IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BAYER HEALTHCARE LLC,

Plaintiff,

v.

BAXALTA INC. and BAXALTA US INC.,

Defendants.

No. 16-cv-1122-RGA

MEMORANDUM OPINION

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August 23, 2019

ANDREWS, U.S. DISTRICT JUDGE:

Presently before the Court is Defendants' motion for judgment as a matter of law and for a new trial concerning invalidity, noninfringement, and damages. (D.I. 434). I have reviewed the parties' briefing. (D.I. 436, 452, 461). I heard oral argument on the issue of nonenablement on August 9, 2019. For the following reasons, Defendants' motion is **DENIED**.

I. BACKGROUND

On December 5, 2016, Plaintiff Bayer Healthcare LLC filed suit against Defendants Baxalta Inc. and Baxalta US Inc. (collectively, "Baxalta") and Nektar Therapeutics for infringement of U.S. Patent No. 9,364,520 ("the '520 patent"). (D.I. 1). The '520 patent is directed to forms of human factor VIII, "a protein necessary for normal blood clotting in response to injury." (D.I. 99 at 1). The patent claims factor VIII conjugates not found in nature, made up of recombinant factor VIII and one or more biocompatible polymers chemically bonded to factor VIII at the protein region known as the "B-domain." (*Id.* at 1, 3). The claimed factor VIII conjugates are formed through a process called pegylation, which is the conjugation of recombinant factor VIII with polyethylene glycol ("PEG"), a biocompatible polymer. (*Id.* at 5).

The accused product is Baxalta's Adynovate, a pegylated factor VIII used to treat hemophilia A. (D.I. 28 ¶ 25; D.I. 247 at 1). Hemophilia A is a congenital bleeding disorder caused by deficient or defective factor VIII. '520 patent at 1:25-32. The FDA approved the Adynovate Biologics License Application ("BLA") on November 13, 2015. (D.I. 28 ¶ 25).

I held a jury trial from January 25 to February 1, 2019.[1] Bayer asserted claims 1-3 and 8 of the '520 patent. (D.I. 398). The jury found that Baxalta infringed all four asserted claims, that none of the claims were invalid for lack of enablement or obviousness, and that Bayer was

[1] I cite to the trial transcript as "Tr."

entitled to $155,190,264 in damages, based on a 17.78% royalty rate and $872,836,128 royalty base. (*Id.*). I granted judgment as a matter of law with respect to induced, contributory, and willful infringement by Nektar, and willful infringement by Baxalta. Tr. at 1134:24-1135:3; (D.I. 412 ¶¶ 2-3). Bayer has no remaining claims against Nektar.

Baxalta now moves for judgment as a matter of law that the '520 patent is invalid, that Adynovate does not infringe, and that the jury's damages award is not supported by substantial evidence. In the alternative, Baxalta moves for a new trial. (D.I. 436).

II. LEGAL STANDARDS

A. Judgment as a Matter of Law

Judgment as a matter of law is appropriate if "the court finds that a reasonable jury would not have a legally sufficient evidentiary basis to find for [a] party" on an issue. Fed. R. Civ. P. 50(a)(1). "Entry of judgment as a matter of law is a 'sparingly' invoked remedy, 'granted only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability.'" *Marra v. Phila. Hous. Auth.*, 497 F.3d 286, 300 (3d Cir. 2007) (citation omitted).

"To prevail on a renewed motion for JMOL following a jury trial, a party must show that the jury's findings, presumed or express, are not supported by substantial evidence or, if they were, that the legal conclusion(s) implied [by] the jury's verdict cannot in law be supported by those findings." *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1348 (Fed. Cir. 1998). "'Substantial' evidence is such relevant evidence from the record taken as a whole as might be accepted by a reasonable mind as adequate to support the finding under review." *Perkin-Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 893 (Fed. Cir. 1984).

In assessing the sufficiency of the evidence, the Court must give the non-moving party, "as [the] verdict winner, the benefit of all logical inferences that could be drawn from the evidence presented, resolve all conflicts in the evidence in his favor and, in general, view the record in the light most favorable to him." *Williamson v. Consol. Rail Corp.*, 926 F.2d 1344, 1348 (3d Cir. 1991). The Court may "not determine the credibility of the witnesses [nor] substitute its choice for that of the jury between conflicting elements in the evidence." *Perkin-Elmer*, 732 F.2d at 893. Rather, the Court must determine whether the evidence supports the jury's verdict. *See Dawn Equip. Co. v. Ky. Farms Inc.*, 140 F.3d 1009, 1014 (Fed. Cir. 1998); *Gomez v. Allegheny Health Servs. Inc.*, 71 F.3d 1079, 1083 (3d Cir. 1995) (describing standard as "whether there is evidence upon which a reasonable jury could properly have found its verdict"); 9B *Charles Alan Wright & Arthur R. Miller, Federal Practice and Procedure* § 2524 (3d ed. 2008) ("The question is not whether there is literally no evidence supporting the party against whom the motion is directed but whether there is evidence upon which the jury might reasonably find a verdict for that party.").

Where the moving party bears the burden of proof, the Third Circuit applies a different standard. This standard "requires the judge to test the body of evidence not for its insufficiency to support a finding, but rather for its overwhelming effect." *Fireman's Fund Ins. Co. v. Videfreeze Corp.*, 540 F.2d 1171, 1177 (3d Cir. 1976) (quoting *Mihalchak v. Am. Dredging Co.*, 266 F.2d 875, 877 (3d Cir. 1959)). The Court "'must be able to say not only that there is sufficient evidence to support the finding, even though other evidence could support as well a contrary finding, but additionally that there is insufficient evidence for permitting any different finding.'" *Id.* at 1177 (quoting *Mihalchak*, 266 F.2d at 877).

