IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JANSSEN PHARMACEUTICALS, INC. and JANSSEN PHARMCEUTICA NV,	§	
Plaintiffs,	§	
v.	§	Civil Action No. 21-1784-WCB
TOLMAR, INC.,	§	
Defendant.	§	

FINDINGS OF FACT AND CONCLUSIONS OF LAW

BACKGROUND

This is a Hatch-Waxman Act case. The plaintiffs, Janssen Pharmaceuticals, Inc. and Janssen Pharmaceutica NV (collectively, "Janssen"), are suing the defendant, Tolmar, Inc., ("Tolmar") for patent infringement under 35 U.S.C. § 271(e)(2).

A. The Statutory Framework

The Hatch-Waxman Act is the name commonly used to refer to the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified at 21 U.S.C. §§ 355, 360(cc), 35 U.S.C. §§ 156, 271, 282), as amended by the Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066. The Hatch-Waxman Act was designed to strike a balance between two competing policy interests: (1) to induce pioneering research and development of new drugs; and (2) to enable competitors to bring low-cost generic copies of those drugs to market rapidly if those drugs are not entitled to patent protection. *See Andrx Pharms., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1371 (Fed. Cir. 2002). To

promote those objectives, the Hatch-Waxman Act provides for a prompt determination of whether particular drugs made and sold by brand-name pharmaceutical companies are protected by valid patents. If the patents are held to be infringed and not invalid, the covered drugs cannot be made and sold by generic manufacturers until the patents expire. If the patents are held to be invalid or not infringed, the Act provides a mechanism for prompt approval of the generic versions of the drugs by the U.S. Food and Drug Administration ("FDA"), which regulates the sale of pharmaceutical drugs in this country.

In order to obtain the necessary FDA approval to market a new drug, a pharmaceutical company must file a New Drug Application ("NDA"). That application is designed to show the FDA, through rigorous testing procedures, that the drug is safe and effective for its proposed uses. After considering the application, and often after extended negotiations with the pharmaceutical company, the FDA may grant the application and authorize the company to market the drug for particular indications. The company is restricted to marketing the drug for those indications, as dictated by FDA regulations that govern both labeling and advertising for all prescription drugs. *See* 21 C.F.R. §§ 201.1–201.327 (labeling); *id.* § 202.1 (advertising).

In an effort to speed up the approval process for generic drugs, the Hatch-Waxman Act provides that a generic drug manufacturer may submit an Abbreviated New Drug Application ("ANDA") for approval by the FDA. If the generic company intends to market a drug that is bio-equivalent to the first pharmaceutical company's approved drug, the ANDA may rely on the safety and efficacy studies previously submitted as part of the first company's NDA.

Under the Hatch-Waxman Act, NDA holders are required to notify the FDA of all patents that "claim[] the drug for which the [NDA] applicant submitted the application . . . and with respect to which a claim of patent infringement could reasonably be asserted." 21 U.S.C. § 355(b)(1),

(c)(2). The FDA lists such patents in a publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations," which is commonly referred to as the "Orange Book." *See Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1318 (Fed. Cir. 2012); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1045 (Fed. Cir. 2010).

The Hatch-Waxman Act creates what is referred to as an "artificial" type of infringement that allows for the adjudication of the parties' rights in patents that would be infringed if the ANDA were issued and the generic product made, used, or sold. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990); *Glaxo Grp. Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1351 (Fed. Cir. 2004). In particular, 35 U.S.C. § 271(e)(2)(A) provides that it shall be an act of patent infringement to submit an ANDA for a drug claimed in a patent or the use of which is claimed in a patent if the purpose of the submission of the ANDA is to obtain approval to engage in the commercial manufacture, use, or sale of the drug claimed in the patent, or the use of which is claimed in the patent, before the patent's expiration.

Janssen is the owner of U.S. Patent No. 9,439,906 ("the '906 patent"), entitled "Dosing Regimen Associated with Long Acting Injectable Paliperidone Esters." The '906 patent is listed in the Orange Book as covering Janssen's Invega Sustenna® brand paliperidone extended-release suspension products. Invega Sustenna® is indicated for the treatment of schizophrenia in adults, for the treatment of schizoaffective disorder in adults as a monotherapy, and as an adjunct to mood stabilizers or antidepressants.

Tolmar filed Abbreviated New Drug Application No. 211995 and notified Janssen of the filing pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(j), on November 21, 2021. Tolmar's ANDA specifically seeks FDA approval to market generic versions of Janssen's Invega Sustenna® brand paliperidone palmitate extended-release injectable

suspension products prior to the expiration of the '906 patent. Based on Tolmar's ANDA filing, Janssen is accusing Tolmar of infringing the '906 patent under 35 U.S.C. § 271(e)(2)(A).

B. Schizophrenia and Anti-Psychotic Drugs

"Schizophrenia is the most serious mental illness." TD3 18:17–19; TD1 359:3–5, 20.[1] Schizophrenia patients are treated with antipsychotic medications such as Invega Sustenna® to relieve their symptoms. TD3 22:16–23:4; *see also* TD1 360:21–361:12. Antipsychotic medications fall into two groups: first and second-generation antipsychotics. First-generation antipsychotics were invented in the 1950s. TD1 365:10–14. Although effective, first-generation antipsychotics "are associated with cognitive slowing and worsening," so their use is discouraged in the early phase of illness. *See* TD3 43:23–44:7. Second-generation, or "atypical" antipsychotics were developed in the 1970s and '80s. TD1 365:15–17. Second-generation antipsychotics work by blocking the neurotransmitter dopamine, TD3 32:7–17, as an overabundance of dopamine is associated with psychotic disorders, *id.* at 67:2–17. Second-generation antipsychotics result in better relief of symptoms with fewer side effects compared to their first-generation predecessors. TD1 365:23–366:5.

One of the main second-generation antipsychotics is a drug called risperidone. *See* '906 patent 1:27–31. Risperidone metabolizes into paliperidone, which is the active moiety for antipsychotic purposes. *Id.* Janssen itself markets an orally administered risperidone product under the name Risperdal Consta®.

Early formulations of risperidone were administered orally. Oral administration proved problematic, however, because as many as 75 to 80 percent of schizophrenic patients are

[1] References to the trial transcript will include the trial day ("TD1" through "TD4") and the page and line numbers of the transcript for that day. The trial transcript can be found on the district court docket sheet for this case at docket entries 145 through 148.

nonadherent to medication, meaning that they are unwilling or unable to take medication on their own as prescribed. TD3 23:21–24:4; *see also* PTX-227 at 3. Nonadherence is especially pronounced among schizophrenic patients because persons with schizophrenia often do not believe they suffer from a disorder. TD3 24:7–9. Some patients even feel that the symptoms have meaning and do not want to rid themselves of the symptoms. TD3 24:11–14. The nonadherence issue is exacerbated by the fact that patients often notice the negative side effects associated with medication before they experience the therapeutic benefits. TD3 25:2–16. As a result, patients often insist that they do not need the medication. *Id.*

Nonadherence problems are the most severe with orally administered medication. *See* JTX-222 at 5; JTX-63 at 7. Long-acting injectables, on the other hand, pose less risk of nonadherence because they present fewer opportunities for patients to resist treatment. TD3 51:16–17. Moreover, the mode of their administration helps facilitate continuity of treatment and certainty of adherence. JTX-240 at 1. Prior to the patent in suit, most antipsychotics were not available in long-acting injectable form. *See* JTX-12B at 23–31.

C. Janssen's Research and Clinical Trials

In view of the problems with oral administration of antipsychotic drugs, Janssen set out to develop a second-generation long-acting injectable antipsychotic that would provide rapid and sustained efficacy without the need for oral supplementation. TD2 152:14–153:3; TD2 223:13–224:24; JTX-601 at 19. Initially, Janssen looked to its own risperidone-based antipsychotic, Risperdal Consta®. As Janssen discovered, however, injectable risperidone has a three-week-long "lag period" after injection before the drug meaningfully releases into the blood. That lag period made Risperdal Consta® a poor candidate for a loading dose strategy without oral supplementation. TD2 169:10–13.

Having recognized the problems with risperidone, Janssen turned to paliperidone palmitate, a related formulation sharing risperidone's active moiety. Paliperidone palmitate "exhibits the characteristic dopamine . . . and serotonin . . . antagonism of the second-generation, atypical antipsychotic drugs." '906 patent at 1:32–36. Unlike risperidone, however, injectable paliperidone palmitate does not exhibit a pronounced lag period. *See* TD2 160:17–161:13. With that advantage in mind, Janssen conducted Phase I clinical trials evaluating the safety of two protocols: a large dose of paliperidone palmitate on day 1; and two small on days 1 and 8 respectively. TD2 167:11–20. Based on the Phase I results, Janssen conducted a Phase II clinical trial studying equal-dose gluteal injections (i.e., injections in the buttocks) in dosages of either 50 mg-eq.[2] or 100 mg-eq. on days 1, 8, and 36 of the treatment period. TD2 170:12–171:4. The Phase II study was successful enough to justify proceeding to Phase III clinical trials, and Janssen commissioned several Phase III trials to test the efficacy of fixed paliperidone dosing regimens against placebo and Risperdal Consta®. TD2 233:18–334:9.[3]

Surprisingly to Janssen, both of the pertinent Phase III clinical trials failed. TD2 173:10–17; TD2 235:21–24. The trials, referred to as PSY-3003 and PSY-3004, showed no efficacy for fixed paliperidone dosing regimens in United States subjects. TD2 239:22–240:2, 236:1–17. In fact, none of Janssen's fixed-dose, gluteal dosing regimens achieved efficacy for any patient population by day 8 of the treatment period, a result that "undermined . . . [the] important

[2] Mg-eq. refers to milligrams equivalent of the active ingredient. In this case, it means the quantity of paliperidone palmitate needed to deliver 50 mg of pure paliperidone.

[3] A Phase I clinical trial is a small trial conducted on healthy volunteers to determine the safety of the proposed treatment. A Phase II clinical trial is a larger trial designed to test the proposed treatment against the standard treatment or placebo. A Phase III clinical trial is a large trial designed to develop data regarding the safety and efficacy of the treatment to be submitted to the FDA for approval of the proposed treatment.

development goal for the product" of rapid efficacy without oral supplementation. TD2 235:21–239:4; TD2 173:17–175:8, 178:18–179:6.

The failed Phase III studies triggered a "crisis" at Janssen. TD2 174:13–17. Janssen witnesses testified that Janssen "had to come up with a solution" to rescue the development program from failure. TD2 175:18–176:4. But it was not clear to Janssen what the solution would be, because Janssen had expected the Phase III studies to succeed. TD2 176:5–8. Only when the results of PSY-3003 were reported did Janssen discover that the proposed dosing protocol was ineffective. As Janssen's scientists viewed it, nothing in the prior art explained how to solve the problem.

To identify factors that might explain the failure, Dr. An Vermeulen, one of the named inventors on the '906 patent, developed a complex population pharmacokinetics model to analyze individual patient data. TD2 180:18–20, 181:11–182:12. Population pharmacokinetics is the study of the sources and correlates of variability in drug concentrations among individuals in are the target patient population who receive clinically relevant doses of a drug of interest. JTX-638 at 6.

Dr. Vermeulen's work revealed two important factors that appeared to contribute to the failures of the PSY-3003 and PSY-3004 studies: First, the population pharmacokinetic study revealed that body weight had a pronounced effect on the efficacy of the tested treatment regimen. TD2 183:5–184:2; JTX-606 at 9. Second, the study disclosed that there was a significant difference in efficacy depending on whether the injections were given in the gluteal or deltoid (shoulder) muscles. TD2 183:5–184:2; JTX-606 at 9. Based on the population pharmacokinetic data, Dr. Vermeulen realized that patients with a higher body mass index were not reaching therapeutic blood levels in the early days of treatment. TD2 199:10–23. And based on comparing

the results of the gluteal injections of PSY-3003 with the results of earlier clinical trials using injections in the deltoid muscle, Dr. Vermeulen recognized that something about the deltoid injection site made administration of paliperidone palmitate in the deltoid muscle much more effective. TD2 184:19–186:13.

