10 ("All concerned parties have waived their right to a hearing and/or participated in a trial on the subject matter of this motion, and they have consented to adding Drs. Gopal and Samtani as inventors of the 906 Patent."). Given the evidence and testimony presented at trial on this issue, however, the Court reviews the substance of the motion to correct inventorship in this Opinion.

examined results of the failed PSY-3002 study, and proposed the claimed dosing regimen. Trial Tr. (Gopal) at 1071:5–16 ("**Q.** Now, did you play a role in selecting the dosing regimen for the new trials? **A.** Yes, I did. **Q.** And what was your role? **A.** So my role was from the perspective of a physician and a clinician treating patients. So we would work closely with the modelers to tell them what was realistic, what potential scenarios to come up with, because they didn't have clinical training by background. So we would tell them what different doses to study, what injection sites, what time periods, and other factors that helped adjust the model."); *id.* at 1089:8–12 (discussing his analysis of results of failed PSY-3002 study: "So I was looking to try to figure out what went wrong in the study because a lot of people were asking me in senior management. So based on my looking at the data, these are the four points that I thought were potentially responsible for it.").

This testimony was corroborated by contemporaneous documents which were admitted into evidence. *See, e.g.*, PTX-235 at 3–4 (PowerPoint presentation created by Dr. Gopal in March 2007 titled "R092670-PSY-3007 Protocol Overview" which instructed investigators running clinical trials on study protocol); PTX-253 at 1 (email from Dr. Gopal regarding results of PSY-3002 study and discussing potential explanations for unexpected failure); PTX-256 at 1 (May 29, 2007 letter to investigators regarding temporary halt of PSY-3006 and PSY-3007 studies as Dr. Gopal and his team considered how to modify these studies in light of PSY-3002 results); PTX-263 at 9–10 (internal Janssen presentation that Dr. Gopal helped prepare, dated June 7, 2007, titled "Paliperidone Palmitate PSY-3002 Results & Implications for PSY-3006").

Dr. Samtani also testified with credibility about his contributions to the '906 Patent in the form of developing dosing windows for claims 2, 10, 13, 20, and 21, and developing the renal impairment dosing regimen. Trial Tr. (Samtani) at 1345:18–1346:8 ("**Q.** I understand you're not

a lawyer, but can you explain to the best of your ability what your significant contributions were to the '906 patent? **A.** So there are two distinct contributions that I can remember. The first one is the development of a dosing recommendation for psychiatric patients who also have mild renal impairment. So this particular dosing recommendation was designed only on the basis of modeling and simulation. And the other piece that I can remember is the designing of dosing windows around the regularly scheduled monthly maintenance injection and also a dosing window around the Day 8 loading dose for paliperidone palmitate. And so it is these dosing recommendations that are contributions that I can recollect are my contributions, among others, to this particular patent."); *id.* at 1349:5–11 (discussing PTX-251, a PowerPoint presentation given in April 2007, and stating, "So I had been working on this project for about two months, and at this point I had made a couple of major breakthroughs that were important findings that I was able to incorporate into the population PK models. And it was this update that I wanted to give to An Vermeulen, and this presentation was prepared as a project update for An Vermeulen in April of 2007.").

This testimony was also corroborated by contemporaneous documents described at trial and admitted into evidence. *See, e.g.*, PTX-251 at 19–20, 27 (presentation authored by Dr. Samtani dated April 27, 2007, titled: "AM&S Application: POP-PK Paliperidone Palmitate" discussing major updates developed through use of deconvolution analysis and the Hirano concept); PTX-278A at 35–36, 118–19 (draft population pharmacokinetic report from August 3, 2007, titled, "Clinical Pharmacology Advanced PK/PD Modeling and Simulation - Population Pharmacokinetic Analysis - R092760 (Paliperidone Palmitate)," which discussed comparisons of initiation regimes and documented that 150/100 mg-eq. day 1/day 8 dosing regimen is optimal); PTX-288 (final report submitted to FDA as part of Janssen's New Drug Application submission in Fall 2007 that included Dr. Samtani's modeling and findings); PTX-294A (PowerPoint sent by

Dr. Samtani to Janssen team in October 2007 summarizing population pharmacokinetic modeling and simulation). Accordingly, the Court finds that based on the testimony and evidence presented at trial, there is clear and convincing evidence that Drs. Gopal and Samtani should be added as inventors of the '906 Patent.[56]