B. New Trial

Federal Rule of Civil Procedure 59(a)(1)(A) provides, in pertinent part: "The court may, on motion, grant a new trial on all or some of the issues—and to any party— . . . after a jury trial, for any reason for which a new trial has heretofore been granted in an action at law in federal court . . . ." The decision to grant or deny a new trial is committed to the sound discretion of the district court. *See Allied Chem. Corp. v. Daiflon, Inc.*, 449 U.S. 33, 36 (1980); *Olefins Trading, Inc. v. Han Yang Chem. Corp.*, 9 F.3d 282, 289 (3d Cir. 1993) (reviewing district court's grant or denial of new trial motion under the "abuse of discretion" standard). Although the standard for granting a new trial is less rigorous than the standard for granting judgment as a matter of law—in that the Court need not view the evidence in the light most favorable to the verdict winner—a new trial should only be granted where "a miscarriage of justice would result if the verdict were to stand," the verdict "cries out to be overturned," or where the verdict "shocks [the] conscience." *Williamson*, 926 F.2d at 1352-53.

III. ASSERTED CLAIMS

Bayer asserted claims 1-3 and 8 of the '520 patent. The claims provide:

> 1. An isolated polypeptide conjugate comprising a functional factor VIII polypeptide and one or more biocompatible polymers, wherein the functional factor VIII polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or an allelic variant thereof and has a B-domain, and further wherein the biocompatible polymer comprises polyalkylene oxide and is covalently attached to the functional factor VIII polypeptide at the B-domain.
>
> 2. The isolated polypeptide conjugate of claim 1, wherein the biocompatible polymer comprises polyethylene glycol.
>
> 3. The isolated polypeptide of claim 2, wherein the polyethylene glycol comprises methoxypolyethylene glycol.
>
> 8. A pharmaceutical composition comprising a therapeutically effective amount of the isolated polypeptide conjugate of claim 1 and a pharmaceutically acceptable adjuvant.

'520 patent at 61:8-20, 62:13-14.

IV. INVALIDITY

Baxalta bears the burden of proof by clear and convincing evidence on invalidity. Therefore, to prevail on JMOL, Baxalta must show "not only that there is sufficient evidence to support the finding, even though other evidence could support as well a contrary finding, but additionally that there is insufficient evidence for permitting any different finding." *Fireman's Fund*, 540 F.2d at 1177. Baxalta moves for judgment of invalidity based on insufficient evidence for the jury to find that Baxalta failed to prove both nonenablement and obviousness. (D.I. 436 at 3-10, 21-24). For the following reasons, Baxalta's motion is **DENIED**.

A. Nonenablement

A patent specification "shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ." 35 U.S.C. § 112, ¶ 1 (2006).[2] "[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1362 (Fed. Cir. 2018) (internal citations and quotation marks omitted). Factors for assessing whether a disclosure would require undue experimentation include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

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[2] Paragraph 1 was later replaced by § 112(a) of the Leahy-Smith America Invents Act ("AIA"), which applies to applications and patents with an effective filing date of March 16, 2013, or later. Pub. L. No. 112–29, §§ 3(n)(1), 4(c), 125 Stat. 284, 293, 296 (2011). The '520 patent has a priority date of November 14, 2005. (D.I. 326, Sched. A ¶ 13). Therefore, the pre-AIA statute applies.

Each of the asserted '520 patent claims requires "an isolated polypeptide conjugate," which I have construed to mean "a polypeptide conjugate where conjugation was not random." (D.I. 200). Specifically, the PEG is conjugated to the B-domain of a functional factor VIII polypeptide. '520 patent at 61:8-15. The claims are not limited by conjugation to particular amino acids such as cysteine or lysine. Baxalta agrees that the '520 patent teaches non-random conjugation through pegylation at cysteine. (D.I. 436 at 5). However, Baxalta asserts that since the claims are not limited to particular amino acids, the full scope of the claims includes non-random pegylation at lysine, which the '520 patent fails to enable. (D.I. 436 at 3-10; D.I. 461 at 1-6).

1. The '520 Patent Must Enable Non-Random Lysine Pegylation at the B-Domain

It is well established that the specification must enable the full scope of the claimed invention. *Everlight*, 896 F.3d at 1364. That means if "the asserted claims are broad enough to cover [both cysteine and lysine pegylation], the ['520 patent] must enable both embodiments." *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 1000 (Fed. Cir. 2008) (internal citation omitted) (addressing an invention for use in both video games and movies); *see also Everlight*, 896 F.3d at 1364 (finding enablement of "five out of the six referenced permutations" in the patent insufficient); *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1378-79 (Fed. Cir. 2007) (where the full scope of the claims included injectors with and without a pressure jacket, finding the claims invalid because the patent only enabled injectors with a pressure jacket). It is undisputed that non-random lysine pegylation is within the scope of the asserted claims as I have construed them. (D.I. 452 at 9-14).[3]

[3] Although Bayer does not explicitly concede this point, it could not plausibly argue otherwise, as Adynovate is the product of lysine pegylation. *See, e.g.*, Tr. at 1236:11-14.

Bayer argues that Baxalta mischaracterizes the novel aspect of the invention to improperly broaden the scope of the claims. (D.I. 452 at 9). According to Bayer, "the key insight of the '520 patent claims was the discovery that PEGylating at the B-domain resulted in the retention of functional activity." (*Id.* (internal citations omitted)). Therefore, the question for enablement is "whether, with the benefit of the '520 patent, a person of ordinary skill could attach PEG at the B-domain of full-length Factor VIII using a conjugation process that is 'not random.'" (*Id.*).