Having identified why the PSY-3003 and 3004 dosing strategies had failed, Dr. Vermeulen and her colleagues recommended a new loading dose strategy featuring a 150 mg-eq. dose in the deltoid on day 1 of the treatment period for all patients, regardless of the monthly maintenance dose, followed by either a 100 or 50 mg-eq. dose on day 8. JTX-236; see also TD2 187:24–188:12; JTX-607. Based on that recommendation, Janssen launched two new Phase III clinical studies. TD2 253:11–254:23. One of the two studies, PSY-3007, featured a 150 mg-eq. dose in the deltoid on day 1, followed by monthly 25, 100, or 150 mg-eq. doses in either the gluteal or the deltoid muscle starting on day 8. PTX-629 at 21. The other study, PSY-3006, differed from the first mainly in that it provided for a 50 mg-eq. dose on day 8 and smaller doses thereafter. TD2 262:10–24; JTX-615 at 9.

Shortly after this second round of Phase III clinical trials began, Janssen received new data causing it to modify the studies. In the spring of 2007, Janssen received the results of a non-inferiority study, entitled PSY-3002, which failed for lack of efficacy. TD2 254:24–256:4; JTX-593 at 1. PSY-3002 compared 50 mg-eq. paliperidone palmitate administered in the gluteal on days 1 and 8 (followed by flexible dosing) to orally administered paliperidone palmitate. TD2 252:14–253:5. The study revealed that injected paliperidone palmitate performed more poorly than the oral version, TD2 254:24–256:4; JTX-593 at 324–25.

Contemporaneously with Janssen's receipt of the PSY-3002 data, another Janssen scientist, Dr. Mahesh Samtani, refined Dr. Vermeulen's population pharmacokinetic model,

increasing its utility. TD2 190:24–191:14; TD2 348:16–350:20. Using his refined model, Dr. Samtani made three key discoveries about paliperidone palmitate. First, he learned that paliperidone palmitate has a biphasic absorption profile, meaning that it is absorbed quickly at first but more slowly thereafter. TD2 351:13–23, 352:24–354:7. Second, he learned that this biphasic absorption profile was more pronounced when the drug was injected in the deltoid muscle than when it was injected in the gluteal muscle. From that evidence, he concluded that rapid efficacy could be better achieved by injections in the deltoid than in the gluteal. TD2 356:11-357:1. Third, he learned that higher doses of paliperidone palmitate do not result in proportionally higher increases in peak concentration; rather, he discovered that as the dose increases, the release curve flattens and the peaks are not as high. TD2 357:2–358:14 (discussing JTX-613 at 27).

Based on the results of PSY-3002 and Dr. Samtani's modeling and simulation work, Janssen revised the dosing regimen for PSY-3006 to increase the day 8 dose from 50 to 100 mg-eq. and to mandate injection in the deltoid. The clinical studies on that formulation were successful, TD2 264:6–266:8; JTX-599 at 99, and that dosing regimen was the regimen that was ultimately claimed in the '906 patent, TD2 263:1–22; TD2 369:6–19; JTX-615 at 9

D. The '918 Provisional Application and the '906 Patent

On December 19, 2007, Janssen filed U.S. Provisional Application No. 61/014,918 ("the '918 provisional application"), which was based on the revised version of the PSY-3006 dosing regimen that produced a positive result in the Phase III study. A year later, on December 17, 2008, Janssen filed the application that became the '906 patent.

The '906 patent is directed to a dosing regimen for a long-acting injectable formulation of paliperidone palmitate. Claim 1 is representative of its dependent claims (1–3). It recites:

> 1. A dosing regimen for administering paliperidone palmitate to a psychiatric patient in need of treatment for schizophrenia, schizoaffective disorder, or schizophreniform disorder comprising
>
> > (1) administering intramuscularly in the deltoid of a patient in need of treatment a first loading dose of about 150 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the first day of treatment;
> >
> > (2) administering intramuscularly in the deltoid muscle of the patient in need of treatment a second loading dose of about 100 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the 6th to about 10th day of treatment; and
> >
> > (3) administering intramuscularly in the deltoid or gluteal muscle of the patient in need of treatment a first maintenance dose of about 25 mg-eq. to about 150 mg-eq. of paliperidone as paliperidone palmitate in a sustained release formulation a month (±7 days) after the second loading dose.

'906 patent at 32:11–30.

The '906 patent contains three other sets of claims that differ from claims 1–3 in ways that are material to this litigation. Claims 5–7 and 15 (the "psychotic disorder claims") depend from representative independent claim 4 and differ from claim 1 in two ways. First, the preamble of claim 4 addresses "psychotic disorder" instead of "schizophrenia, schizoaffective disorder, or schizophreniform disorder." *Compare* '906 patent at 32:40–41 *with id.* at 32:12–14. Second, the body of claim 4 recites a second loading dose administered on the eighth day of treatment, rather than on a day between the 6th and 10th day of treatment, as recited in claim 1. *Compare* '906 patent at 32:51 *with id.* at 32:24. The remaining psychotic disorder claims do not differ from claim 4 in any way that Tolmar has identified as meaningful. Claims 8–14 and 16 (the "renal impairment claims") mirror claims 1–7 and 15. The only material difference between the two sets of claims is that the renal impairment claims call for up to a 50 percent reduction in dose volume when treating renally impaired patients. *See* '906 patent at 32:66–34:3. Claims 17–21 (the "formulation claims") all depend from claims 1, 4, 8, or 11. *See* '906 patent at 34:15–51. Those dependent

claims recite the formulation of the aqueous nanoparticle solution called for in the earlier dosing claims. *Id.*

The disclosure of the '918 provisional application, to which the '906 patent claims priority, differs from that of the '906 patent in one respect material to this case. The specifications of both the '918 provisional application and the '906 patent describe administering loading doses "approximately once a month." '906 patent at 5:29; *id.* at 6:4; '918 provisional application at 5:9–10, 6:3. However, the '906 patent clarifies, by way of example, that administering doses approximately once a month means once during each period of one month plus or minus seven days. '906 patent at 5:29; *id.* at 6:4. And that "month (±7 days)" window after the second loading dose is what was ultimately claimed in the '906 patent. '906 patent at 32:29. By contrast, the '918 provisional application claims a maintenance dose administered "on about the 34th to about the 38th day of treatment" i.e., 26 to 30 days after the second loading dose. '918 provisional at 29:19–20. Elsewhere, the '918 provisional application claims a maintenance dose administered "after the 30th day of treatment," *id.* at 29:22–24, 34:17–19, 38:26–28.

DISCUSSION

To simplify the issues for trial, the parties stipulated as to all issues relating to infringement. Tolmar agreed to a judgment of infringement with respect to claims 1–7, claim 15, and the portions of claims 17–21 that depend from claims 1 and 4 of the '906 patent. Dkt. No. 86 at ¶ 1. Janssen stipulated to entry of a judgment of noninfringement with respect to claims 8–14, 16, and the portions of claims 17–21 that depend from claims 8 and 11 (collectively the "renal impairment claims"). *Id.* at ¶¶ 5–6.[4] Although judgment was entered in Tolmar's favor with respect to the

[4] The parties' stipulation was conditioned on the court's subsequent claim construction ruling. Each side agreed that infringement of the renal impairment claims depends entirely on the claim construction issue. Judge Andrews adopted Tolmar's construction of the phrase "of from

renal impairment claims, Janssen reserved the right to appeal the court's claim construction ruling. For that reason, Tolmar still challenges the validity of those claims. In light of those stipulations, the issues for trial related exclusively to invalidity, and Tolmar challenged the validity of each claim of the '906 patent.

Tolmar argues that the claims of the '906 patent are invalid for three reasons. First, Tolmar argues that the claims would have been obvious over a combination of two main references and several secondary references pertaining to the dependent claims. Second, Tolmar argues that the claimed ±7-day maintenance doses and the claimed scope of psychotic disorders are not adequately described in the '906 specification under 35 U.S.C. § 112. And third, Tolmar argues that the specification fails to enable a person of ordinary skill to practice the claimed invention.

I. Obviousness

Obviousness under 35 U.S.C. § 103 is a question of law based on underlying findings of fact. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The underlying factual considerations "include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations" of nonobviousness. *Apple Inc. v. Samsung Elecs. Co*., 839 F.3d 1034, 1052–53 (Fed. Cir. 2016) (en banc); *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 736 (Fed. Cir. 2013) (citing *Graham*, 383 U.S. at 17–18, and *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007)). "The obviousness analysis should not be conducted 'in a narrow, rigid manner,' but should instead focus on whether a claimed invention is merely 'the result of ordinary innovation,' which is not entitled to patent protection." *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F. Supp. 3d 566,

about 75 mg-eq.," Dkt. No. 93 at 1 (claim construction order); *see also* Dkt. No. 40 at 4 (parties' proposed constructions), after which Janssen conceded noninfringement of those claims. In July 2023, this case was transferred to me for trial.

595 (D. Del. 2018), aff'd sub nom. *Persion Pharms. LLC v. Alvogen Malta Operations Ltd.*, 945 F.3d 1184 (Fed. Cir. 2019) (quoting *KSR*, 550 U.S. at 427–28).

"A party seeking to invalidate a patent as obvious 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 from doing so.'" *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 973 (Fed. Cir. 2014) (quoting *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009)). Although the patent owner bears the burden of production as to secondary considerations of nonobviousness, the party challenging the patent bears the ultimate burden of proving obviousness. *Galderma*, 737 F.3d at 738.

Based on the evidence at trial, I find that one of Tolmar's principal references, referred to as "Kramer," is not prior art to the '906 patent. I also find that a person of ordinary skill in the art would not have found the claimed dosing regimens obvious over the remaining references without Kramer.

A. Person of Ordinary Skill in the Art

Janssen's proposed definition of a person of ordinary skill in the art with regard to the technology at issue in this case is a person with an "M.D., Ph.D., Pharm.D., or equivalent work experience in drug formulation, pharmacy, pharmacokinetics, or medicine and [] capable of working in a team comprising others in the field or related fields." Dkt. No. 118-1, Ex. 1 at 3. Janssen's definition "accounts for various factors, including the educational background of the inventors, the level of education and experience of those working in the field, the types of problems faced by those working in the field, solutions known by those working in the field to those problems, and the sophistication of the technology that is the subject of the patent." *Id.*

Tolmar's proposed definition of a person of ordinary skill in the art with regard to the technology at issue in this case is a person with "an advanced degree, such as an M.D., Ph.D., PharmD, master's degree, or other advanced degree, in subject matter related to chemistry, medicine, pharmaceutics, pharmacokinetics, or related discipline, with several years of experience in the relevant field and [] capable of working in a team with others in the field or related fields." *Id.*

The parties agree that the two definitions are materially identical and that "the opinions offered by the parties' experts as to the validity of the '906 Patent would not change based on which of the definitions in paragraphs 16 and 17 above is applied." *Id.* Following the proposed definitions, I find that a person of ordinary skill in the art is one with an M.D., Ph.D., Pharm.D., or equivalent work experience in drug formulation, pharmacy, pharmacokinetics, or medicine, who is capable of working in a team comprising others in the field or related fields.