F. Teva's Motion to Amend the Pleading

On July 7, 2021, Teva filed a motion to amend pursuant to Federal Rule of Civil Procedure 15(b)(2), asking the Court to deem its pleadings amended with a count for patent invalidity due to incorrect inventorship under 35 U.S.C. § 102(f), and to enter judgment in its favor on that claim. ECF No. 244. In its brief in support (ECF No. 245), Teva argues that Janssen both "expressly consented to trying the issue of inventorship" and conceded that the inventive entity of the '906 Patent is incorrect by seeking an order to correct inventorship under 35 U.S.C. § 256. *Id.* at 2–3. Teva makes a number of arguments in support of its motion. Teva argues that Janssen did not meet its burden under section 256 to add Drs. Gopal and Samtani as inventors of the '906 Patent. *Id.* at 4. In connection with this argument, Teva asserts that even adding Drs. Gopal and Samtani as inventors does not properly correct inventorship because Janssen previously indicated (in its now withdrawn pretrial motion) that there were four inventors to be added to the '906 Patent. *Id.* at 5–6. Teva also contends that Janssen did not offer any testimony or evidence as to Dr. Lewyn-Briscoe or Dr. Kusumakar despite previously indicating that they are also inventors of the '906 Patent. *Id.* Additionally, Teva argues that the record evidence presented at trial demonstrates that tens of people inside and outside Janssen contributed to the '906 Patent and that these people

[56] Teva also argues that Dr. Gopal at one point pushed for a higher second loading dose and only "acquiesced" to the dosing regimen in Claim 2. Def. Reply Br. at 45. This argument misses the focus of joint inventorship analysis, and fails to acknowledge the difficult and fluid process that Janssen went through in developing Invega Sustenna. Teva's arguments regarding Dr. Samtani's modeling efforts (*id.* at 46) similarly miss the mark.

should also be named as inventors. *Id.* at 4–5.

Janssen filed its brief in opposition on August 2, 2021. ECF No. 252. Janssen argues that Teva cannot assert a section 102(f) defense because it did not raise such a defense in its invalidity contentions as required by Local Patent Rule 3.3 and that Teva waived this argument by failing to include it in the Final Pretrial Order, raise it at trial, or brief the issue post-trial. *Id.* at 13–15. Janssen further argues that it did not consent to trying a section 102(f) defense, that no section 102(f) defense was implicitly tried, and that it would be greatly prejudiced if such a defense were introduced into the case at this time. *Id.* at 16–18. Janssen also asserts that there is no trial evidence to support a section 102(f) defense and that Teva has the burden of proof on this issue. *Id.* at 19–20. Finally, Janssen argues that even if the Court were to reach the merits of the section 102(f) invalidity challenge, the '906 Patent would not be rendered invalid under any potential scenario. *Id.* at 20–23.

Teva filed its reply in support on August 9, 2021. ECF No. 258. Echoing its original arguments, Teva maintains that Janssen placed inventorship at issue during trial, Janssen failed to provide evidence showing that Drs. Gopal and Samtani should be added as inventors of the '906 Patent, and that Teva has carried its burden of establishing invalidity by showing that inventorship of the '906 Patent is incorrect. *Id.* at 2–4.[57]

Rule 15(b)(2) allows for amendment of a complaint during or after trial when a claim not included in the complaint is tried by express or implied consent. *Swiatek v. Bemis Co.*, 542 F. App'x 183, 188 (3d Cir. 2013). It is difficult to find that Janssen expressly consented to Teva

[57] While Teva attempts to frame this amendment request solely in terms of inventorship, they in fact ask the Court "to deem Teva's pleadings amended with a count for patent invalidity under 35 U.S.C. § 102(f)." ECF No. 245 at 1. Thus, the correct inquiry here is whether Janssen gave express or implied consent to trying the issue of invalidity based upon incorrect inventorship.

raising a section 102(f) invalidity challenge. As Janssen noted in its opening post-trial brief, "Teva has not asserted an inventorship defense pursuant to 35 U.S.C. § 102(f)" prior to its pending motion. Pls. Br. at 74. Thus, Janssen did not raise any arguments against a section 102(f) challenge in any of its post-trial submissions, as would be expected if the issue had been raised, or if evidence relevant to such a challenge had been presented at trial. *Id*.

In determining whether there was implied consent to try an issue, the court must consider "whether the parties recognized that the unpleaded issue entered the case at trial, whether the evidence that supports the unpleaded issue was introduced at trial without objection, and whether a finding of trial by consent prejudiced the opposing party's opportunity to respond." *Liberty Lincoln-Mercury, Inc. v. Ford Motor Co.*, 676 F.3d 318, 327 (3d Cir. 2012) (internal citations and quotation marks omitted). Neither party appeared to recognize that a section 102(f) invalidity challenge entered the trial as this topic was never meaningfully discussed, and the only evidence and testimony relevant to inventorship heard at trial was presented in connection with adding Drs. Gopal and Samtani to the '906 Patent, as discussed above. Furthermore, "[t]he main consideration in determining whether leave to amend under Rule 15(b) should be granted is prejudice to the opposing party." *Swiatek*, 542 F. App'x at 188. Janssen argues persuasively that it would be greatly prejudiced by allowing Teva to amend its pleadings as it would "have prepared for and proceeded at trial much differently," including by calling witnesses and presenting evidence as to Drs. Lewyn-Briscoe and Kusumakar. ECF No. 252 at 18–19 (citing *Swiatek*, 542 F. App'x at 188).