Bayer's "novel aspect" theory stems from the Federal Circuit's decision in *Automotive Technologies*. There, the court found the scope of the claims included both mechanical and electronic side impact sensors. 501 F.3d at 1285. Use of the claimed "velocity-type" side impact sensors was the "novel aspect" of the invention. *Id.* at 1283. The court found that the electronic sensor was "not just another known species of a genus consisting of sensors," but "a distinctly different sensor compared with the [mechanical sensor]." *Id.* at 1285. Thus, the court held that the specification had to enable both the electronic and mechanical sensors. *Id.* Because the court determined that the specification failed to enable the electronic sensor, it affirmed the district court's judgment of invalidity for nonenablement. *Id.*

Bayer relies on my opinion in *Delaware Display Grp. LLC v. VIZIO, Inc.*, 2017 WL 784988 (D. Del. Mar. 1, 2017), which distinguished *Automotive Technologies*. The asserted claims covered lighting displays, which included a "light source" limitation. *Id.* at *3. The light source was applicable to displays of all sizes. *Id.* at *4. I granted summary judgment of enablement despite the fact that, at the time of the invention, one skilled in the art could not have made a light source for certain larger displays. *Id.* at *5. In contrast to *Automotive*

Technologies, I found that the light source was a "tangential limitation" and not the novel aspect of the asserted claims. *Id.* I explained:

> To hold otherwise would drastically alter the law of enablement. Suppose I had a product claim that claimed a camera where the novel aspect was a design that allows it to take improved pictures. As an additional limitation, I require a battery for the camera. The only role the battery plays is to supply the power to the camera. The battery plays no other meaningful role. It is clear that the battery is not the focus of the invention. My specification allows one skilled in the art to make the battery technology of the time and implement my novel design. Years later, novel battery technology is developed. It would be very harsh for enablement law to render my product claim invalid for lack of enablement because my patent did not teach the new battery technology when batteries were not even the focus of my claim. The law of enablement does not command that result, nor should it.

Id.

Delaware Display is inapposite. Even under Bayer's view, the novel aspect of the claimed invention is the non-random pegylation of factor VIII at the B-domain. This is not a situation where the parties only dispute the enablement of a "tangential limitation," such as a generic light source or battery. *See Delaware Display*, 2017 WL 784988, at *5.

The facts of this case are analogous to those in *Automotive Technologies*. As in *Automotive Technologies*, the scope of the asserted claims includes two distinct embodiments of the claimed invention—factor VIII conjugates with non-random pegylation at the B-domain via (1) cysteine pegylation and (2) lysine pegylation. It is undisputed that "different amino acids have different reactivities under different conditions." Tr. at 1343:7-11. Therefore, like the sensors in *Automotive Technologies*, a conjugate with non-random lysine pegylation is "not just another known species of a genus consisting of" conjugates with non-random pegylation, but "a distinctly different" conjugate compared to the conjugate with non-random cysteine pegylation. *See Automotive Technologies*, 501 F.3d at 1285. Thus, to enable the asserted claims, the '520

patent must teach a person of ordinary skill in the art to practice the claimed conjugates with both cysteine and lysine pegylation.[4]

2. The '520 Patent Specification Supplies the "Novel Aspect" of the Claimed Invention

Enablement does not require the specification to disclose what is well known in the art. *Everlight*, 896 F.3d at 1364. "'[T]he artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending on the predictability of the art.' But this gap-filling is merely supplemental; it cannot substitute for a basic enabling disclosure." *Id.* (quoting *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)). "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." *Automotive Technologies*, 501 F.3d at 1283; *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997).

The '520 patent does not disclose an embodiment for non-random lysine pegylation. (*See* D.I. 452 at 10-11). All of the specification's embodiments relate to non-random cysteine pegylation. Therefore, the knowledge of one skilled in the art is required to fill the gap between the specification and the full scope of the claims.

At the August 9, 2019 hearing, Baxalta argued that the specification itself must provide the full enabling disclosure because non-random lysine pegylation relates to the novel aspect of the claimed invention. I think that is too narrow a view of enablement. Although the novel aspect of the claimed invention is non-random pegylation at the B-domain, that does not mean

[4] It would follow that, since the claims are not limited to any amino acid, the scope of the claims includes not just non-random pegylation at lysine, but non-random pegylation at any amino acid in the B-domain. Whether those other embodiments are enabled is irrelevant for purposes of JMOL, however, as Baxalta attempted to prove its case by focusing on lysine.

the specification must disclose an embodiment for non-random pegylation at each amino acid in the B-domain. The specification provides detailed disclosures on how to practice the claimed invention with cysteine. *E.g.*, '520 patent at 20:56-21:5. I think that qualifies as a sufficient disclosure of the "novel aspect" of the invention. Thus, it is appropriate to consider the knowledge in the art to determine whether, in view of the cysteine disclosure, undue experimentation was required to practice the invention with lysine.

3. Baxalta Fails to Meet Its Burden on JMOL

Baxalta bears the burden of proof on invalidity. Thus, Baxalta can only prevail on JMOL if it shows that a reasonable jury could not have found that Baxalta failed to meet its burden to prove nonenablement by clear and convincing evidence.[5] *Fireman's Fund*, 540 F.2d at 1177.

Baxalta argues that, under the *Wands* analysis, the record overwhelmingly shows that a person of ordinary skill in the art could not practice non-random lysine pegylation without undue experimentation. I have already addressed the nature of the claimed invention (*Wands* factor 4) and the scope of the asserted claims (*Wands* factor 8). For the remaining factors, Baxalta asserts that the inventors did not know how to achieve non-random lysine pegylation (*Wands* factors 1-3), and that the '520 patent is silent on non-random lysine pegylation and teaches against lysine pegylation generally (*Wands* factors 5-7). (D.I. 436 at 3-4).

First, Baxalta asserts that the '520 patent inventors, Drs. Pan and Murphy, did not know how to make the claimed invention using lysine pegylation. (*Id.* at 4-6). Dr. Pan was the lead inventor on the '520 patent. (D.I. 461 at 4). Dr. Pan stated in an October 2005 email that he believed previous attempts at pegylating factor VIII failed because they relied on lysine pegylation that was "random PEGylation and not controlled." Tr. at 989:2-990:10. Instead, Dr.