B. The Main Prior Art References

Tolmar relies primarily on two prior art references in support of its obviousness argument. The first reference is an overview of National Clinical Trial No. 210,548 ("NCT 548"), published on September 20, 2005, on the clinicaltrials.gov website. JTX-23. NCT 548 describes the protocol for Janssen's PSY-3003 Phase III clinical trial. TD2 268:20–270:4. The second reference, referred to as the "Kramer" reference, is a poster purportedly displayed by a group of Janssen researchers at the 20th U.S. Psychiatric and Mental Health Congress in Orlando, Florida, on October 13, 2007. The poster was entitled "Efficacy and Tolerability of Two Fixed Dosages of Paliperidone Palmitate in the Treatment of Schizophrenia: Results of a 9-Week Placebo-Controlled Trial." JTX-36. It reports the results of Janssen's Phase II clinical trial.

Janssen's PSY-3003 clinical trial, as described in NCT-548, was a 14-week study on paliperidone palmitate injections, designed to test the hypothesis that three "fixed doses of paliperidone" of varying quantity "are each more efficacious than placebo in treating subjects with schizophrenia." *Id*. The three fixed doses were 50, 100, and 150 mg-eq. of paliperidone palmitate administered on days 1, 8, 36, and 64 of the treatment period. *Id*; *see also* TD1 155:18–22. NCT 548 did not provide for mixing and matching the doses. That is, a patient who received a 50 mg-eq. dose on day 1 would receive 50 mg-eq. doses for the remainder of the study. Similarly, patients who received a 100 mg-eq. dose on day 1 would continue to receive 100 mg-eq. doses throughout the treatment period, and patients who received a 150 mg-eq. dose on day 1 would continue to receive 150 mg-eq. doses throughout the treatment period.

A person of ordinary skill in the art would understand that the formulation called for in NCT 548 must be a sustained-release formulation, because anything else would fail to maintain a therapeutically effective plasma concentration of paliperidone for a month-long period. TD1 157:13–23.

Although NCT 548 describes the dosing regimens of Janssen's PSY-3003 study, it contains no information about the study's results. NCT 548 only states Janssen's hypothesis: "that the 3 fixed doses of paliperidone are each more efficacious than placebo in treating subjects with schizophrenia." JTX-23 at 1. Because NCT 548 states that it is a Phase III clinical trial, a person of ordinary skill in the art would recognize that the safety and efficacy of the proposed protocol was supported by Phase I and Phase II studies. They would further recognize, based on the enormous cost of conducting Phase III clinical trials, that Janssen had good reason to believe its hypothesis to be correct.

The second primary reference, Kramer, reported the results of a study using a dosing regimen of intramuscular injections of 50 and 100 mg-eq. of paliperidone palmitate on days 1, 8, and 36 of treatment. JTX-36 at 3. Like NCT 548, the Kramer protocol employed gluteal injections and doses of equal size across all time points. *Id.*; *see also* TD2 170:12–171:4. Unlike NCT 548, however, Kramer reported the results of the study. *See* JTX-36 at 4–6. Importantly, Kramer reported that only 51% of the enrolled patients completed the study. TD1 139:14–140:1. The most common reason given for withdrawal was lack of efficacy. *Id*.

A significant issue at trial was whether the Kramer poster was actually published at all. Tolmar argues that the evidence shows that the poster was published by being presented for several hours on October 13, 2007, at the Orlando Congress. Janssen argues that the evidence shows, at most, that the poster was intended to be displayed at that time, but that the evidence does not prove that the poster was actually shown as planned.

The alleged publication of the Kramer poster predates the filing of both the '906 patent and the December 19, 2007, provisional to which it claims priority, but it does not predate the provisional by more than a year.

C. Kramer's Status as Prior Art

I find that Tolmar did not meet its burden of proving Kramer's status as prior art to the '906 patent for two independent reasons. First, I find that Tolmar did not prove by clear and convincing evidence that the '906 patent is not entitled to the filing date of the '918 provisional application. Second, I find that Tolmar did not prove by clear and convincing evidence that Kramer was actually presented at the 2007 Congress Orlando. Either finding is sufficient to exclude Kramer as prior art to the '906 patent.

1. Priority to the Filing Date of the '918 Provisional Application

The version of 35 U.S.C. § 102 that was in effect prior to the enactment of the America Invents Act ("Pre-AIA section 102") is the version of the statute that applies in this case. Under Pre-AIA section 102(b), a printed publication qualifies as prior art only if it was published "more than one year prior to the date of the application for patent in the United States." As such, Kramer falls within the one-year grace period set forth in Pre-AIA section 102(b) of the Patent Act and therefore does not constitute prior art unless Tolmar can show that the '906 patent is not entitled to the filing date of the '918 provisional application.[5]

For a patent to benefit from the filing date of an earlier application, including a provisional application, the earlier application must satisfy the written description and enablement requirements for each claim. *New Railhead Mfg., L.L.C. v. Vermeer Mfg. Co.*, 298 F.3d 1290, 1294 (Fed. Cir. 2002). Tolmar argues that the '918 provisional application fails to satisfy either requirement with respect to the plus or minus seven-day limitation of the '906 claims.

a. Burden of Proof

To establish that the '906 patent is not entitled to priority as of the filing date of the '918 provisional application, Tolmar must prove by clear and convincing evidence that the '918 provisional application does not fully support or enable the '906 claims. *See Tech. Licensing Corp.*

[5] In my order addressing Janssen's motion for summary judgment, I held that the '906 patent was reduced to practice by no later than June 2007. Dkt. No. 114 at 7. Thus, Kramer does not qualify as prior art under Pre-AIA section 102(a), either. *Id*. In that order, I did not rule as to priority under section 102(b), because at the time Janssen did not argue that Kramer was published (if at all) within the grace period of the '918 provisional application. *See* Dkt. No. 102. In that motion, Janssen erroneously stated that the filing date for the provisional application was in December 2008. *See* Dkt. No. 102 at 14 ("Tolmar contends that the Kramer Document is prior art under pre-AIA § 102(b) because it was allegedly published in a printed publication in October 2007, more than one year before the December 2008 Provisional filing date."). In fact, the filing date of the provisional application was December 19, 2007, JTX-22, less than a year after the alleged publication date of the Kramer poster in October 2007.

v. Videotek, Inc., 545 F.3d 1316, 1327 (Fed. Cir. 2008); *see also Gen. Hosp. Corp. v. Sienna Biopharmaceuticals, Inc.*, 888 F.3d 1368, 1371 (Fed. Cir. 2018) ("Sufficiency of written description [in a patent application] is a question of fact.").

How the burden of proof is allocated between the parties depends on whether the patent office has addressed the issue. If the patent office has already found that an application supports an issued patent, the challenger bears both the burden of production and the burden of persuading the finder of fact, by clear and convincing evidence, that the patent is not entitled to the priority date of the earlier application. *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1573–74 (Fed. Cir. 1985); *Tech. Licensing Corp.*, 545 F.3d at 1328. If the patent office has not addressed the issue, the patent owner bears the burden of production of showing that the patent is entitled to the benefit of an earlier filing date, including that the written description in the earlier application supports the asserted claim. *See PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1303–06 (Fed. Cir. 2008) (affirming the district court's conclusion that "when a dispute arises concerning whether a CIP patent is entitled to priority to the date of the original application and the Patent Office has not addressed the issue, the burden of proof ordinarily should rest with the party claiming priority to the date of the original application."); *Tech. Licensing Corp.*, 545 F.3d at 1328–29 (reading *PowerOasis* as applying to the burden of production).

In this case the Patent and Trademark Office, in the person of the examiner, considered the '906 patent's validity over references that were prior art to the patent, but not to the '918 provisional application. The examiner concluded that "the ['906 patent] claims are fully supported by [the '918 provisional application]." JTX-2 at 1414. Because the patent office has already determined that the claims are fully supported by the disclosure in the provisional application, Tolmar bears both the burden of production and the burden of proving, by clear and convincing

evidence, that the patentee is not entitled to the filing date of the '918 provisional application as the priority date for the '906 patent. *Tech. Licensing Corp.*, 545 F.3d at 1327.

b. Written Description

For the claims of the '906 patent to benefit from the filing date of the '918 provisional application, the provisional application must provide written description support for the claims in question. As to that issue, Tolmar argues that the provisional application does not support the claimed "(±7 days)" window for the monthly maintenance doses. *See* TD1 327:1–6 (conceding that "everything other than the monthly plus or minus seven-day maintenance window is taught and supported by the disclosure in the '918 provisional application"). All independent claims of the '906 patent contain the plus or minus seven-day limitation, so Tolmar's argument applies equally to all the asserted claims.

The written description requirement is satisfied if "the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* "The written-description analysis is highly dependent on the facts of each case." *Biogen Int'l GmbH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1342 (Fed. Cir. 2021).

The '906 patent claims a protocol in which the first maintenance dose is administered "a month (±7 days) after the second loading dose." '906 patent at 32:29–30. The '918 provisional application describes maintenance doses that are administered "approximately once a month." '918 provisional application at 5:9–10, 6:3. The provisional application claims a maintenance

dose administered "on about the 34th to about the 38th day of treatment," i.e., 26 to 30 days after the second loading dose. *Id.* at 29:19–20.

The inventors indisputably had possession of at least one embodiment of the '906 claims. Tolmar argues, however, that the provisional application did not show that the inventors possessed the entire range recited in the '906 patent.

Applying the governing legal principles to the facts of this case, the written description question is: Does "approximately once a month" convey to a person of ordinary skill in the art that maintenance doses of the claimed formulation can be administered up to a week early or late, as needed?

The meaning of the word "approximately," much like the meaning of the word "about," depends on "the technological facts of the particular case." *Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008) (discussing the meaning of "about"). The only expert who offered an express opinion on this issue was Tolmar's witness, Dr. Lisa Coles, who testified that "the '918 [provisional application] does not support the '906 [patent] in either enablement or written description regarding these widened dosing windows." TD1 88:16–18; *see also* TD1 84:8–11. In explaining her conclusion, Dr. Coles credited the "substantial increase in dosing window" between the provisional application and the claims of the patent. TD1 84:14. On that point, she explained that a person of ordinary skill in the art "would understand that the drug concentrations that would be attained . . . with such a large window would be affected" and that such a person would not know "whether those drug concentrations [would still be] within an effective dosing window." TD1 84:16–22.

Dr. Coles' testimony is unpersuasive because it assumes an ordinary artisan would understand the four-day monthly window claimed in the '918 provisional application to define the

outer boundary at which a correct concentration of paliperidone can be achieved. In other words, Dr. Coles assumed that an ordinary artisan would view the day 34–38 window of the '918 claims as a strict limiting requirement. But that is an implausible assumption. Instead, an ordinary artisan would understand the term "approximately once a month," as used in the specification of the '918 provisional application, to mean that once a month is the ideal timing for administering a maintenance dose, but that some deviation from that dosing interval is permissible.

The '918 provisional application itself, together with testimony from Janssen's experts in a related context, support that conclusion. The '918 provisional application reports that the half-life of paliperidone is "40–49 days (median) after the 100 and 150 mg eq. dose." '918 provisional application at 27:10–13. Based on the half-life reported in the '918 provisional application, a skilled artisan would understand that "[w]ithin a week, the drop [in plasma level] is going to be minuscule," and a skilled artisan could thus "predict that the [treatment] window will be one week." TD2 375:2–376:18; *see also* TD3 219:11–220:4 (given "such a long half-life," plasma fluctuations within a ±7-day window "would be minor").