While there are certainly fairness and prejudice concerns implicated by allowing Teva to assert a new invalidity defense approximately four months after closing arguments, six months after the close of briefing, and nine months after the conclusion of live testimony, the Court finds that even considering Teva's invalidity defense based upon incorrect inventorship, Teva has

clearly failed to carry its burden on this point. The trial record contains testimony and evidence which support granting Janssen's motion to correct inventorship by adding Drs. Samtani and Gopal as inventors (as discussed and analyzed above), but the record is devoid of any testimony or evidence showing that there are additional issues with inventorship of the '906 Patent. Teva attempts to avoid this dearth of support by citing to arguments outside of the trial record, largely focused on Janssen's withdrawn initial motion to correct inventorship. Such attempt to rely on materials outside of the trial record is improper and is rejected. *See Mass Engineered Design, Inc. v. Planar Sys., Inc*., No. 16-1510, 2018 WL 3323762, at *5 (D. Or. July 6, 2018) ("Moreover, at the bench trial, the Court will only consider admissible evidence in making its findings of fact and conclusions of law."); *Deere & Co. v. FIMCO Inc.*, 260 F. Supp. 3d 830, 835 (W.D. Ky. 2017) ("Initially, the Court notes that both parties should be mindful that this case is set for a bench trial rather than a jury trial. As such, the Court can and will only consider the evidence it has found to be relevant and admissible at trial."); *Armco, Inc. v. Burns & McDonnell, Inc*., 809 F. Supp. 43, 45 n.3 (S.D. Ohio 1992) ("At the bench trial of this case, this Court will be careful to only consider evidence ultimately admitted into evidence in rendering its decision."); *see also Caldwell-Baker Co. v. S. Illinois Railcar Co.*, 225 F. Supp. 2d 1243, 1259 (D. Kan. 2002) ("Withdrawal of a motion has a practical effect as if the party had never brought the motion."). Here, the Court must determine whether Teva has shown by clear and convincing admissible evidence that the '906 Patent is invalid for failing to name the correct inventors. *See Pannu*, 155 F.3d at 1350 ("When a party asserts invalidity under § 102(f) due to nonjoinder, a district court should first determine whether there exists clear and convincing proof that the alleged unnamed inventor was in fact a co-inventor."). The Court finds that Teva has not done so.

Teva's section 102(f) invalidity challenge relies almost exclusively on testimony and

evidence presented during its cross-examination of Janssen's witnesses that briefly addressed named and unnamed individuals' work on developing Invega Sustenna. These cursory exchanges regarding "teamwork," and touching upon other individuals who worked in largely unspecified capacities on Invega Sustenna, are wholly inadequate to support a section 102(f) challenge. *See* Trial Tr. (Vermeulen) at 755:11–16, 1004:21–1005:5, 1005:18–21, 1013:14–17, and 1024:13–17; *see also* Trial Tr. (Gopal) at 1172:3–16. This testimony does not show that a correct inventor of the '906 Patent has been omitted as clearly not every person who works on an invention that is later patented is an inventor in the eyes of the law. *Fina Oil & Chem. Co.*, 123 F.3d at 1473 ("[T]o be a joint inventor, an individual must make a contribution to the conception of the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention."). Teva presents no persuasive argument or evidence to show that any of the other individuals involved with Invega Sustenna should be named as inventors, as mere testimony confirming that individuals worked on a project in some capacity falls woefully short of the required clear and convincing evidence required to show inventorship is incorrect. *See, e.g.*, *Gemstar-TV Guide Int'l, Inc. v. Int'l Trade Comm'n*, 383 F.3d 1352, 1382 (Fed. Cir. 2004) ("[A]lleged co-inventors must prove their contribution to the conception of the invention with more than their own testimony concerning the relevant facts.").

Additionally, while Teva states without any legal or factual support that inventorship of the '906 Patent is "uncorrectable," (ECF No. 245 at 4), the Court rejects this meritless argument. It is well-settled that even if the Court were to find incorrect inventorship, Janssen would be given an opportunity remedy this issue. *See Pannu*, 155 F.3d at 1350 ("Upon such a finding of incorrect inventorship, a patentee may invoke section 256 to save the patent from invalidity. Accordingly, the patentee must then be given an opportunity to correct inventorship pursuant to that section.");

Roche Palo Alto LLC v. Ranbaxy Lab'ys Ltd., 551 F. Supp. 2d 349, 359 (D.N.J. 2008) (A patent owner is "entitled to an opportunity to correct inventorship through the district court, even if it did absolutely nothing to correct the improper inventorship beforehand"). While Teva has failed to meet its burden on its section 102(f) challenge, it has also failed to show that Janssen would not be able to cure inventorship.

Accordingly, the Court has considered Teva's invalidity challenge under section 102(f) despite the issues noted with its motion to amend the pleadings pursuant to Rule 15(b)(2) (ECF No. 244), and finds that the trial record does not contain adequate evidence or testimony to show that the '906 Patent is invalid due to failure to include all proper inventors.

IV. CONCLUSION

For the foregoing reasons, the Court finds that Defendant has failed to show by clear and convincing evidence that the Patent-in-Suit is invalid. An appropriate Order accompanies this Opinion.

DATE: October 8, 2021

s/ Claire C. Cecchi
CLAIRE C. CECCHI, U.S.D.J.