[5] I prefer not to use a "triple negative," but I think that is what the law requires.

Pan used a method that targeted pegylation of the four free cysteines in the B-domain of factor VIII. *Id.* at 983:24-984:21. When asked whether he "ever consider[ed] lysine PEGylation as an option for meeting the goals of the KG-N project[6]," he responded, "I didn't think it was possible." *Id.* at 972:11-15.[7] He explained that he "really thought especially for Factor VIII, such a complex protein with so many lysines, it would not be a feasible way to make that work." *Id.* at 972:14-16, 973:3-8. Dr. Murphy also stated in a 2007 email, "For the majority of PEGylated products, PEG is conjugated to free amines (usually lysine residues) on the surface of a protein. This results in random PEGylation since there are generally multiple potential attachment sites." *Id.* at 381:21-382:2.[8]

Second, Baxalta argues that the '520 patent is silent on non-random lysine pegylation. (D.I. 436 at 6-9). As discussed, the '520 patent does not disclose an embodiment of the claimed invention using lysine pegylation. However, "[a] patentee is not required to provide actual working examples" to show enablement. *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1189 (Fed. Cir. 2014).

Baxalta also argues that the '520 patent teaches against lysine pegylation generally. The patent's only discussion of lysine pegylation is in the "Background of the Invention," which explains, "Random modification of [factor VIII] by targeting primary amines (N-terminus and lysines) with large polymers such as PEG . . . has been attempted with varying degree of success." '520 patent at 3:50-53. The patent notes, however, "This random approach" is

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[6] KG-N stands for "Kogenate New." Kogenate was Bayer's prior factor VIII product. Tr. at 328:20-23. Bayer began the KG-N project around 2002 or 2003 to develop a factor VIII with longer circulation time. Tr. at 273:6-8, 274:14-17. The '520 patent resulted from Bayer's work on the KG-N project. *Id.* at 348:13-15.

[7] Bayer asserts that Dr. Pan made this statement in the limited context of a 2004 proposal relating to the use of B-domain deleted factor VIII, which is not relevant to the '520 patent. (D.I. 452 at 13); Tr. at 353:13-16, 983:24-984:11, 1003:15-24. I do not think the testimony is that limited. Although Dr. Pan had been discussing the 2004 proposal, counsel's question referred broadly to "the goals of the KG-N project." Tr. at 966:20-973:8.

[8] Dr. Murphy noted at trial that while he agreed with what he wrote, the use of "generally" made it a "broad statement." Tr. at 382:3-6.

"problematic" because "[factor VIII] has hundreds of potential PEGylation sites, including the 158 lysines . . . , all of which could potentially be PEGylated with reagents primarily targeting primary amines." *Id.* at 3:63-4:1. Drawbacks of not controlling the site of pegylation include "potential activity reduction if the PEG were to be attached at or near critical active sites," and "enormous heterogeneity in product profile [that] will make consistent synthesis and characterization of each lot nearly impossible." *Id.* at 4:7-16.

Expert testimony was thin on both sides. Baxalta's expert, Dr. Zalipsky, merely recited the *Wands* factors and opined, without further explanation, that the '520 patent specification does not teach how to do non-random pegylation with lysines on factor VIII. *Id.* at 1211:3-1212:11. Dr. Zalipsky's testimony is so conclusory as to be virtually worthless.[9] Baxalta relies heavily on inventor fact testimony in its post-trial briefing. Dr. Zalipsky did not address that testimony in his nonenablement opinion. Plaintiff's experts implied that a person of ordinary skill in the art would have known how to alter reaction conditions to practice the claimed invention with lysine. Tr. at 1306:20-1307:7, 1341:25-1343:23; *see also id.* at 433:9-449:22, 490:7-17 (discussing reaction conditions for Adynovate). As discussed, the '520 patent specification provides detailed instructions on the reaction conditions required for cysteine. *E.g.*, '520 patent at 20:56-21:5.

At most, Baxalta has shown that a reasonable jury *could* have found nonenablement by clear and convincing evidence. The enablement issue comes down to a factual dispute over the level of experimentation required to practice the claimed invention with lysine. The parties presented conflicting and unfocused testimony—the jury was not obligated to credit Baxalta's witnesses over Bayer's or to draw the conclusions that Baxalta now argues for. In addition, the

[9] In closing argument, Baxalta did not mention Dr. Zalipsky or his opinion in connection with its nonenablement argument. Tr. at 1523:23-1525:2, 1554:20-1559:9; *see also id.* at 1544:22-1545:7 (discussing noninfringement).

fact that the '520 patent specification teaches against *random* lysine pegylation does not mean, as a matter of law, that the patent is not enabled as to non-random lysine pegylation. Therefore, Baxalta has failed to meet its high burden on JMOL.

B. Obviousness

Baxalta argues that the '520 patent is obvious in view of the Bossard patent (DTX 6), the Bossard work,[10] and what was known in the art. (D.I. 436 at 22-24; D.I. 461 at 11-12).

A patent claim is invalid as obvious under 35 U.S.C. § 103 "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103; *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406–07 (2007). "Obviousness is a question of law based on underlying facts." *Samsung Elecs. Co. v. Elm 3DS Innovations, LLC*, 925 F.3d 1373, 1380 (Fed. Cir. 2019). "[T]he scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." *KSR*, 550 U.S. at 406 (citation and quotation marks omitted). A court is also required to consider secondary considerations, or objective indicia of nonobviousness, as a "check against hindsight bias." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1078-79 (Fed. Cir. 2012); *see also Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966).[11]

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[10] The Bossard work was done by Dr. Bossard and others at Nektar under a 2003 research agreement between Nektar and Bayer. *See* Tr. at 224:11-25. Baxalta asserts that the Bossard work is prior art under 35 U.S.C. § 102(f). (D.I. 436 at 23).