Additionally, the provisional application incorporates another patent by reference. *See* '918 provisional application at 7:21–22 (incorporating JTX-20). The incorporated patent states that such formulations are "therapeutically effective for at least three weeks or more, in particular about 1 month." JTX-20 at 2:38–43, 8:17–19. Because the referenced material is a U.S. patent, it is properly treated as part of the disclosure for priority purposes. *See Droplets, Inc. v. E*TRADE Bank*, 887 F.3d 1309, 1318 (Fed. Cir. 2018). Based on the disclosure in the incorporated patent, a person of ordinary skill in the art would understand that the difference between administering the drug once every three weeks, as opposed to once a month, is not a critical one. At a minimum, a

person of skill in the art would recognize that there is flexibility of up to a week on the "minus" side of one month. TD1 328:19–329:5.

Lastly, the provisional application claims a maintenance dose administered monthly "after the 30th day of treatment." '918 provisional application at 29:22–24, 34:17–19, 38:26–28. Reading the two claimed windows ("after the 30th day" and "on about the 34th to 38th day") together with the "approximately once a month" disclosure in the specification of the '918 provisional application, a person of ordinary skill in the art would recognize that the day on which maintenance doses are administered may vary up to one week before or after the day falling exactly one month after the previous dose.

There is no evidence in the record suggesting that a variation in the date of treatment by plus or minus seven days is critical to the claimed method. There is no evidence that telling an ordinary artisan to administer doses once a month, plus or minus seven days, would be meaningfully different from directing that doses be administered "approximately" once a month. Rather than indicating a technical or scientific distinction, the difference in language likely reflects a strategic choice in drafting claims designed to avoid indefiniteness challenges based on the use of the term "approximately," while refraining from reciting the "once a month" limitation for maintenance doses so narrowly as to make evasion of the claims easy.

For the reasons described above, it is implausible that an ordinary artisan would read the '918 provisional application as disclosing only a strict 4-day maintenance window. As such, I find that Tolmar has not met its burden of proving that the provisional application's reference to the dosage intervals as being "approximately once a month" indicates that the provisional application fails to provide written description support for the recited dosage interval of "a month ±7 days" in the '906 patent.

c. Enablement

Tolmar next argues that the '918 provisional application does not enable a person of ordinary skill in the art to practice the '906 invention with respect to the plus or minus seven-day limitation. In support, Tolmar cites testimony from Dr. Coles that an ordinary artisan would not know whether the drug concentrations were within the effective therapeutic window. TD1 84:8–22.

To satisfy the enablement requirement of 35 U.S.C. § 112, "the specification must enable the full scope of the invention *as defined by its claims*." *Amgen Inc. v. Sanofi*, 598 U.S. 594, 610 (2023) (emphasis added). The claims of the '906 patent say nothing about drug concentrations or a therapeutic window. As the Federal Circuit noted in *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1370 (Fed. Cir. 2023), concerns of the type raised by Dr. Coles "may be an issue for the FDA," but they have no bearing on a person's ability to practice the claims and therefore have no bearing on enablement.

An ordinary artisan knows how to administer an intramuscular injection. The claim merely says to do so within a certain date range. Regardless of when the injection is administered, patients are "given the same dose that they would normally be given." TD3 222:14–15. As such, I find that the claims of the '906 patent are fully enabled by the '918 provisional application.

2. Whether the Kramer Poster Was Actually Published

For Kramer to qualify as prior art, Tolmar must also show, by clear and convincing evidence, that Kramer was published by being presented at the October 2007 Congress. *See Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1578 (Fed. Cir. 1996) ("[The accused infringer] must persuade the trier of fact by clear and convincing evidence that the [contested reference] was published prior to [the] invention date" to establish its status as prior art.).

That question, it turns out, is not a simple one to answer. There is ample evidence that the Kramer poster was prepared and was intended to be displayed at the conference. Whether it was actually displayed or not is another matter. The problem is that, while there is little doubt that the poster was intended to be displayed, there is no direct evidence that the poster was in fact displayed.

Tolmar cites three pieces of evidence in support of its argument that the poster was actually displayed at the 2007 Congress. The first piece of evidence is an information disclosure statement filed by Janssen during the prosecution of the '906 patent citing Kramer as prior art. JTX-2 at 183. The second consists of two emails, both received by Dr. David Hough, a Janssen researcher. Attached to one of the emails was a copy of the Kramer poster, which the email characterized as one of the "final [2007 Congress] posters." DTX-697 at 1. The other email contained a press release, prepared in advance of the 2007 Congress, which referred to the presentation of the Kramer poster. DTX-698; *see also* TD2 332:9–333:12. Tolmar's third piece of evidence is a poster index, prepared by the organizers of the 2007 Congress, stating that Kramer would be presented on October 13, 2007, from 2:15 to 5:15 p.m. DTX-39 at 1–2.

There are problems with each of Tolmar's items of evidence. Although Tolmar has shown that Janssen *intended* to present Kramer at the 2007 Congress, no direct evidence shows that Kramer was, in fact, presented. Tolmar's circumstantial evidence permits a reasonable inference in its favor but does satisfy its high "clear and convincing" burden.

a. The Information Disclosure Statement

Tolmar's first piece of evidence is Janssen's own information disclosure statement, which lists Kramer, in a column entitled "non-patent literature documents," as being published at the 2007 Congress. JTX-2 at 183. It is well established that "mere submission of an IDS to the

USPTO does not constitute the patent applicant's admission that any reference in the IDS is material prior art." *ResQNet.com, Inc. v. Lansa, Inc.*, 594 F.3d 860, 866 (Fed. Cir. 2010) (quoting *Abbott Lab'ys v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1279 (Fed. Cir. 2003)). Nonetheless, the information disclosure statement is relevant insofar as it suggests that Kramer was actually presented.

While the information disclosure statement is relevant, it is entitled to little weight. Kramer was one of 28 non-patent literature documents identified in the statement, the overwhelming majority of which were posters. *See* JTX-2 at 181–85. It is implausible that the prosecutor of the '906 patent did serious due diligence with respect to each listed poster to confirm that each was, in fact, presented, as opposed to merely scheduled for presentation. As such, Janssen's inclusion of Kramer in the information disclosure statement is only minimally probative as to whether Kramer was actually presented.

b. The Emails to Dr. Hough

Tolmar's second piece of evidence consists of two emails sent to Dr. Hough in October 2007. At trial, Janssen asked Dr. Hough, one of the authors of the Kramer study, whether he knew if he or any of his co-authors presented the Kramer poster at the 2007 Congress. Dr. Hough responded that he did not. TD2 230:1–16. Tolmar challenged that contention on cross-examination, over Janssen's objection, by calling Dr. Hough's attention to two emails sent to Dr. Hough regarding the Kramer poster.

The first of the two emails was an October 11, 2007, email to Dr. Hough from Maria Kyriazis-Christidou. DTX-697. It contained, as an attachment, a copy of the Kramer poster. That copy of the poster was the same as copy that Tolmar introduced into evidence as JTX-36. The email thus confirmed the contents of the Kramer poster and that it was scheduled for presentation

"at USP&MHC: Orlando, October 11-14, 2007." JTX-36 at 7; DTX-697.[6] The email with the attached copy of the Kramer poster constitute further evidence that the Janssen scientists intended to present Kramer at the 2007 Congress, but it says nothing about whether the poster was actually presented.

The other email was sent to Dr. Hough from Ambre Morley on October 1, 2007. DTX-698. It contained, as an attachment, a press release concerning the Kramer poster. *Id.* The press release was embargoed until October 13, 2007, at 2:15 p.m., the time at which the Kramer poster was scheduled for presentation. *Id.* at 3. Dr. Hough testified at trial that it was normal, routine practice for Janssen to send out press releases highlighting poster presentations after the fact. TD2 329:22–330:6. But the press release that was entered into evidence was obviously prepared in advance of the conference, as it was marked "embargoed" until October 13, 2007. The embargoed press release therefore supported the inference that Kramer was scheduled for presentation at the 2007 Congress, but it did not establish that Kramer was actually presented at the conference.

Janssen objected to the admission of the two email exhibits at trial because of Tolmar's failure disclose the exhibits to Janssen prior to Dr. Hough's trial testimony. *See* TD2 313:18–24.Tolmar's counsel responded that he had discovered the emails on the night before Dr. Hough testified at trial, among materials that Janssen had produced during discovery. Counsel explained that despite their late production, Tolmar sought to offer the emails into evidence, not merely to use them in cross-examination of Dr. Hough. TD2: 314–15. I admitted the two exhibits conditionally, subject to further consideration of Janssen's objections.

[6] The Kramer poster does not state that it was "scheduled for presentation"; it states that it was "presented." Because the poster was obviously created before its presentation, however, the fact that the poster says it was presented deserves no weight beyond suggesting that the poster was intended to be presented.

Tolmar offers two arguments as to why the court should not exclude the undisclosed emails from evidence. The first is that Tolmar identified the emails only at midnight the night before Dr. Hough was scheduled to testify. TD2: 316–17. Tolmar's second argument, advanced in its post-trial brief, is that it had "good cause" because it did not know Dr. Hough would testify on the issue of whether Kramer was presented at the 2007 Congress, so it had no reason to anticipate that it would need to cross-examine him on that subject. Dkt. No. 140 at 15. The general question of whether exhibits that were not on a party's exhibit list could be added at trial was addressed at the pretrial conference, in which I explained that exhibits not disclosed in a party's proposed exhibit list could be added for "good cause." 9/29/23 Pretrial Conference Tr. 15:17–16:3; *accord* Fed. R. Civ. P. 16(e).

As I stated during trial, Tolmar should have advised Janssen of the possibility that DTX-697 and DTX-698 might be offered into evidence as soon as Tolmar discovered them and considered using them as affirmative evidence. *See* TD2 317:2–22. Nonetheless, Tolmar's handling of the issue does not warrant the severe sanction of excluding the evidence. "[E]xclusion should be reserved for circumstances amounting to 'willful deception or flagrant disregard of a court order by the proponent of the evidence.'" *Integra Lifesciences Corp. v. Hyperbranch Med. Tech., Inc.*, No. CV 15-819-LPS-CJB, 2017 WL 11558096, at *4 (D. Del. Dec. 11, 2017) (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 792 (3d Cir. 1994)).

I credit the representation by Tolmar's trial counsel that the emails came to his attention late the night before the emails were offered into evidence. Tolmar's failure to disclose the emails thus does not amount to "willful deception or flagrant disregard of a court order." Moreover, even if Tolmar had disclosed the emails to Janssen, it is unlikely that Janssen could have done anything to mitigate their impact. The emails show that the version of Kramer discussed at trial is the same

version that the Janssen scientists intended to present at the 2007 Congress. There is no way to explain away that fact.

Because Tolmar's failure to make timely disclosure of the exhibits does not appear to have been in bad faith, and because the lack of disclosure did not significantly prejudice Janssen by depriving Janssen of an opportunity to respond to the evidence, the emails regarding the Kramer poster will not be excluded. With that said, however, it is important to note that the effect of the emails is largely cumulative: they provide support for a proposition that was otherwise well established: that the Kramer reference was intended to be presented at the Orlando conference; they do not, however, go the further step of showing that the Kramer reference was actually displayed at the conference.

iii. The Poster Index

Tolmar's final piece of evidence on this issue is a poster index from the 2007 Congress stating that Kramer "will be presented" on October 13, 2007, from 2:15 to 5:15 p.m. DTX-39 at 1–2. The poster index is consistent with other evidence on this issue. It confirms that Kramer is poster number 313 and was scheduled to be presented at the Congress. Like Tolmar's other evidence, however, it does not show that Kramer was, in fact, presented.

Prior to trial, and again at trial, Janssen objected to the admission of the poster index on hearsay and authentication grounds. I rejected the hearsay objection prior to trial, based on Rule 803(3) of the Federal Rules of Evidence. I postponed ruling on Janssen's authentication objection until trial, to determine what evidence Tolmar would introduce on the authentication issue. At trial, I conditionally admitted the poster index over Janssen's authentication objection. In its proposed findings of fact and conclusions of law, Janssen has renewed its objections to the poster index on hearsay and authentication grounds.