[11] Bayer only raised one objective indicia of nonobviousness—unexpected results—which was addressed by a special interrogatory on the verdict form. Tr. at 1414:22-1415:7; (D.I. 398 at 4). The jury found that "the claimed inventions of the '520 patent achieve unexpected results." (*Id.*).

Bayer argues that Baxalta asserts a new obviousness combination, which was not raised at trial or in Baxalta's pre-verdict JMOL. (D.I. 452 at 4-5). "[A] party must file a pre-verdict JMOL motion on all theories, and with respect to all prior art references, that it wishes to challenge with a post-verdict JMOL." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 845 (Fed. Cir. 2010), *aff'd*, 564 U.S. 91 (2011) (finding a pre-verdict JMOL on anticipation insufficient to preserve the right to a post-verdict JMOL on a different theory (obviousness) or different prior art). Baxalta relied on four obviousness references at trial—the Bossard patent, the Bossard work, the Gruppo reference (DTX 80), and the Mosesson reference (DTX 107)—and moved for pre-verdict JMOL based on all four references. Tr. at 1210:12-16; (D.I. 390 at 3-4). Baxalta specifically relied on both Gruppo and Mosesson:

> A POSA would have been motivated to use full-length Factor VIII based on Gruppo's teaching that full-length Factor VIII has fewer bleeding incidences and that the B-domain protects Factor VIII from premature thrombin cleavage. Moreover, based on Gruppo, a POSA would have been motivated to PEGylate the B-domain because it is not required for coagulation activity. Mosesson teaches that the B-domain is surface-exposed and accessible, which would have provided a reasonable expectation of success that the B-domain could be PEGylated.

(D.I. 390 at 3-4 (citations omitted)). Baxalta now asserts that Gruppo and Mosesson merely "reiterate[] cumulative principles over what was otherwise known in the art." (D.I. 461 at 12).

Baxalta's present theory appears to be that the '520 patent claims are obvious in view of the Bossard patent and the knowledge in the art, wherein the knowledge in the art provided motivation to combine and the Bossard work provided a reasonable expectation of success. (D.I. 436 at 22-24). Baxalta does not even mention Gruppo and Mosesson in its opening brief and instead relies on the '520 patent specification as its sole evidence of the knowledge in the art. (D.I. 436 at 22). On reply, Baxalta argues that its discussion of Gruppo and Mosesson at trial is reflected in the '520 specification. (D.I. 461 at 12). Baxalta essentially replaces Gruppo and Mosesson with a general assertion of knowledge in the art based on the '520 patent—a new

theory that Baxalta failed to preserve in its pre-verdict JMOL. (*See* D.I. 390 at 3-4). Therefore, Baxalta has waived its right to challenge the jury's verdict under its new obviousness theory.

In the alternative, I find that Baxalta's JMOL fails on the merits.

Baxalta argues that a person of ordinary skill in the art would have been motivated to apply the Bossard patent to conjugate at the B-domain of full-length factor VIII. (D.I. 436 at 22). The Bossard patent taught conjugation of factor VIII but did not specifically teach conjugation at the B-domain. The patent disclosed the use of full-length factor VIII, including its amino acid sequence and thus the location of lysines and cysteines in the protein. DTX 6 at 9:38-41, 10:16-19, 16:44-45, 73:18-20 (claim 15), SEQ ID NO: 1; Tr. at 1214:24-1215:12. Baxalta argues that the Bossard patent taught "conjugation at 'desired' sites on Factor VIII, including lysine and cysteine sites." (D.I. 436 at 22); DTX 6 at 12:9-11. A substantial number of the lysine sites are in the B-domain. (*See* D.I. 436 at 22).

Bayer asserts that the Bossard patent was directed to random pegylation, not pegylation targeted to the B-domain. (D.I. 452 at 6). Baxalta's invalidity expert, Dr. Zalipksy, admitted that "the lysine PEGylation disclosed in Bossard is not within the scope of the claims of the '520 patent because it yields a random conjugation." Tr. at 1246:12-21. He also agreed that the example in the patent that disclosed cysteine pegylation used a factor VIII without the B-domain ("B-domain deleted"). Tr. at 1214:16-1215:1; '520 patent, Ex. 7. Bayer's expert Dr. Russell opined that the reaction conditions discussed in the Bossard patent—long reaction times with a large excess of PEG—were consistent with random pegylation. *Id.* at 1296:21-1297:9. He further testified that none of the Bossard patent's examples analyzed where the PEG attached to the proteins, and in fact, all of the examples used B-domain deleted factor VIII. *Id.* at 1295:17-19, 1297:10-1298:6.

Based on the testimony from Drs. Zalipsky and Russell, a reasonable juror could have concluded that the Bossard patent was directed to random pegylation without regard for the B-domain. Therefore, the jury did not have to find that the Bossard patent taught a person of ordinary skill in the art to pegylate at the B-domain of factor VIII. Without such a finding, the jury had no basis to conclude that the '520 patent claims are invalid as obvious.[12]

V. NONINFRINGEMENT

The jury found that Baxalta infringed each of the asserted claims. (D.I. 398 at 2). Baxalta now moves for JMOL of noninfringement. Specifically, Baxalta argues that the record cannot support a finding that Adynovate meets the "isolated polypeptide conjugate," "SEQ ID NO:4" or "at the B-domain" limitations. (D.I. 436 at 10-11). For the following reasons, Baxalta's motion is **DENIED**.

A. "isolated polypeptide conjugate" ("where conjugation was not random")

Baxalta argues that Adynovate does not meet the "isolated polypeptide conjugate" limitation, because there is insufficient evidence to support finding that Adynovate is the result of non-random pegylation.

Baxalta appears to assume that non-random pegylation requires knowing where each PEG will attach on factor VIII, even within the B-domain. (*See* D.I. 436 at 11-12). I do not think my construction requires that level of precision. As discussed on summary judgment, evidence that Adynovate was made to be "predominantly" and "preferentially" pegylated at the B-domain created a genuine dispute of fact as to whether Adynovate is the result of non-random pegylation. (D.I. 319 at 9). Further, I reiterated that non-random conjugation does not require

[12] Baxalta only relies on the Bossard work as evidence of a reasonable expectation of success. (D.I. 436 at 23-24). Since I find that Baxalta has failed to show that the Bossard patent, in combination with what was known in the art, discloses the claimed invention, I need not reach Baxalta's arguments relating to the Bossard work.

total homogeneity, either among the factor VIII conjugates in the product or within each individual factor VIII conjugate. (*Id.*). In other words, the claims do not require each factor VIII in Adynovate to be pegylated in the same places (homogeneity among conjugates in the product), nor do they require every PEG on each factor VIII to be in the B-domain (homogeneity within each conjugate).

Bayer presented substantial evidence at trial to support finding that Adynovate is the result of non-random pegylation. In its submissions to the FDA, Baxalta described Adynovate as having PEGs "targeted to the B-domain," asserted that "the consistency of the region-specific PEGylation predominantly on the B-domain was confirmed," and provided a site analysis report stating that 73% of all identified sites of pegylation were located within the B-domain. Tr. at 534-536:11, 553:4-554:13; *see also* PTX 446 at 6-7; PTX 441 at 15, PTX 879 at 64, PTX 607 at 22. Bayer's expert Dr. Ravetch explained that if Adynovate were made under conditions where all sites were normalized, only 51% of the pegylation sites would have been in the B-domain. Tr. at 607:9-12. Therefore, a reasonable juror could conclude that Adynovate was designed to have PEGs targeted to the B-domain, and thus was not the result of random pegylation.

B. "SEQ ID NO:4" (2,332 amino acids)

The asserted claims require a factor VIII polypeptide comprising the amino acid sequence of "SEQ ID NO:4 or an allelic variant thereof."[13] '520 patent at 61:8-12. The '520 patent defines "SEQ ID NO:4" as human full-length factor VIII and lists its entire 2,332 amino acid sequence. '520 patent at 9:36-37, SEQ ID NO:4. Baxalta argues that Adynovate does not meet the "SEQ ID NO:4" limitation as a matter of law, because Bayer failed to present substantial evidence that Adynovate contains full-length factor VIII. (D.I. 436 at 19).

[13] Allelic variants are the slight differences between individuals due to "genetics." Tr. at 638:10-13.

It is undisputed that Adynovate is made by pegylating Advate, an earlier generation drug, and that Advate contains some percentage of full-length factor VIII. (*Id.*). The Adynovate label also states, "ADYNOVATE is a recombinant full-length human coagulation factor VIII (2,332 amino acids . . .)." PTX 905 at 3. Baxalta argues, however, that Bayer failed to present any evidence that the full-length factor VIII present in Advate is retained after pegylation in Adynovate. (D.I. 436 at 19). Baxalta also asserts that, in view of *PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007), "advertising and other materials" such as the Adynovate label are insufficient to support a finding of infringement. (D.I. 436 at 19).

PharmaStem did not create a per se bar on the use of marketing materials to show infringement. "To be sure, there is no prohibition against using the admissions of a party, whether in the form of marketing materials or otherwise, as evidence of an infringement action; such admissions are entitled to weight along with all other evidence of infringement." *PharmaStem*, 491 F.3d at 1351. The court simply held that, given the facts of that case, the marketing materials presented at trial were insufficient to support a finding of infringement. *Id.*

Here, the Adynovate label is evidence of infringement as a party admission that Adynovate contains full-length factor VIII. Based on that admission and the undisputed fact that Adynovate is made using some amount of full-length factor VIII, a reasonable juror could have found that Adynovate meets the "SEQ ID NO:4" limitation.[14]

[14] Baxalta also argues that Bayer is barred from relying on the doctrine of equivalents to meet the "SEQ ID NO:4" limitation. (D.I. 436 at 19-20). The jury found literal infringement and did not address the doctrine of equivalents. (D.I. 398 at 3). Because I find the jury's verdict supported by substantial evidence, I do not reach Baxalta's doctrine of equivalents argument.

C. "at the B-domain" ("retains functional factor VIII activity")

The Court construed "at the B-domain" to mean "attachment at the B-domain such that the resulting conjugate retains functional factor VIII activity." (D.I. 200). The parties dispute whether Adynovate "retains functional factor VIII activity."

The '520 patent describes "functional factor VIII" as including variations on factor VIII "that have the biological activity of correcting human factor VIII deficiencies." '520 patent at 9:46-50. It is undisputed that Adynovate has factor VIII activity such that it can be used to treat patients. (D.I. 436 at 21; D.I. 452 at 21). In fact, Baxalta has admitted that Adynovate "retains functional Factor VIII activity." Tr. at 557:24-558:11 (PTX 1200 at 7); (*see also* D.I. 326, Sched. A ¶ 22 ("Adynovate contains functional factor VIII conjugated with [PEGs]."). Baxalta argues, however, that not all activity is sufficient to show infringement. Rather, the claims require retention of "substantial" factor VIII activity. (D.I. 436 at 20-21).

Baxalta relies on the '520 patent specification. The specification describes the invention as "maintain[ing] substantial [factor VIII] activity," including derivatives of factor VIII, "so long as they contain the functional segment of human factor VIII and the essential, characteristic human factor VIII functional activity remains unaffected in kind." '520 patent at 8:25-26, 9:46-55. In addition, Table 4, which measures "specific activity"[15] before and after pegylation of factor VIII, shows about 100% activity retention post-pegylation. '520 patent at 25:40-57; Tr. at 1202:24-1203:11.