As for hearsay, Janssen argues that the poster index was not properly admitted under Rule 803(3), which provides that a "statement of the declarant's then-existing state of mind (such as motive, intent, or plan)" is admissible over a hearsay objection. Fed. R. Evid. 803(3). Prior to the promulgation of the Federal Rules of Evidence, the Supreme Court held in *Mutual Life Insurance Co. v. Hillmon*, 145 U.S. 285 (1892), that a declarant's statement of future intent is admissible over a hearsay objection, and the Advisory Committee on the Rules of Evidence confirmed in the Advisory Committee Note on the proposed rule that the rule of the Hillmon case was "left undisturbed." *See* 30B Charles Alan Wright & Jeffrey Bellin, *Federal Practice & Procedure* § 6831, at 301 (2017).

Janssen argues, however, that Rule 803(3) was intended to codify the *Hillmon* rule only to the extent that it applies to statements reflecting the intent of the declarant, not to statements regarding the intent of a third party.[7] Under that interpretation of Rule 803(3), Janssen argues that the poster index is inadmissible because it was prepared by 2007 Congress representatives, yet it was offered as proof of the intent of the Janssen scientists to show that they intended to display the poster (and, thus, to support Tolmar's theory that they did so).

[7] In the *Hillmon* case itself, the Supreme Court addressed the admissibility of a statement by the declarant relating not only his own intentions, but also the intentions of a third party. The Court held that the statement was admissible for both purposes. While the Advisory Committee Note on Rule 803(3) said that the purpose of the Rule was to leave the *Hillmon* rule "undisturbed," the House Judiciary Committee Report on Rule 803(3) stated that the Committee intended the new Rule to limit the doctrine of *Hillmon* "so as to render statements of intent by a declarant admissible only to prove his future conduct, not the future conduct of another person." 30A Wright & Bellin, *supra*, at 301. Cognizant of the tension between the two statements as to the intended scope of the Rule, courts have struggled to define the outer limits of the Rule's reach. *See, e.g.*, Robert P. Mosteller, *McCormick on Evidence* § 275 (8th ed. 2020). Because the poster index was clearly admissible for the relevant purpose of proving the intent of its drafter, however, it is admissible even under a narrow construction of the Rule, so it is not necessary here to explore the limits of admissibility under Rule 803(3).

That argument fails, however, because the poster index constitutes a statement by the conference representatives that the 2007 Congress would feature the display of the Kramer poster at a particular date and time. As such, the poster index was admissible as a statement by the declarants (the conference representatives) regarding the declarants' intent, which was to have various posters on display at specified times during the conference. It is therefore unnecessary to decide whether Rule 803(3) would allow the admission of a statement regarding the declarant's state of mind to prove the state of mind of a third party, or to help prove that either the declarant or the third party acted consistently with that intent.

As for authentication, Rule 901(a) of the Federal Rules of Evidence requires the proponent of evidence to "produce evidence sufficient to support a finding that the item is what the proponent claims it is." Fed. R. Evid. 901(a). In this case, the poster index was not authenticated by any witness with personal knowledge of the document. In place of a witness with personal knowledge, Tolmar relied on Rule 901(b)(4) for authentication.

Rule 901(b)(4) allows for authentication by circumstantial evidence, including "[t]he appearance, contents, substance, internal patterns, or other distinctive characteristics of the item." The rules requiring proof of authenticity do not impose an exacting standard. "The only requirement [under Rule 901] is that there has been substantial evidence from which [the finder of fact] could infer that the document was authentic." *Link v. Mercedes-Benz of N. Am.*, 788 F.2d 918, 927 (3d Cir. 1986). That is not an exacting standard. As the Third Circuit has explained, "[t]he burden of proof for authentication is slight." *McQueeney v. Wilmington Tr. Co.*, 779 F.2d 916, 929 (3d Cir. 1985); *see also Lexington Ins. Co. v. W. Pa. Hosp.*, 423 F.3d 318, 328–29 (3d Cir. 2005); *United States v. Reilly*, 33 F.3d 1396, 1404 (3d Cir. 1994); *Link*, 788 F.2d at 927; *LG Display Co. v. AU Optronics Corp.*, 265 F.R.D. 189, 196 (D. Del. 2010); *United States v. Lamm*,

5 F.4th 942, 947 (8th Cir. 2021) ("To authenticate evidence, a party must clear only a 'low bar.'"). Three factors support admission of the poster index.

First, the Poster Index appears authentic on its face. For example, it bears the letterhead of the 2007 Congress. Letterhead alone is generally insufficient to establish authenticity, *see Orr v. Bank of Am.*, *NT & SA*, 285 F.3d 764, 777 (9th Cir. 2002), but is "an important characteristic" favoring admission where additional circumstances corroborate its authenticity, *Denison v. Swaco Geolograph Co.,* 941 F.2d 1416, 1423 (10th Cir.1991). Thus, the poster's appearance of authenticity favors admission.

Second, the poster is consistent with other evidence in the case. The Poster Index, the Kramer poster itself, and the emails to Dr. Hough all state that Kramer was scheduled for presentation at the 2007 Congress. Consistency with other evidence in the case favors admissibility for purposes of authentication. *See United States v. Goichman*, 547 F.2d 778, 784 (3d Cir. 1976) (holding documents sufficiently authenticated, in part because they accurately stated defendant's children's names and were consistent with allegations in a separate legal proceeding and with related bank statements); *United States v. McGlory*, 968 F.2d 309, 329 (3d Cir. 1992) (finding no abuse of discretion in admitting handwritten notes whose character was consistent with other admissible evidence, even though the government's handwriting expert could not say they were written by the defendant).

Third, the poster index was obtained by Tolmar under circumstances consistent with authenticity. The poster index was found by Tolmar in a notice of opposition filed against European Patent No. 2,234,617. DTX-62. Though not alone sufficient to establish authenticity, *see Ex parte Zhang*, No. 2021-000087, 2021 WL 633718, *2–3 (PTAB Feb. 16, 2021), those

circumstances are consistent with it. The circumstances of discovery by Tolmar thus further suggest authenticity.

The combination of authentic appearance, consistency with other evidence in the case, and credible circumstances of discovery are sufficient to satisfy Rule 901. *See, e.g., United States v. Turner*, 718 F.3d 226, 233 (3d Cir. 2013) (holding foreign bank records admissible where those records bore the insignia of the foreign bank, were consistent with other evidence in the case, and were seized by the government under circumstances consistent with authenticity). The poster index therefore was adequately authenticated.

In a separate challenge to the admissibility of the poster index, Janssen argues that the poster index was improperly admitted because Dr. Coles, who was the sponsor of the evidence, testified that she found the poster index in an opposition to a European counterpart of the '906 patent. TD1 106:19–22 (referring to DTX-62). The European opposition itself was qualified for admission by agreement of the parties prior to trial. Thus, Janssen did not object to the admission of the European opposition itself; instead, Janssen objected to the fact that Dr. Coles sponsored the introduction of the opposition, even though the opposition was not described in Dr. Coles' expert report. The failure to refer to the Poster Index in Dr. Coles' expert report, Janssen argues, violated Tolmar's expert disclosure obligations under Rule 26 of the Federal Rules of Civil Procedure. *See* Fed. R. Civ. P. 26(a)(2)(B); TD1 107:2–23.

Although Dr. Coles' report did not discuss the European opposition directly, the "materials considered" portion of Dr. Coles' report included the invalidity contentions that Tolmar submitted to Janssen, which included the poster index. TD1 108:2–13. Dr. Coles' testimony about where she found the materials she considered was therefore within the scope of her report. For that reason, her limited testimony regarding the European opposition did not violate Rule 26(a)(2)(B).

iv. Conclusion

Tolmar has clearly proved that the authors of the Kramer poster intended to display the poster at the 2007 Congress. But the only evidence that goes to the question of whether Kramer was actually presented is Janssen's own information disclosure statement. As noted, a reference in an information disclosure statement does not qualify as an admission, *ResQNet*, 594 F.3d at 866, and by itself it did not clearly establish that the poster was presented.

Tolmar has not introduced a copy of a press release or other documentary evidence issued after the conference. The only press release offered by Tolmar was the embargoed version of the press release that was sent to Dr. Hough in advance of the presentation. DTX-698. Moreover, and importantly, Dr. Hough denied having any memory of whether Kramer was presented at the 2007 Congress, TD2 331:14–16, and none of the other six authors listed on the face of the poster testified that the poster was presented as scheduled. Thus, there was no direct evidence at trial that the Kramer poster was actually presented. "The absence of a record of an event which would ordinarily be recorded gives rise to a legitimate negative inference that the event did not occur." *AZ v. Shinseki*, 731 F.3d 1303, 1315 (Fed. Cir. 2013) (quoting *United States v. Robinson*, 544 F.2d 110, 114 (2d Cir.1976)). The fact that Tolmar failed to obtain testimony from any of the participants or attendees at the conference, or to obtain any physical evidence supporting Tolmar's contention that the poster was displayed at the October 2007 conference suggests that the Kramer poster may not have actually been presented.

Even if the Kramer poster was in fact displayed, there is very little evidence relating to how long the poster was on display or who may have seen it, factors that bear on whether the poster would be regarded as a "printed publication" for purposes of section 102(b). *See In re Klopfenstein*, 380 F.3d 1345, 1350–52 (Fed. Cir. 2004). The poster index indicated that the poster

was scheduled to be on display for a three-hour period on October 13, 2007, and Dr. Coles testified that posters at such conferences are typically displayed for a period to allow persons attending the conferences to view them and ask questions of the poster presenters. TD1 102:20–105:19. And there was no indication that the poster presentations were intended to be confidential or that viewers would have understood that further dissemination of the information on the posters was forbidden.

In the end, there was no direct evidence that the Kramer poster was actually displayed, that it was displayed for a period of time long enough for a substantial number of conference attendees could view it, and under circumstances that did not discourage further dissemination of the poster information—all factors bearing on the "printed publication" issue, *see Klopfenstein*, 380 F.3d at 1350–51; *Grünenthal GmbH v. Antecip Bioventures II LLC*, PGR2017-00022, 2018 WL 599257, at *7 (PTAB Nov. 14, 2018) (circumstantial evidence that a poster might have been displayed a three-hour period not sufficient to render the poster a "printed publication").

In sum, it is unclear whether Kramer was actually presented at the 2007 Congress or that it was presented in a manner that would have qualified it as a "printed publication" within the meaning of pre-AIA section 102(b). Consequently, I find that Tolmar has not met its burden of showing by clear and convincing evidence that the Kramer poster was disseminated and publicly accessible at the 2007 Congress. *See Norian Corp. v. Stryker Corp.*, 363 F.3d 1321, 1330 (Fed. Cir. 2004); *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560 (Fed. Cir. 1988) ("dissemination and public accessibility are the keys to the legal determination whether a prior art reference was 'published.'"). The absence of proof that the Kramer poster qualifies as a printed publication therefore provides a second independent reason that Kramer is not prior art to the '906 patent.