I do not find Baxalta's arguments persuasive. My construction of "at the B-domain" only requires retention of factor VIII activity at a level that is "functional." It does not require any

[15] There is some dispute over whether "specific activity" is a relevant measure at all. Dr. Ravetch indicated that specific activity reflects the purity of the product, as opposed to its ability to clot blood. Tr. at 648:20-25, 686:16-22. Baxalta's scientist, Dr. Mitterer, also discussed specific activity in the context of purification. *Id.* at 899:17-22.

specific ratio of pre-pegylation to post-pegylation activity. (D.I. 200). Nor do I think the '520 patent specification supports such a limiting construction. Table 4 describes the experimental results of a particular embodiment and is not necessarily limiting. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005); (*see also* D.I. 452 at 22). The other portions of the specification merely indicate that the invention maintains "substantial" factor VIII activity and that "functional" factor VIII activity is "unaffected." I do not think either statement is inconsistent with maintaining "functional" factor VIII activity; neither requires retention of a particular level of activity beyond being "functional." Baxalta has admitted that Adynovate "retains functional factor VIII activity." Tr. at 557:24-558:11 (PTX 1200 at 7). Therefore, a reasonable juror could find that Adynovate meets the "at the B-domain" limitation.

VI. DAMAGES

The jury awarded $155,190,264 in damages calculated from a 17.78% royalty rate and $872,836,128 royalty base. The royalty base is not in dispute. Bayer's expert, Dr. Addanki, opined that a reasonable royalty would fall between 5.1% and 42.4%, and would depend on the parties' relative bargaining powers. Tr. at 749:22-750:4, 792:22-25. He initially took an additional step of calculating the mid-point rate, 23.75%, but I excluded that portion of his opinion on *Daubert* as an impermissible use of the Nash Bargaining Solution. (D.I. 372 at 12-16). Based on Dr. Addanki's testimony, the jury awarded a royalty of 17.78%.

Baxalta argues that the jury's award cannot stand as a matter of law because it is (1) speculative, (2) based on previously undisclosed expert opinions, (3) an impermissible disgorgement of profits, (4) based on improper exclusion of costs, and (5) not apportioned to the value of the '520 patent. As such, Baxalta moves for judgment that Bayer is only entitled to

nominal damages, or alternatively, for a new trial on damages. (D.I. 436 at 25-26). For the following reasons, Baxalta's motion on damages is **DENIED**.

A. Speculative Damages

Baxalta argues that, because Dr. Addanki did not opine on a specific rate within the 5.1% to 42.4% range, the jury was required to speculate as to damages. (D.I. 436 at 26-27).

A jury determines damages based on the totality of the evidence and is not required to choose from either party's suggested figures. *Fuji Photo Film Co. v. Jazz Photo Corp.*, 394 F.3d 1368, 1378 (Fed. Cir. 2005) ("[T]he jury is not bound to accept a rate proffered by one party's expert but rather may choose an intermediate royalty rate."); *Unisplay, S.A. v. Am. Elec. Sign Co.*, 69 F.3d 512, 519 (Fed. Cir. 1995) ("[A] jury's choice simply must be within the range encompassed by the record as a whole."); *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 926 F.2d 1161, 1168 (Fed. Cir. 1991) ("[T]he determination of a reasonable royalty must be based upon the entirety of the evidence and the court is free to, indeed, must reject the royalty figures proffered by the litigants, as the district court did in this case, where the record as a whole leads the court to a different figure."). The totality of the evidence may include expert testimony suggesting a reasonable royalty range. *See Powell v. Home Depot U.S.A., Inc.*, 663 F.3d 1221, 1241 (Fed. Cir. 2011) (upholding a jury damages award where plaintiff's expert testified that a reasonable royalty would be between $2,180 and $8,500 per unit). Therefore, the jury's royalty rate is not speculative simply because it was not suggested by either party or because Dr. Addanki gave his reasonable royalty opinion in the form of a range.

Bayer presented substantial evidence at trial to support finding a 17.78% royalty, which is "within the range encompassed by the record as a whole." *Unisplay*, 69 F.3d at 512. As discussed on *Daubert*, Dr. Addanki did substantial analyses in his expert reports to determine the

end points of the reasonable royalty range. (D.I. 372 at 13-14). He gave comparable testimony at trial. Tr. at 747:22-25, 759:7-784:8, 787:24-792:19. As for selecting a value within the range, Dr. Addanki explained, "[W]here you end up in any negotiation depends on the relative bargaining positions that each party has. . . . In a nutshell, how important it is to each party to close the deal is inversely related to how strong their bargaining position is." *Id.* at 745:4-746:1.

To help the jury determine the parties' relative bargaining positions, Dr. Addanki discussed the factual circumstances under which each party approached the June 2016 hypothetical negotiation. *Id.* at 806:6-8. He noted that Bayer would not typically license out its intellectual property, especially to a competitor. *Id.* at 750:11-751:2. Bayer and Baxalta had been competitors for twenty-five years and Bayer had never licensed the '520 patent. *Id.* Referring to testimony from Mr. Fournel, a senior vice president at Bayer, Dr. Addanki explained, "Bayer's attitude towards its intellectual property was it used it to prevent competitors from stealing its inventions and copying them. So it would not have been very important to Bayer to license [to] a competitor." *Id.*

In contrast, Dr. Addanki opined that the hypothetical license would have been very important to Baxalta because it enabled Baxalta to make and sell Adynovate. *Id.* at 751:3-752:18. He relied on internal documents from Baxalta's parent company, Shire, which indicated that Shire believed Adynovate had substantial business value. Dr. Addanki explained that the documents, from the months following the hypothetical negotiation but prior to Adynovate's launch, showed that Adynovate was to replace Advate as the flagship brand and that it was expected to increase "patient growth and market share." *Id.* at 753:24-754:13, 755:8-17 (PTX 817). The documents also noted growing competition in the recombinant factor VIII market. *Id.*

at 756:5-757:2 (PTX 617). Dr. Addanki thus opined that Shire viewed Adynovate as a means to meet increasing competitive pressures. *Id.* at 757:3-6.