D. Obviousness of Claims 1–7 and 15 Based on NCT 548 Alone

Even without Kramer as a prior art reference, Tolmar maintains that claims 1–7 and 15 of the '906 patent would have been obvious based on the NCT 548 prior art reference alone. *See* Dkt. No. 140 at 43; TD5 22:6–18. The 150 mg-eq. dosing regimen in NCT 548, which was one of the three dosage regimens hypothesized to achieve positive therapeutic effect over placebo, closely resembles the regimen set forth in the claims. The NCT 548 regimen differs from the one described in claim 1 of the '906 patent, however, in two main ways. First, the patent claims loading doses administered in the deltoid, '906 patent at 32:15, 32:20, whereas NCT 548 calls for gluteal injections, JTX-23 at 1. Second, NCT 548 calls for equal doses throughout the treatment regimen, whereas the '906 claims call for unequal doses. The patent recites an initial loading dose of 150 mg-eq., followed by a day 8 loading dose of only 100 mg-eq. '906 patent at 32:22. The 150 mg-eq. regimen described in NCT 548, by contrast, calls for both an initial loading dose of 150 mg-eq. and a day 8 loading dose of 150 mg-eq. In addition, the maintenance doses claimed in the patent are independent of the loading doses and can range from "about 25 mg-eq. to about 150 mg-eq.," '906 patent at 32:27–28, whereas the NCT 548 calls for maintenance doses to be the same as the loading doses, JTX-23 at 1.

Tolmar argues that it would have been obvious to try injections in the deltoid because the deltoid is one of only two common sites for intramuscular injections—the gluteal being the other. As for the quantity of paliperidone in each dose, Tolmar makes two arguments. Tolmar's first argument is that an ordinary artisan would have been motivated to select the 150 mg-eq. initiation loading dose from NCT 548 and would have had a reasonable expectation of success in trying a dosing regimen with a modified 100 mg-eq. day 8 dose and with maintenance doses unequal to the two loading doses. Tolmar's second argument is that the ranges allegedly taught by NCT 548

create a presumption of obviousness as to the dosage amounts of the '906 claims, which Janssen has failed to rebut. For these reasons, Tolmar argues that a person of ordinary skill in the art would arrive at the claimed invention based on NCT 548 combined with their general background knowledge of the field.

1. Deltoid Limitation

The first difference between the NCT 548 dosing regimen and that of the claims is that the claims call for the loading doses administered to the deltoid. On this issue, Tolmar argues that a person of ordinary skill in the art would have been motivated to pursue deltoid injections and would have had a reasonable expectation of success in doing so.

Prior to the claimed invention, "[i]t was the norm" to administer long-acting antipsychotics in the gluteus. TD1 429:23–430:3. It was common, however, to use the deltoid for a variety of intramuscular injections. TD1 368:19–370:16, 372:8–17. Although deltoid injections are more painful than gluteal injections, TD3 200:21–201:6; TD1 370:10–12, 438:6–15, Tolmar offered evidence that most patients prefer deltoid injections for modesty reasons. TD1 370:1–16. As one of Tolmar's witnesses put it, patients typically prefer injections in which "they don't have to take their pants off." TD1 370:15–16. That preference is more exaggerated in schizophrenia patients, the witness explained, because such patients are often agitated and apt to refuse medication. *See* TD1 371:21–372:2. "When patients are agitated, requiring four or five staff to subdue them, it's really hard to pick locations." *Id.* For those reasons, the court finds that a person of ordinary skill in the art would have been motivated to develop a long-acting injectable that is administrable in the deltoid.

Although "there was nothing out there in the literature for paliperidone palmitate" regarding deltoid injections, TD3 174:8–16, it was well known that the deltoid and gluteal muscles

were the two main sites for intramuscular injections generally. TD1 151:11–16. And it was likewise known that the deltoid muscle had better absorption kinetics than the gluteal muscle. TD1 403:1–5; *but see* TD1 153:13–18 (conceding that dissolution, rather than absorption, is the rate-limiting step in the claimed injections). Tolmar's evidence showed that a skilled artisan "wouldn't expect worse absorption in the deltoid," i.e., that an ordinary artisan would expect the two sites to be interchangeable. TD1 153:1–9. Based on that evidence, I find that a person of ordinary skill in the art, who would have expected NCT 548 itself to succeed, would likewise have had a reasonable expectation of success in administering the NCT 548 injections to the deltoid.

While ordinary artisans would have a motivation to explore the deltoid as an injection site and an expectation of interchangeability, they would not have expected the markedly superior results that the claimed dosing regimen delivered relative to the NCT 548 protocols. Surprisingly, paliperidone palmitate has a biphasic absorption profile, meaning that it is absorbed rapidly at first but slowly thereafter. That feature, which is more prominent in the deltoid than the gluteal, TD2 351:13–23, 352:24–354:7, allows for rapid efficacy without compromising tolerability, making the deltoid a markedly better loading dose site. Tolmar introduced no persuasive evidence showing why an ordinary artisan would understand the deltoid limitation to be critical to the success of Janssen's invention; rather, Tolmar's experts characterized such modification of NCT 548 as merely an "option" ordinary artisans could pursue. TD1 255:23–256:8.

Because a person of ordinary skill in the art would have had both a motivation and an expectation of achieving at least equal results in changing the injection site from the NCT 548 prior art, however, the deltoid limitation by itself does not render claims 1–7 and 15 of the '906 patent nonobvious over NCT 548. The unexpectedly favorable results Janssen observed from use

of the deltoid injections are relevant as an objective indicator of nonobviousness, but do not outweigh the ordinary artisan's motivation and expectation of success.

2. Dose Size Limitations

The more persuasive difference between NCT 548 and the claimed dosing regimen is the size of the doses at each point in time. Tolmar argues (1) that a person of ordinary skill in the art would have had a motivation and a reasonable expectation of success in trying the claimed dosing regimen, and (2) that overlapping ranges of various parameters render the claims prima facie obvious. Neither argument is persuasive.

a. Motivation and Reasonable Expectation of Success

A person of ordinary skill in the art would not have had a reason to modify the dosing sizes of NCT 548 to reach the claimed invention because such a person would not have known that the clinical trial described in NCT 548 (the PSY-3003 trial) ultimately failed. For a person to have a reasonable expectation of success generally requires that there be a reason to deviate from the prior art to reach the claimed invention. *See Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1356–57 (Fed. Cir. 2013); *see also PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007) ("[T]he burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to . . . carry out the claimed process."). Because no evidence suggested a reason to deviate from the protocol set forth in NCT 548, Tolmar has not met its burden on that issue.

The fact that NCT 548 states only a hypothesis and reports no results makes this an unusual case. Courts generally must "take account of the inferences and creative steps that a person of ordinary skill in the art would employ" when presented with a prior art reference. *KSR*, 550 U.S. at 418. Consistent with this principle, prior art "must be considered not only for what it expressly

teaches, but also for what it fairly suggests" to a skilled artisan. *Bradium Techs. LLC v. Iancu*, 923 F.3d 1032, 1049 (Fed. Cir. 2019). Normally, this means that a person of ordinary skill in the art would view a reference, understand its strengths and weaknesses, its advantages and deficiencies, and attempt to overcome the flaws in the prior art by employing ordinary creativity, related references, and general background knowledge. But NCT 548 is more a prior hypothesis than prior art. Because NCT 548 was only a proposed testing protocol unaccompanied by any results, all it teaches an ordinary artisan is that Janssen thought the proposed dosing regimens would be safe and effective. To be sure, an ordinary artisan would know that similar Phase I and II studies showed promise and that Janssen would not invest in a Phase III clinical trial without good reason to believe its hypothesis was correct. But without knowing the results of the Phase III clinical trial, a person of ordinary skill in the art would have learned nothing from NCT 548 beyond crediting Janssen's hypothesis.

Beyond that, persons of ordinary skill in the art considering NCT 548 would likely balk at selecting the 150 mg-eq. regimen as a starting point for loading doses without having efficacy and safety data on paliperidone palmitate injections to guide them. It was known at the time that the occurrence of drug-induced movement disorders, known as extrapyramidal symptoms, generally increased with increases in the dosage of dopamine-receptor-inhibiting drugs. TD2 225:11–15; TD3 30:2–4, 47:9–49:2. For that reason, researchers in the field would have been more likely to select 100 mg-eq., the midpoint of the three regimens described in NCT 548, as a starting point. In fact, the evidence suggests that 150 mg-eq. would have been the least promising initial loading dose, because using such a high loading dose would have run counter to the conventional wisdom at the time that clinicians should "start low and go slow" with antipsychotics. TD3 28:22–29:3, 49:1–5; TD2 225:22–226:4. Illustrating that point, a panel of outside experts reviewing Janssen's

data was "not convinced" that the first dose of 150 mg-eq. was safe or necessary; instead, the panel proposed "a more conservative [100 mg-eq.] approach to avoid putting patients at risk." TD2 189:17–190:7. Even after Janssen received FDA approval for Invega Sustenna®, physicians' "first reaction [to Invega Sustenna®] was skepticism" and "reluctan[ce] to use a high initiation dose, let alone two doses one week apart." TD3 48:16–50:18.

Even if the ordinary artisan had selected NCT 548's 150 mg-eq. regimen as a starting point, Tolmar has pointed to no reason why an ordinary artisan would have modified the second loading dose and subsequent maintenance doses to obtain the claimed invention. As noted, NCT 548 states only a hypothesis; it contains no data. *See* TD1 254:16–255:9; TD1 440:24–441:8; TD3 171:1–2. Tolmar's experts conceded that there is nothing in the prior art to suggest that the dosing regimens described in NCT 548 would fail, and thus no reason to modify the NCT 548 protocol. TD1 255:17–22; TD1 442:11–20 ("A POSA without any results from this study would have no reason to alter any of those dosing regimens."). In the absence of a reason to modify the NCT dosing regimens, NCT 548 would not render the '906 claims obvious. *See InTouch Techs., Inc. v. VGo Commc'ns, Inc.*, 751 F.3d 1327, 1352 (Fed. Cir. 2014).

Only Janssen knew that PSY-3003, the clinical study that NCT 548 describes, failed for lack of efficacy. TD2 251:24–252:16. As such, only Janssen had a motivation to modify the NCT 548 dosing regimens. Even armed with that proprietary knowledge, identifying parameters to change required Janssen to conduct complex population pharmacokinetic modeling using unpublished results from unpublished clinical trials. TD2 180:18–20, 181:11–182:12. And arriving at the claimed method required Janssen to be aware of the results of Janssen's proprietary PSY-3002 non-inferiority study, which compared 50 mg-eq. paliperidone palmitate injections in

the gluteal muscle on days 1 and 8 to orally administered paliperidone palmitate, TD2 252:14–253:5, and failed for lack of efficacy. TD2 254:24–256:4; JTX-593 at 1.

To be sure, there is no "rigid rule categorically precluding obviousness determinations without [pharmacokinetic or pharmacodynamic] data." *Yeda Rsch. V. Mylan Pharms. Inc.*, 906 F.3d 1031, 1043 (Fed. Cir. 2018). However, without Janssen's proprietary clinical study data and Janssen's proprietary pharmacokinetic model used to interpret that data, a person of ordinary skill in the art would not have even known that there was a problem with NCT 548 in the first place, much less how to solve it. "[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) (quoting *Leo Pharm. Prods.*, 726 F.3d at 1357); *Avanir Pharms., Inc. v. Actavis S. Atl. LLC*, 36 F. Supp. 3d 475, 506–07 (D. Del. 2014), *aff'd sub nom. Avanir Pharms. Inc. v. Par Pharm. Inc.*, 612 F. App'x 613 (Fed. Cir. 2015); *Novartis Pharms. Corp. v. Watson Lab'ys, Inc.*, 611 F. App'x 988, 996 (Fed. Cir. 2015) (finding that the invention was not obvious where, "[a]lthough the addition of an antioxidant would have been an obvious solution for a formulation with known oxidation problems, [the challenger] failed to prove that [the] formulation was known to be susceptible to oxidative degradation."); *see also Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1377 (Fed. Cir. 2012) ("Often the inventive contribution lies in defining the problem in a new revelatory way.").