A reasonable juror could rely on Dr. Addanki's testimony to conclude that a reasonable royalty would fall between 5.1% and 42.4% and, based on the parties' relative bargaining positions, the hypothetical negotiation would result in a rate of 17.78%.

B. Newly Disclosed Expert Opinions

Baxalta asserts that Dr. Addanki only disclosed one reasonable royalty in his expert reports—the mid-point of the bargaining range, 23.75%. (D.I. 436 at 28). In contrast, at trial Dr. Addanki opined that a reasonable royalty could be any value within the bargaining range. (*Id.*). Baxalta thus argues that Dr. Addanki presented new opinions at trial in violation of Federal Rules of Civil Procedure 26(a)(2)(B) and 37(c). (*Id.* at 28-30).

I already heard and rejected this argument at trial. (D.I. 373, 374); Tr. at 3:4-12:10, 784:22-787:7. Dr Addanki opined in his expert report that his analysis of the bargaining range provided the "feasible outcomes of the hypothetical negotiation," wherein "[t]he final outcome of the negotiation depends on the bargaining power that each party has." (D.I. 274, Ex. A ¶¶ 18-19). That is consistent with Dr. Addanki's testimony at trial. Tr. at 747:22-25, 749:18-750:4. Therefore, Dr. Addanki provided sufficient disclosure to support his reasonable royalty testimony, consistent with Rules 26(a)(2)(B) and 37(c).

C. Disgorgement of Profits

Baxalta argues that the high end of Dr. Addanki's royalty range, 42.4%, is a legally impermissible disgorgement of Baxalta's profits from Adynovate. (D.I. 436 at 31).

Baxalta relies entirely on *Hughes Tool Co. v. Dresser Industries, Inc.*, 816 F.2d 1549 (Fed. Cir. 1987). In *Hughes*, the Federal Circuit set aside the district court's royalty award as

arbitrary because it was based on a clearly erroneous profits figure. 816 F.2d at 1558. In doing so, the court briefly discussed *Georgia-Pacific Corp. v. U.S. Plywood-Champion Papers Inc.*, 446 F.2d 295 (2d Cir. 1971). As in *Hughes*, the district court in *Georgia-Pacific* had accepted that a reasonable royalty must leave the infringer a reasonable profit. *Hughes*, 816 F.2d at 1558. Also as in *Hughes*, the district court relied on an erroneous profits figure, which left the infringer no profit. *Id.* Therefore, the *Georgia-Pacific* court set aside the royalty award as excessive on appeal. *Id.* Contrary to Baxalta's suggestion, *Hughes* did not hold that a reasonable royalty that leaves an infringer with no profit is excessive as a matter of law.

The Federal Circuit has since made clear that "an infringer's net profit margin is not the ceiling by which a reasonable royalty is capped." *Powell v. Home Depot U.S.A., Inc.*, 663 F.3d 1221, 1238 (Fed. Cir. 2011); *State Indus., Inc. v. Mor-Flo Indus., Inc.*, 883 F.2d 1573, 1580 (Fed. Cir. 1989) ("The determination of a reasonable royalty, however, is based not on the infringer's profit margin, but on what a willing licensor and licensee would bargain for at hypothetical negotiations on the date infringement started."). Therefore, the fact that a 42.4% royalty equals Baxalta's entire profit margin, if true, is not a basis for overturning the jury's damages award.

D. Exclusion of Costs

Baxalta argues that Dr. Addanki failed to account for certain costs when determining his bargaining range. (D.I. 436 at 32-33). Dr. Addanki and Baxalta's expert, Dr. Rausser, presented conflicting testimony on which costs should have been incorporated into the reasonable royalty analysis. Tr. at 772:25-777:25 (Addanki), 1259:21-1261:20 (Rausser). The jury was not required to credit Dr. Rausser over Dr. Addanki. Therefore, the jury could properly rely on Dr. Addanki's testimony to support its damages award.

E. Failure to Apportion

Baxalta argues that Dr. Addanki failed to apportion his damages. I already found Dr. Addanki's apportionment analysis sufficient under *Daubert*:

> Dr. Addanki opines that Adynovate is the smallest salable unit practicing the '520 patent. Dr. Addanki accounts for apportionment by comparing Baxalta's profits from Adynovate to its profits from Advate, an older generation product. Dr. Addanki considers Adynovate and Advate materially identical aside from Adynovate's infringing features. He thus estimates the value of the '520 patent by calculating the incremental value of Adynovate over Advate. . . . Dr. Addanki conducts detailed economic analyses to determine Baxalta's incremental profits from Adynovate, including consideration of sales and patient data for Adynovate, Advate, and other factor VIII products.

(D.I. 372 at 16-17 (citations omitted)). Baxalta's new arguments are based on Dr. Rausser's alternative apportionment analysis. (*See* D.I. 436 at 33-34; D.I. 452 at 34). The fact that Dr. Addanki took a different apportionment approach than Dr. Rausser does not make Dr. Addanki's opinions inadmissible. Therefore, the jury could properly rely on Dr. Addanki's apportionment analysis to support its damages award.

VII. NEW TRIAL

The decision to grant or deny a new trial is within the discretion of the district court. *Allied Chem.*, 449 U.S. at 36. Baxalta has not shown that "a miscarriage of justice would result if the verdict were to stand," the verdict "cries out to be overturned," or the verdict "shocks [the] conscience." *Williamson*, 926 F.2d at 1352-53. Therefore, Baxalta's motion for a new trial is **DENIED**.

VIII. CONCLUSION

A separate order will be entered.