Lastly, even assuming there was a reason to modify NCT 548, persons of ordinary skill in the art would not have known which of the many parameters they should alter to improve upon NCT 548. It required Dr. Vermeulen's population pharmacokinetic model, as modified by Dr. Samtani, for Janssen to identify the most promising variables to alter. "[A] conclusion of

obviousness does not follow from merely 'varying all parameters or trying each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.'" *Grünenthal GmbH v. Alkem Lab'ys Ltd.*, 919 F.3d 1333, 1345 (Fed. Cir. 2019) (quoting *In re Kubin*, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009)) (cleaned up). With nothing to suggest which modifications to make to the NCT 548 regimen, a person of ordinary skill in the art would be limited to the guess-and-check approach rejected in *Grünenthal.* Such an approach is not sufficient to show obviousness in any field of technology, but it is especially unsuitable to apply such an approach in the pharmaceutical arts, where testing individual modifications to known prior art formulations typically involves the commitment of substantial time and resources. As an example, evidence at trial showed that each of Janssen's Phase III clinical trials in this case cost approximately $15 million. TD2 232:16–18.

Tolmar's arguments regarding motivation and a reasonable expectation of success depend heavily on Kramer, which studied similar dosing regimens and reported lack of efficacy. With the Kramer data, a person of ordinary skill in the art would at least be motivated to modify the Kramer and NCT 548 regimens, though not necessarily in ways that would yield the claimed method. Because Kramer does not qualify as prior art, however, Tolmar's contention that an ordinary artisan would find it obvious to modify NCT 548 to arrive at the claimed method is unconvincing.

Ultimately, Tolmar's experts provided no persuasive reason to believe that the fixed-dose regimens of NCT 548 alone would have led a skilled artisan to use a high 150 mg-eq. loading dose, followed by a lower 100 mg-eq. second loading dose and varying maintenance doses as claimed in the '906 patent. As such, I find that a person of ordinary skill in the art would have had no reason to modify the NCT 548 dosing regimens. The claimed dosing regimen solved a "problem

. . . not known in the art," and the solution to the unknown problem would not have been obvious. *Forest Lab'ys*, 918 F.3d at 935; *Leo Pharm. Prods.*, 726 F.3d at 1356–57; *Avanir Pharms.*, 36 F. Supp. 3d at 506–07; *Novartis Pharms.*, 611 F. App'x. At 996.

b. Overlapping Ranges

Tolmar's "overlapping ranges" theory of obviousness is incorrect as a matter of law. "A prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *E.I. du Pont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) (quoting *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003)); *see also In re Applied Materials*, 692 F.3d 1289, 1295 (Fed. Cir. 2012); *Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1340–41 (Fed. Cir. 2020). "[S]uch overlap creates a presumption of obviousness," which can be rebutted by a patentee's showing of unexpected results, *E.I. du Pont*, 904 F.3d at 1006 (citing *In re Aller*, 220 F.2d 454, 456 (CCPA 1955), teaching away, *id.* (citing *Ormco Corp. v. Align Technology Inc.,* 463 F.3d 1299, 1311 (Fed. Cir. 2006), or that "the parameter was not recognized as result-effective, *id.* (citing *Applied Materials*, 692 F.3d at 1295). But this burden-shifting framework applies only where "the only difference from the prior art is a difference in the range or value of a particular variable." *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005); *see also Tris Pharma, Inc. v. Actavis Lab'ys FL, Inc.*, 503 F. Supp. 3d 183, 203 (D. Del. 2020) ("[T]he presumption attaches only when the range or value of a particular variable is *the* difference between the claimed invention and the prior art.") (cleaned up) (emphasis in original), *aff'd*, No. 2021-1495, 2022 WL 2525318 (Fed. Cir. July 7, 2022). Where there are additional differences between the prior art and the patented invention, the presumption of obviousness may not be invoked. *Pharmacyclics LLC v. Alvogen, Inc.*, No. 2021-2270, 2022 WL 16943006, at *9 (Fed. Cir. Nov. 15, 2022).

Even if I were to agree with Tolmar's characterization of NCT 548 as disclosing ranges of paliperidone to be included in each dose, there can be no prima facie case of obviousness because the claimed method requires administration to the deltoid rather than to the gluteal muscle. As such, the overlapping ranges component, to the extent that there is one, is not the "only difference from the prior art." *Kumar*, 418 F.3d at 1366. For this reason, the prior art does not establish a prima facie case of obviousness, and the burden remains on Tolmar to prove obviousness by clear and convincing evidence.

3. Secondary Considerations

Two secondary considerations in particular reinforce the nonobviousness of claims 1–7 and 15. First, the success of using a large loading dose in the deltoid on day one of the treatment was an unexpected positive result of Janssen's invention. TD2 165:13–166:10; TD3 224:13–226:2; TD1 296:22–297:4. Second, the undisputed commercial success of Invega Sustenna® favors nonobviousness. *See* TD4 83:2–6; TD4 84:13–17 (no dispute over sales figures), 86:13–16 (no dispute over accuracy of data), 85:23–86:5 (no dispute over market share).

Unexpected results suggest nonobviousness because "that which would have been surprising to a person of ordinary skill in a particular art would not have been obvious." *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995). The conventional thinking at the time of the invention was that large loading doses would be accompanied by an unacceptable level of adverse side effects. As noted, a panel of outside experts reviewing Janssen's data in February 2007 proposed "a more conservative [100 mg-eq.] approach to avoid putting patients at risk." TD2 189:17–190:7. The FDA initially suggested that Janssen go even lower, with doses of 75 mg-eq. on days 1 and 8. And even after Janssen received FDA approval for Invega Sustenna®, Janssen's evidence showed

that physicians reacted with skepticism and were reluctant to use such a high initiation dose. TD3 48:16–50:18.

Janssen's decision to start with a loading dose of 150mg-eq. and follow it with a second loading dose of 100 mg-eq. was based in part on Dr. Samtani's discovery that higher doses of paliperidone palmitate do not result in proportionally higher increases in peak concentration in the patient's body, but can facilitate more rapid onset of the therapeutic effects of the drug. TD2 357:2–358:14. That characteristic of Janssen's paliperidone palmitate formulation, according to Dr. Samtani, was not known in the art before Dr. Samtani's work. TD2 358:11-14. *See Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1351 (Fed. Cir. 2012) (crediting inventor's testimony about industry praise and unexpected results). The surprising efficacy and safety of large initiation doses of paliperidone palmitate supports Janssen's nonobviousness argument.

Tolmar argues that Janssen's results were not unexpected, in part because errors in conducting the PSY-3003 Phase III clinical trial led to that trial's failure and in part because the use of loading doses and once-monthly injectables were known in the prior art. As Janssen points out, however, the testing error Tolmar refers to affected only one arm of one of the failed Phase III studies, and there was no basis in the prior art to expect the dramatic difference in results between NCT 548's fixed-dose, gluteal regimen and the claimed dosing regimens.

Commercial success is another of the "objective indicia of nonobviousness." *Chemours Co. FC, LLC v. Daikin Indus., Ltd.*, 4 F.4th 1370, 1378 (Fed. Cir. 2021). In 2012, Invega Sustenna® replaced Risperdal Consta® as the leading antipsychotic. TD3 296:2–7; JTX-12B at 102–03, 123–32. Invega Sustenna® continues to command the largest market share among long-acting injectable antipsychotics by both revenue and days of treatment. TD3 292:9–22, 293:12–

294:7, 295:21–296:7. Annual net sales of Invega Sustenna® were $2 billion in 2022, and the total net sales of the product between 2009 and 2022 were almost $15 billion. JTX-12B at 18. By any metric, Invega Sustenna® has been a commercial success. And its commercial success is largely driven by the benefits of the patented invention—rapid and sustained efficacy without oral supplementation. TD3 57:2–58:5.

Tolmar offered evidence at trial that the commercial success of Invega Sustenna® was not attributable to its superiority over prior art treatments, but to other factors. Those factors, according to Tolmar, include Janssen's status as a market leader in second-generation long-acting injectables prior to the introduction of the claimed invention, Janssen's marketing practices, such as discounting and market spending, and the presence of "blocking patents" owned by Janssen that deterred others from developing competing products.

Those factors may have had some marginal effect in the market, but not enough to negate the probative force of the huge commercial success of Invega Sustenna®. The patented invention need not be "solely responsible for the commercial success, in order for this factor to be given weight." *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991). Based on careful consideration of the competing evidence on this issue, I am persuaded that the commercial success of Janssen's product was mainly attributable the claimed dosage regimen in the '906 patent. As for Tolmar's arguments regarding the three alleged "blocking patents," Tolmar's evidence failed to show that those patents prevented competitors from developing a competing paliperidone palmitate product before the priority date of the '906 patent. That is particularly true in light of the statutory "safe harbor" provision for research and development, 35 U.S.C. § 271(e)(1); see TD3 331:22–332:23. Thus, the commercial success of Invega Sustenna® supports the nonobviousness of claims 1–7 and 15 of the '906 patent.

E. The Renal Impairment and Formulation Claims

Claims 8 through 14 and claim 16 of the '906 patent are directed to the treatment of renally impaired patients. Those claims start with the methods described in claims 1–7 and 15 and direct that the dose sizes be reduced to account for decreased capacity for renal filtration in patients suffering from chronic renal impairment. Tolmar's nonobviousness argument as to the renal impairment claims is that a person of ordinary skill in the art would simply start with the non-renal-impairment claims and reduce the dose volume by up to 50 percent for renally impaired patients. To succeed, Tolmar's argument requires (1) that the non-renal-impairment claims would have been obvious and (2) that reducing dose size to account for decreased renal filtration would have been obvious over two references: Cleton 46 and Snoeck (the "renally impaired prior art"). Because I have ruled against Tolmar on the first issue, I need not reach the second to conclude that the renal impairment claims are not obvious over NCT 548, the renal impairment prior art, and the general knowledge of an ordinary artisan.

The formulation claims, claims 17–21, depend from claims 1, 4, 8, or 11, and add additional limitations as to the composition of the dose to be administered. Because I have held claims 1, 4, 8, and 11 nonobvious, so too are claims 17–21. "Dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious." *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988); *see also* Manual of Patent Examining Procedures § 2143.03 ("If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious" so long as the claim is properly dependent.); *Comaper Corp. v. Antec, Inc.*, 596 F.3d 1343, 1350 (Fed. Cir. 2010) ("A broader independent claim cannot be nonobvious where a dependent claim stemming from that independent claim is invalid for obviousness."); *Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331, 1344 (Fed. Cir. 2009) (same). Thus, because I have

concluded that claims 1, 4, 8, and 11 would not have been obvious, and because Tolmar does not dispute that the formulation claims are properly dependent, claims 17–21 would not have been obvious.

For the foregoing reasons, I conclude that claims 1–21 of the '906 patent would not have been obvious over NCT 548, the renal impairment and formulation prior art, and the knowledge of the ordinary artisan.

II. Written Description

Apart from obviousness, Tolmar argues that the claims of the '906 patent are invalid for lack of an adequate written description and lack of enablement. Neither argument is persuasive. Section 112(a) of the Patent Act provides, in pertinent part, that the specification "shall contain a written description of the invention." 35 U.S.C. § 112(a). The purpose of the written description requirement is to ensure that the "inventor actually invented the invention claimed." *Ariad Pharm.,* 598 F.3d at 1351. The specification's disclosure is sufficient when it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art," *id.*, and is "highly dependent on the facts of each case." *Biogen Int'l GmbH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1342 (Fed. Cir. 2021). As with the other issues in this case, Tolmar's burden on this issue is to prove invalidity by clear and convincing evidence. *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1364 (Fed. Cir. 2003).

Tolmar argues that the '906 patent fails to demonstrate that the inventors possessed a dosing regimen in which 25–150 mg-eq. maintenance doses are administered 21–38 days after the second loading dose, Dkt. No. 140 at 72, or that the inventors possessed a dosing regimen for

treating the full scope of psychiatric disorders claimed, *id.* at 80. With respect to maintenance doses, Tolmar argues that the specification describes administering maintenance doses only on "day 36, monthly, or every 4 weeks," which is "insufficient to show the inventors possessed a 17-day[8] dosing window." *Id.* at 73. As for psychotic disorders, Tolmar argues that "possession of the treatment for schizophrenia is not tantamount to possession of treatment of all psychotic disorders." *Id.* at 80 (citing *FWP IP ApS v. Biogen MA., Inc.*, 749 F. App'x 969, 975–76 (Fed. Cir. 2018). The maintenance dose argument applies to all claims, whereas the psychotic disorders argument applies only to claims 4–7, 11–14, and 17–21 insofar as they depend from claims 4 or 11.

A. Maintenance Doses

As an initial matter, the '906 patent refers to a monthly ±7-day maintenance dosing window throughout the specification. *See* '906 patent at 5:17–23, 5:26–30, 5:38–41, 6:3–5, 6:20–24. That is sufficient to show possession of the invention. Dr. Coles admitted as much. As she testified, "[T]here are multiple, multiple, multiple places in the '906 Patent where it describes giving . . . a maintenance dose monthly plus or minus seven days." TD1 331:6–18).

Even assuming Tolmar's characterization of the specification's disclosures is correct, however, the written description requirement of section 112 does not require disclosure of every claimed embodiment. The written description requirement is satisfied if the specification provides a sufficient number of representative embodiments to show that the inventor possessed the full scope of the claim, or for the described embodiments to have shared features, from which a person of skill in the art could infer possession of the entire claim scope. *Idenix Pharms. LLC v. Gilead*

[8] As construed, a month (±7 days) means "21 to 38 days." Dkt. No. 93. That is the 17-day window to which Tolmar refers.

Scis., Inc., 941 F.3d 1149, 1164 (Fed. Cir. 2019); *Ariad*, 598 F.3d at 1350; *see also Allergan, Inc. v. Sandoz, Inc.*, 796 F.3d 1293, 1308 (Fed. Cir. 2015) ("[T]he proper inquiry is whether the patentee has provided an adequate description that in a definite way identifies the claimed invention in sufficient detail that a person of ordinary skill would understand that the inventor had made the invention at the time of filing."). The claims Tolmar seeks to invalidate for lack of written description are exactly the types of claims that justify not requiring disclosure of every embodiment. *See Lipocine Inc. v. Clarus Therapeutics, Inc.*, 541 F. Supp. 3d 435, 457 (D. Del. 2021) (Providing written description support for every embodiment "would be impossible in many instances, such as for a claim to a pharmaceutical product that is defined by features spanning a numerical range of dose amounts [or] dosing frequency.").

Tolmar concedes that the '906 patent discloses administering a maintenance dose every four weeks, which is in the middle of the claimed range of dosage intervals. A skilled artisan reading the specification would recognize that the purpose of the ±7-day window is "[t]o avoid a missed monthly dose." '906 patent at 6:22–24 ("To avoid a missed monthly dose, patients may be given the injection up to 7 days before or after the monthly time point."); *see also* TD2 374:16–376:18 (purpose of the ±7-day window is to avoid missed doses). As such, a person of skill in the art would understand that the inventors had possession of the claimed dosing regimen even if the inventors did not test repeated dosing at the fringe of the claimed maintenance dose period, i.e., every three weeks or every five weeks. Accordingly, the court finds that the inventors had possession of the claimed maintenance doses.

B. Psychotic Disorders

Tolmar is correct that the '906 specification does not describe treatment of each and every psychotic disorder; Tolmar is incorrect, however, that treatment of every psychotic disorder is

required by the claims. Tolmar's argument is based on Dr. Jacinto Dizon's testimony that many of the "[p]athologic psychological conditions" described in columns 12–14 of the '906 patent are not suitable for treatment with a long-acting injectable antipsychotic. TD1 406:1–411:8. If treatment of all those disorders were required, the claims addressing "psychotic disorders" could well be invalid. *FWP IP ApS*, 749 F. App'x at 975–76 (finding written description inadequate where it did not show that claimed compounds "were in fact effective for treating the entire list of enumerated conditions" in the claims). But the issued claims do not address treatment of all the enumerated disorders.

The claims of Janssen's original application recited the entire list of conditions. *See* JTX-2 at 56–58, 64–67; TD1 454:4–14. The examiner, however, rejected those claims for lack of enablement and written description support. *See* JTX-2 at 170–72 (enablement rejection); *id.* at 173 (written description rejection); TD1 454:23–455:3. Following that rejection, the claims were amended to their current form, which calls for the claimed method where the psychiatric patient is "in need of treatment for psychotic disorder." *See* JTX-2 at 554–62 (amendment); *id.* at 565–74 (allowance); TD1 455:4–20.

Tolmar's argument requires that an ordinary artisan understand the psychotic disorder claims to incorporate the broader list about which Dr. Dizon testified. In other words, Tolmar's argument is predicated on a form of claim construction. But the court previously construed the term "psychotic disorder" in the '906 patent to mean "a disorder characterized by psychotic symptoms, such as delusions, hallucinations, disorganized speech, or disorganized or catatonic behavior." Dkt. No. 93 at 1. Dr. Dizon's reliance on an unclaimed list of psychiatric conditions undermines his opinion on this issue. Moreover, "just as prosecution history estoppel may act to estop an argument under the doctrine of equivalents, positions taken before the PTO may bar an

inconsistent position on claim construction under § 112." *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1457 (Fed. Cir. 1998) (en banc). Interpreting the psychotic disorder claims to incorporate the broad list from the specification would be contrary to the prosecution history of the '906 patent. Aside from Dr. Dizon's testimony, Tolmar has presented no evidence that the inventors did not possess a means of treating psychotic disorders, as that term was construed in the '906 patent.

For those reasons, I find that a person of ordinary skill in the art would understand from the specification that the inventors of the '906 patent possessed the claimed dosing regimen. At a minimum, Tolmar has not met its burden of proving otherwise by clear and convincing evidence. As such, I conclude that Tolmar has not proved that any of the '906 claims are invalid for lack of an adequate written description.

III. Enablement

To satisfy the enablement requirement of section 112 of the Patent Act, the specification must disclose "the manner and process of making and using [the invention], in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." 35 U.S.C. § 112(a).

In order to show lack of enablement, Tolmar must prove "by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Allergan*, 796 F.3d at 1309 (quoting *In re Wands*, 858 F.2d 731, 736–37 (Fed. Cir. 1998)). "Whether undue experimentation is required . . . is a conclusion reached by weighing many factual considerations." *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013) (cleaned up). As such, "whether a patent satisfies the enablement

requirement is a question of law based on underlying factual findings." *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1096 (Fed. Cir. 2020).

Tolmar argues that the '906 patent does not enable a person of ordinary skill in the art to practice the claimed invention, for two main reasons. First, Tolmar argues that an ordinary artisan would not be able to administer maintenance doses within the claimed 17-day window because it would not be clear which dose volume to select or how frequently to administer the doses. Dkt. No. 140 at 66 (citing TD1 201:15–202:17, 344:14–20); *see also* Dkt. No. 140 at 74; *id.* at 69 (explaining that an ordinary artisan would not know how to "maintain or achieve target plasma concentrations of paliperidone" using the claimed method "without undue experimentation"). Second, Tolmar argues that a person of ordinary skill in the art would not be able to treat all psychotic disorders with the claimed dosing regimen, as both paliperidone palmitate and long-acting injectables are unsuitable for many applications. Dkt. No. 140 at 74; *id.* at 77 (citing both parties' experts agreeing that they "would not treat a patient with substance-induced psychotic disorder with a long-acting injectable" as described by the claims). As in the case of Tolmar's written description arguments, the first enablement argument applies to all claims, whereas the second applies only to claims 4–7, 11–14, and 17–21 insofar as they depend from claims 4 or 11. Neither argument is persuasive.

Both arguments incorrectly assume that enablement requires disclosure of how to achieve a *desirable* result using the invention. Enablement requires only that the specification impart to a person of skill in the art the ability to practice "the invention *as defined by its claims*." *Amgen Inc. v. Sanofi*, 598 U.S. 594, 610 (2023) (emphasis added). It is not necessary to "maintain or achieve target plasma concentrations of paliperidone" in order to practice the claims. Nor is it necessary that it be good practice to treat a patient with every psychotic disorder according to the claimed

method. As such, neither of Tolmar's arguments is directed to enabling the person of ordinary skill in the art to practice the invention as defined by its claims.

To the contrary, the claims themselves are sufficiently clear that an ordinary artisan would plainly be capable of practicing them. As Janssen's witness Dr. Patrick Sinko explained, the claims are "almost like a recipe," "a series of steps that you have to follow," and "it's very easy to follow those steps." TD3 213:2–15; *see also* TD3 214:19–215:6. Tolmar's witness, Dr. Coles, agreed. See TD1 331:9–332:1 ("Q: And if a POSA was given an instruction to give a maintenance dose of paliperidone palmitate monthly plus or minus seven days, they would not need any additional information to be able to do that; right? A: Well, if they're told to do it, they could do it . . . ."). Practicing the claimed regimen does not require any experimentation at all, let alone undue experimentation. Because Tolmar has not demonstrated any need for experimentation, it has not met its burden of proving lack of enablement. *Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1189 (Fed. Cir. 2014) (reversing finding of no enablement where defendant "failed to make the threshold showing that . . . experimentation is necessary to practice the claimed methods").

As stated above with respect to the '918 provisional application, Tolmar's concerns "may be an issue for the FDA," but they have no bearing on a person's ability to practice the claims and therefore have no bearing on enablement. *See United Therapeutics*, 74 F.4th at 1370. An ordinary artisan knows how to administer an intramuscular injection. The claims merely say to do so within a certain date range, which is well within the capability of a person of ordinary skill in the art. As such, I find that an ordinary artisan could practice the claims of the '906 patent without undue experimentation. I therefore conclude that all the claims of the '906 patent are adequately enabled by the specification.

IV. Conclusion

For the foregoing reasons, I hold that Tolmar has failed to prove, by clear and convincing evidence, that Janssen's '906 patent, or any claim of that patent, is invalid.

Janssen is directed to file a proposed form of judgment in accordance with these Findings of Fact and Conclusions of Law within 10 days of the issuance of this order.

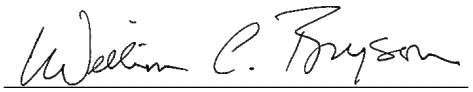
* * * * *

There is an appeal pending before the Federal Circuit in *Janssen Pharmaceuticals, Inc. v. Teva Pharmaceuticals USA, Inc.*, No. 22-1258, a case raising issues that may bear upon the issues raised in this case. I have not obtained any information about that case other than information that is on the public record. Because this case is an ANDA case, for which an expedited decision is required, I have not postponed deciding this case until after the Federal Circuit acts in the *Teva* case. In the event the Federal Circuit's decision in the *Teva* appeal has an effect on the proper disposition of this case, that question can be addressed through post-decisional motions in this case or through an appeal from the judgment.

The briefs in this case were submitted under seal. For that reason, I have filed this opinion under seal. Within three business days of the issuance of this order, the parties are directed to advise the court by letter whether they wish any portions of this order to remain under seal, and if so which portions. Any request that portions of the order remain under seal must be supported by a particularized showing of need to limit public access to those portions of the order.

IT IS SO ORDERED.

SIGNED this 26th day of February, 2024.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE