IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC., AMGEN MANUFACTURING, LIMITED, and AMGEN USA INC.,

Plaintiffs;

v.

SANOFI, SANOFI-AVENTIS U.S. LLC, AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., and REGENERON PHARMACEUTICALS, INC.,

Defendants.

Civil Action No. 14-1317-RGA

MEMORANDUM OPINION

Melanie K. Sharp, James L. Higgins, and Michelle M. Ovanesian, YOUNG CONAWAY STARGATT & TAYLOR, LLP, Wilmington, DE; William G. Gaede, III (argued), MCDERMOTT WILL & EMERY LLP, Menlo Park, CA; Sarah Chapin Columbia and K. Nicole Clouse, MCDERMOTT WILL & EMERY LLP, Boston, MA; Rebecca Harker Duttry, MCDERMOTT WILL & EMERY LLP, Washington, DC; Christopher B. Mead, LONDON & MEAD, Washington, DC; Keith R. Hummel, David N. Greenwald, Lauren A. Moskowitz, Geoffrey G. Hu, and Sharonmoyee Goswami, CRAVATH, SWAINE & MOORE LLP, New York, NY; Lauren Martin and Megan Y. Yung, QUINN EMANUEL URQUHART & SULLIVAN, LLP, Boston, MA, attorneys for Plaintiffs.

David E. Wilks and Scott B. Czerwonka, WILKS, LUKOFF & BRACEGIRDLE, LLC, Wilmington, DE; Matthew M. Wolf (argued), ARNOLD & PORTER KAYE SCHOLER LLP, Washington, DC; David K. Barr and Daniel L. Reisner, ARNOLD & PORTER KAYE SCHOLER LLP, New York, NY; Deborah E. Fishman, ARNOLD & PORTER KAYE SCHOLER LLP, Palo Alto, CA; John Josef Molenda and Vishal Chandra Gupta, STEPTOE & JOHNSON LLP, New York, NY, attorneys for Defendants.

August 28, 2019

ANDREWS, U.S. DISTRICT JUDGE:

Currently pending before the Court are Defendants' Renewed Motion for Judgment as a Matter of Law ("JMOL") that the Asserted Patent Claims are Invalid and, in the alternative, Motion For a New Trial.[1] (D.I. 883, 886). I have reviewed the briefing for these motions. (D.I. 885, 888, 922, 923, 982, 983). I heard helpful oral argument on August 8, 2019. (Hr'g Tr.). The Parties submitted supplemental letters after argument. (D.I. 1045, 1046).

I. BACKGROUND

Plaintiffs Amgen, Inc., Amgen Manufacturing, Ltd., and Amgen USA Inc. filed suit against Defendants Sanofi, Sanofi-Aventis U.S. LLC, Aventisub LLC, and Regeneron Pharmaceuticals, Inc. on October 17, 2014 alleging infringement of U.S. Patent Nos. 8,583,698 ("the '698 patent"), 8,829,165 ("the '165 patent"), and 8,859,741 ("the '741 patent"). (D.I. 1, 10, 184). Plaintiffs later amended the Complaint to add claims of infringement of U.S. Patent Nos. 8,871,913 ("the '913 patent"), 8,871,914 ("the '914 patent"), 8,883,983 ("the '983 patent"), and 8,889,834 ("the '834 patent"). (D.I. 184). The parties stipulated to infringement of selected claims for trial,[2] (D.I. 235), and tried issues of validity to the jury in March 2016. During trial, the Court granted JMOL of non-obviousness and no willful infringement. (D.I. 345 at 1076:6-1077:6; D.I. 302). The issue of damages was not tried to the jury. (D.I. 346 at 1285:16-20). The jury determined the patents were valid. (D.I. 303). Plaintiffs moved for a permanent injunction (D.I. 306), which was granted (D.I. 392), and then stayed. (D.I. 401). Defendants appealed. (D.I. 402).

On appeal, the Federal Circuit affirmed the grant of Plaintiffs' JMOL of non-obviousness and the denial of Defendants' JMOL of no written description and enablement but reversed for

[1] Plaintiffs' Motion for a Permanent Injunction is also pending. (D.I. 870).
[2] The selected claims for the first trial were claims 2, 7, 9, 15, 19, and 29 of the '165 patent, claim 7 of the '741 patent, and claim 24 of the '914 patent. (D.I. 235).

errors made in evidentiary rulings and jury instructions and remanded the case for a new trial on written description and enablement. *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1381-82 (Fed. Cir. 2017). The Federal Circuit also vacated the permanent injunction. *Id.*

On remand, the Parties tried the issues of written description and enablement to the jury.[3] The jury verdict found claim 7 of the '741 patent and claims 19 and 29 of the '165 patent valid, but invalidated claims 7 and 15 of the '165 patent for lack of written description. (D.I. 817). Defendants now ask that the Court overturn the jury verdict under Federal Rule of Civil Procedure 50(b) or grant a new trial under Rule 59. (D.I. 883, 886).

The claims of the '165 patent still in dispute read as follows:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> **19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.**
>
> **29. A pharmaceutical composition comprising an isolated monoclonal antibody, wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3 and blocks the binding of PCSK9 to LDLR by at least 80%.**

('165 patent, cls. 1, 19, 29 (disputed claims bolded)). The claim of the '741 patent still in dispute reads as follows:

---

[3] Plaintiffs further narrowed the claims for the remand trial to claims 7, 15, 19, and 29 of the '165 patent and claim 7 of the '741 patent. (D.I. 759; D.I. 768).

> 1. An isolated monoclonal antibody that binds to PCSK9, wherein the isolated monoclonal antibody binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 2. The isolated monoclonal antibody of claim 1, wherein the isolated monoclonal antibody is a neutralizing antibody.
>
> **7. The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.**

('741 patent, cls. 1-2, 7 (disputed claim bolded)).

II. LEGAL STANDARD

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) (cleaned up).

"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) (alterations in original). "'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 . . . ." Among the most common reasons for granting a new trial are: (1) the jury's verdict is against the clear weight of the evidence, and a new trial must be granted to prevent a miscarriage of justice; (2) newly discovered evidence exists that would likely alter the outcome of the trial; (3) improper conduct by an attorney or the court unfairly influenced the verdict; or (4) the jury's verdict was facially inconsistent. *See Zarow-Smith v. N.J. Transit Rail Operations, Inc.*, 953 F. Supp. 581, 584–85 (D.N.J. 1997).

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. DISCUSSION

A. Judgment as a Matter of Law of No Written Description

Defendants argue that no reasonable jury could conclude that the claims are supported by written description under either the representative species test or the structural features test. (D.I. 888 at 4-5).

The written description requirement contained in 35 U.S.C. § 112, ¶ 1 requires that the specification "clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad Pharm., Inc., v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (cleaned up). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "This inquiry, as we have long held, is a question of fact. Thus, we have recognized that determining whether a patent complies with the written description requirement will necessarily vary depending on the context." *Ariad*, 598 F.3d at 1351 (internal citations omitted). For patents that claim a broad genus (a major class or kind of thing) while disclosing only species of that genus (subclasses), the written description requirement is more specific. There are two tests. They are the representative species test and the structural features test. The Federal Circuit has summarized their requirements as follows:

> Demonstrating possession "requires a precise definition" of the invention. To provide this "precise definition" for a claim to a genus, a patentee must disclose "a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus."

Amgen, 872 F.3d at 1373 (quoting *Ariad*, 598 F.3d at 1350).

The representative species test does not require disclosure of every species in the genus and there is no bright-line rule "governing [] the number of species that must be disclosed to

describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in a field." *Ariad*, 598 F.3d at 1351. However, "merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species." *Id.* at 1350. "One needs to show that . . . one has conceived and described sufficient representative species encompassing the breadth of the genus." *AbbVie*, 759 F.3d at 1300.

Under the structural features test, "[f]unctional claim language can meet the written description requirement when the art has established a correlation between structure and function," such that disclosure of the function implicitly discloses the common structural features of the genus. *Ariad*, 598 F.3d at 1350.

"A party must prove invalidity for lack of written description by clear and convincing evidence." *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 682 (Fed. Cir. 2015). Because lack of written description, "like any other ground of invalidity, must be established by clear and convincing evidence," Defendants' burden on a JMOL motion is "doubly high: it must show that no reasonable jury could have failed to conclude that [Defendants'] case had been established by clear and convincing evidence." *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1353 (Fed. Cir. 2003) (internal citation omitted).

I start with the representative species test. Defendants argue that to satisfy the representative species test in the antibody context, the patentee "must adequately describe representative antibodies to reflect the structural diversity of the claimed genus" and "describe some species representative of antibodies that are structurally similar to" infringing antibodies. *AbbVie*, 759 F.3d at 1301. Defendants argue that Plaintiffs have not satisfied the representative species test because the undisputed evidence at trial indicated that the amino acid sequences of the

disclosed antibodies and the infringing Competitor Antibodies[4] were completely different from one another. (D.I. 888 at 6-7). Plaintiffs argue that there was substantial evidence submitted at trial supporting a jury finding that the disclosed antibodies were representative of the structural diversity of the genus, including the Competitor Antibodies. (D.I. 923 at 5-6).

I agree with Plaintiffs that substantial evidence supports the jury verdict under the representative species test. The record contains contradictory evidence on (1) what the appropriate comparison metric was, (2) whether there was sufficient similarity between the amino acid sequences of the Competitor Antibodies and the disclosed examples in the patents, and (3) whether there was functional similarity between the Competitor Antibodies and the disclosed examples in the patents.

First, Plaintiffs' experts repeatedly disputed the use of amino acid sequence as an appropriate comparison to determine whether the disclosed species were representative of the genus. (D.I. 865 at 638:8-11, 768:18-20, 765:10-766:12, 769:14-770:24). Plaintiffs' experts testified that three-dimensional structure was the appropriate metric for comparison and presented substantial evidence of similarity in the three-dimensional structure of the antibodies disclosed in the patent and the Competitor Antibodies.[5] (*Id.* at 621:5-629:1, 633:12-637:17, 764:6-767:15, 724:9-10, 725:21-727:4, 772:154-775:17; D.I. 864 at 449:5-9).

Second, even if amino acid sequence was the appropriate metric for comparison, substantial evidence supported a finding of structural similarity between the Amgen Antibodies and the Competitor Antibodies. The amino acid sequence differences between the Competitor

[4] I adopt the Parties' terminology from trial. The Competitor Antibodies are infringing antibodies developed by Plaintiffs' competitors, Merck, Pfizer, and Defendant. They are Praluent, 1D05, AX132, and J16. (D.I. 888 at 6).
[5] Defendants argue that Plaintiffs were improperly permitted to enter into evidence post-priority-date evidence about the three-dimensional structure. As Defendants include this challenge in their Rule 59 Motion for a New Trial, I will address it there.

Antibodies are not as extreme as in *AbbVie*. In *AbbVie*, the Court determined that "[a]ll of the antibodies described in AbbVie's patents were derived from Joe-9 and have VH3 type heavy chains and Lambda type light chains" and "the patents [did] not describe any example [] of fully human IL-12 antibodies having heavy and light chains other than the VH3 and Lambda types." *AbbVie*, 759 F.3d at 1300. Unlike there, here there was testimony of 80% similarity between the disclosed antibodies and the Competitor Antibodies' amino acid sequences, (D.I. 864 at 371:2-10, 374:19-24), and the disclosed antibodies cover more classes of antibodies than the patent disclosed in *AbbVie*. (D.I. 865 at 771:3-11). Dr. Rees testified that there are eight different families of binding and blocking antibodies disclosed by the patents. (D.I. 865 at 771:3-11).

Third, Plaintiffs presented substantial evidence of functional similarity. There was significant testimony that the antibodies disclosed in the 2008 patent application, while binding to different residues[6] across the "sweet spot," blocked PCSK9 binding to LDL-R through a variety of binding interactions. (D.I. 864 at 471:24-372:6; D.I. 865 at 630:14-25, 649:10-650:1, 651:1-652:11).

The jury was entitled to credit the testimony of Plaintiffs' experts. Thus, substantial evidence in the record supports the jury verdict of validity under the representative species test.

Because satisfaction of the representative species test is sufficient to support a finding of validity under written description, I need not address the Common Structural Features Test. Defendants have failed to show "that no reasonable jury could have failed to conclude that [Defendants'] case [for lack of written description] had been established by clear and convincing

[6] Residues are amino acids that make up the PCSK9 protein, and in the context of the patent, are within the "sweet spot" where PCSK9 would bind with an LDL receptor. (D.I. 863 at 194:22-196:1).

evidence." *Boehringer*, 320 F.3d at 1353 (internal citation omitted). I will therefore deny Defendants' motion for JMOL on the issue of written description.

B. Judgment as a Matter of Law of No Enablement

Defendants argue that no reasonable jury could conclude that the asserted claims were enabled. (D.I. 888 at 13-14). Defendants advance two arguments: (1) the claims are not enabled because the vast majority of antibodies within the full scope of the claims are impossible to make, and (2) undue experimentation is required to make antibodies within the claimed genus. (*Id.* at 14). The Parties agreed at oral argument that the disputed claims rise and fall together for the purposes of enablement. (Hr'g Tr. at 6:16-18, 6:23-7:8).

The enablement requirement, considered a separate and distinct requirement contained in 35 U.S.C. § 112, ¶ 1, assesses whether "one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008). "To be enabling, the specification must teach those skilled in the art how to make and use the *full scope* of the claimed invention without undue experimentation." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012) (internal quotation marks omitted; emphasis added). Because the enablement inquiry takes into account what is known to one skilled in the art, the Federal Circuit has "repeatedly explained that a patent applicant does not need to include in the specification that which is already known to and available to one of ordinary skill in the art." *Koito Mfg. Co. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1156 (Fed. Cir. 2004). "Enablement is a legal question based on underlying factual determinations." *Vasudevan*, 782 F.3d at 684. On a motion for JMOL, I must defer to the jury's underlying factual determinations, *Williamson*, 926 F.3d at 1348, but review the legal question *de novo*. *Pannu*, 155 F.3d at 1348. Factors considered in assessing the enablement requirement 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). "A party must prove invalidity for lack of enablement by clear and convincing evidence." *Vasudevan*, 782 F.3d at 684. Because lack of enablement, "like any other ground of invalidity, must be established by clear and convincing evidence," Defendants' burden on a JMOL motion is "doubly high: it must show that no reasonable jury could have failed to conclude that [Defendants'] case had been established by clear and convincing evidence." *Boehringer*, 320 F.3d at 1353 (internal citation omitted).

To enable the "full scope" of the claims, it is not required that the specification "provide[s] a detailed recipe for preparing every conceivable permutation" of a claimed embodiment. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App'x 961, 967 (Fed. Cir. 2014). Yet, merely enabling a person of ordinary skill to practice an embodiment, or even several embodiments, is not always sufficient. *See, e.g.*, *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013) (determining that the specification provided "only a starting point for further iterative research in an unpredictable and poorly understood field"); *MagSil*, 687 F.3d at 1382-83 (patent claims on "change in the resistance level by at least 10%" with no upper boundary were not enabled because specification did not explain any way to achieve levels above a certain threshold); *Sitrick*, 516 F.3d at 999-1001 (not enabled because the specification did not explain how to integrate "user image" in movies). Thus, "the full scope of a claim is not enabled when there is an embodiment within the claim's scope that a person of ordinary skill, reading the specification, would be unable to practice without undue experimentation." *MorphoSys AG v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 368-69 (D. Del. 2019).

1. Impossibility

Defendants argue that "the vast majority of antibodies within the full scope of the claims are impossible to make" and thus, the claims are not enabled. (D.I. 888 at 14). Defendants assert that *Trustees of Boston University v. Everlight Electronics Co.*, 89 F.3d 1357 (Fed. Cir. 2018), controls the inquiry. In *Everlight*, the Federal Circuit held a patent claim invalid for lack of enablement where the experts agreed that one out of six permutations of the claim was "physically impossible." *Id.* at 1362. Plaintiffs disagree, arguing, "Defendants have provided no evidence that any embodiments that *satisfy [Plaintiffs'] Claims* are impossible to make." (D.I. 923 at 19).

First, Defendants point to testimony elicited on cross-examination from Plaintiffs' witnesses about two hypothetical antibodies: (1) an antibody that binds to only two of the specified residues on opposite sides of the "sweet spot" without touching any of the other thirteen residues, and (2) an antibody binding only to D238 and no other claimed residues. (D.I. 864 at 540:7-21; D.I. 865 at 796:9-12). In regards to the first hypothetical antibody, Dr. Rees testified, "I won't say its impossible, but I don't believe based on good protein structural principle an antibody could bridge across without also interacting with those amino acids in between." (D.I. 865 at 796:23-797:1). In regards to the second hypothetical antibody, Dr. Jackson testified, "An antibody wouldn't bind if it's just binding with one amino acid residue, it wouldn't have the binding strength." (D.I. 864 at 540:19-21).

These statements do not support the "impossibility" theory Defendants advance. Dr. Rees' testimony does not state that it would be impossible to make the first hypothetical embodiment, just unlikely. Dr. Jackson's testimony indicates that an antibody that binds to just one amino acid residue would not fall within the scope of the claims because it would not actually bind to PCKS9 or block the binding of PCKS9 to the LDL receptor. (*See* '741 patent, cl. 1-2, 7).

Second, Defendants' reliance on *Everlight* is unavailing. In *Everlight*, the claims were drafted to cover six enumerated permutations of the patented invention. *Everlight*, 896 F.3d at 1360, 1364. In contrast, here, Plaintiffs' patent claims are drafted to require both (1) binding to "at least" one or two specified residues and (2) blocking PCSK9 from binding to the LDL-R. ('741 patent, cl. 1-2, 7; '165 patent, cl. 1, 19, 29).). This patent language does not claim a full scope of binding to only one or two specified residues and nothing more. Thus, *Everlight* does not require a determination of no enablement as a matter of law.

2. Undue Experimentation

Defendants argue that the *Wands* factors require a conclusion of non-enablement as a matter of law. (D.I. 888 at 15). The *Wands* factors are used to determine whether the amount of experimentation required to practice the claims' full scope is "undue." *See Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014). As noted, the *Wands* factors are:

> (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.

858 F.2d at 737.

a. Breadth of the Claims

After careful review of the evidence, I conclude that a reasonable factfinder could only have found that the scope covered by the claims is broad. Plaintiffs' relies on Dr. Rees' testimony that "the genus . . . would be narrow," (*See* D.I. 923 at 4 (citing D.I. 865 at 725:4-5, 731:16-17, 732:7-8)), because an antibody scientist would not engage in random mutations to the disclosed antibodies. (D.I. 865 at 733:6-11). But this testimony does not aid in the inquiry of what the full scope is of the *claims* of the asserted patents. Except for product-by-process claims or product

claims with a process limitation, the method by which the patented product is made has no effect on the scope of the product claim. *Abbott Labs. v. Sandoz*, 566 F.3d 1282, 1293 (Fed. Cir. 2009) (en banc). An antibody scientist's refusal to engage in random mutations does not mean that there could not be embodiments of the claims that could only be discovered by performing a random mutation. Dr. Rees did not testify that every antibody within the scope of the claims could be made through intelligent substitution, nor did he testify as to how many antibodies would result from making "intelligent substitutions," other than that it would not result in "millions" of antibodies. (*Id.* at 732:7-8). Dr. Rees' testimony that the genus is "narrow" falls short because it does not actually address the breadth of the claims; it is at most merely a conclusory statement that the claim scope is not as large as Defendants' expert testified it was. The quantity that Dr. Rees meant by "narrow" is unknown. Such conclusory expert testimony is insufficient to support a factual determination that the claimed genus is in fact "narrow."

Additionally, part of Dr. Rees' testimony relied on Dr. Jackson's testimony regarding the development stages of Plaintiffs' antibody project. Dr. Jackson testified that the initial testing processes determined that 3,000 of the antibodies created from immunizing ten mice bound to PCSK9. (D.I. 864 at 351:12-15, 351:24-352:3). Further testing revealed that 384 antibodies blocked interaction of PCSK9 with the LDL receptor, and that 84 antibodies were strong blockers. (*Id.* at 352:4-17). Dr. Rees also testified that "if the millions of antibodies that Dr. Boyd described . . . continued [] to bind and block . . . they would [] fall within the claims." (D.I. 865 at 733:2-7). Thus, Dr. Rees tacitly admitted that the potential scope of the claims could be broader than just those generated by intelligent substitution.

Dr. Boyd testified that if a person of ordinary skill in the art only created new antibodies by substituting amino acids per Table 1 of the patents in the sequence of a single disclosed

antibody, the person of ordinary skill would obtain 97,000 antibodies that she would then have to test to see whether they bound to PCKS9 and blocked binding to LDL receptors. (*Id.* at 802:12-23). After doing these substitutions for every disclosed antibody, Dr. Boyd testified that the person of ordinary skill in the art would get "millions" of antibodies. (*Id.*). Even assuming a majority of these millions of antibodies would not satisfy the claim requirements for blocking interaction between PCSK9 and the LDL receptor, there does not appear to be a genuine dispute between the parties as to the scope of antibodies that would need to be tested to determine whether they fell within the claims. (D.I. 865 at 740:18-21, 779:10-20). The Federal Circuit has repeatedly endorsed the consideration of the "number of possible candidates falling within the claimed genus" in the enablement inquiry. *Enzo Life Scis., Inc. v. Roche Molecular Sys., Inc.*, 928 F.3d 1340, 1346 (Fed. Cir. 2019); *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1385 (Fed. Cir. 2013) ("even if potential rapamycin compounds must have a molecular weight below 1,200 Daltons, there are still at least tens of thousands of candidates"). That is, even if potential antibodies must block PCSK9 from binding to LDL receptors, there are still at least millions of candidates.[7] Plaintiffs have repeatedly asserted that a person of ordinary skill in the art would not make substitutions by rote substitution following Table 1 of the patent, but instead, use their knowledge to make a smaller subset of "intelligent substitutions." (Hr'g Tr. at 75:13-17, 98:23-99:10). However, Dr. Rees has never testified as to how a person of ordinary skill would determine what subset of substitutions from Table 1 should be made. (D.I. 865 at 733:12-15). Thus, there is not a genuine material dispute of fact as to the breadth of the claims, and a reasonable factfinder could only conclude on this factual record that the scope of the claims is vast.

[7] Per Dr. Boyd's calculations from just the substitutions suggested by the patent specification. *See* '165 patent, tbl. 1.

b. Predictability of the Art

Defendants contend that the art was "highly unpredictable" as "even the most highly skilled person could not determine [where an antibody will bind] from its [amino acid sequence]." (D.I. 888 at 16). The Parties disagree as to how to assess this factor. Defendants argued that under *Enzo* and *Wyeth*, the question is, when looking at the input, which "in this case [is] an antibody, how predictable is it by looking at it that it will or won't meet the functional limitation." (Hr'g Tr. at 34:6-21). Plaintiffs argued that predictability should be assessed by looking at the maturity and relative skill of those in the art.[8] (Hr'g Tr. at 69:3-6, 9-11, 20-24). However, the state of the art and the relative skill of those in the art are separately enumerated factors under the *Wands* test.[9]

There was conflicting testimony as to the predictability of the art at the time of the 2008 patent application. Dr. Boyd testified that the amino acid sequences for antibodies are generally unpredictable because the unpredictability best serves the immune system; in his words, "If the antibodies were always predictable then the viruses and bacteria could figure out a way to get around them." (D.I. 863 at 225:9-17). Dr. Mehlin of Amgen, one of the inventors, testified:

> in general conservative mutations are going to be better tolerated by a protein than nonconservative mutations. But I'm always surprised. I mean, I have been surprised in the past where sometimes what you think is a conservative mutation is not conservative at all, you know, in terms of the protein function. . . . [T]he only way to know in the end is to test it, right. You can't tell a priori that your mutation will be tolerated.

---

[8] Plaintiffs argued at oral argument that both *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), and *Johns Hopkins Univ v. CellPro, Inc.*, 152 F.3d 1342 (Fed. Cir. 1998), were cases finding patents enabled in the context of antibody technology decades earlier. (Hr'g Tr. at 65:5-23). However, the patent in *In re Wands* was a method patent, 858 F.2d at 734, and in *Hopkins*, the finding of enablement was based on Defendants' failure to raise a genuine issue of material fact. 152 F.3d at 1359-60. Similarly, Plaintiffs also cited to *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 663 (E.D. Tex. 2017). However, as in *Wands*, the claim at issue was a method claim rather than a genus claim. *Id.* at 640-41.

[9] Similarly, Plaintiffs' brief groups together four of the *Wands* factors: nature of the invention, state of the art, relative skill of those in the art, and predictability of the art. (D.I. 923 at 15). However, the entirety of Plaintiffs' discussion on these factors is, "the level of skill in the art was high, the art was advanced, and the techniques involved in Amgen's roadmap were routine and well-known." (*Id.*). None of Plaintiffs' assertions address the predictability of the art.

(D.I. 864 at 388:21-389:8).

Dr. Rees testified that the art is "a highly predictable area" because of the maturity of the art and the disclosures in the patent. (D.I. 865 at 757:2-11). However, he also testified that "the way in which you get from sequence to the three-dimensional structure isn't fully understood today." (*Id.* at 765:15-16). Dr. Rees also admitted that a person of ordinary skill would not know the exact substitutions needed in the amino acid sequence to alter the residues of PCSK9 to which the antibody will bind.[10] (*Id.* at 792:12-20, 793:5-13, 794:6-16). Dr. Rees' assertion that the art is "highly predictable," even taken in the light most favorable to Plaintiffs, is thus a conclusory assertion inconsistent with the rest of his testimony. At best, Dr. Rees' testimony indicates that a person of ordinary skill in the art would understand that conservative substitution could be used to make different antibodies that had the same or improved binding to the antigen. (D.I. 865 at 733:14-22). However, this testimony does not support Plaintiffs' position that testing would not be necessary for conservative substitutions and the position is contradicted by other testimony in the record from Plaintiffs' other expert, Dr. Petsko. Dr. Petsko testified that substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be required to ensure that a substitution does not alter the binding and blocking functions. (D.I. 865 at 688:21-689:10).

Plaintiffs, at oral argument, attempted to distinguish this case from *Enzo*, *Idenix Pharms. LLC v. Gilead Scis., Inc.*, 2018 WL 922125 (D. Del. Feb. 16, 2018), and *Morphosys*, arguing that the evidence in this case displays a structure-function relationship that was absent in those cases. (Hr'g Tr. at 77:16-78:3; 85:22-24). Plaintiffs assert that expert testimony established "that all

[10] There was no explicit testimony from Dr. Rees at trial that antibodies resulting from "intelligent substitutions" in known antibodies would not require testing to ensure that they had the binding and blocking functions required by the asserted claims.

antibodies that bind to the sweet spot have common structures – both three-dimensional shape and chemical structural features – that allow them to bind there." (D.I. 923 at 11). The experts' testimony, as Plaintiffs tacitly admitted in their briefing, focused upon the "sweet spot" of the *antigen* and its "unique three dimensional and chemical structure" that conveys the "structural information (common shape and chemical complementarity) of the antibodies that bind to it." (*Id.*). Defendants' experts hotly contested the existence of such a structure-function relationship for the purposes of written description. (D.I. 888 at 9-13).

In the enablement context, there is no testimony from any expert that the structure-function relationship would eliminate the need for testing newly-created antibodies to determine whether they had the functions of blocking and binding. The Federal Circuit has "concluded that instead of analogizing the antibody-antigen relationship to a 'key in a lock,' it was more apt to analogize it to a lock and 'a ring with a *million* keys on it.'" *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1377 (Fed. Cir. 2017) (cleaned up). Here, while the shape of the "key" or antibody may help narrow the number to be tested in the "lock" or antigen, the expert testimony offered by Plaintiffs is that how to make a "key" or antibody in the correct shape is not "fully understood" (D.I. 865 at 765:15-16), from which it follows that the structure-function relationship is unpredictable.

Therefore, a reasonable factfinder could only find that the art is unpredictable.

c. Nature of the Invention; State of the Prior Art; Relative Skill of Those in the Art

The evidence indicates that the methods disclosed in the patent for making the invention were routine and well-known in the prior art. (D.I. 864 at 347:9-12, 347:18-22, 348:16-24; D.I. 865 at 713:15-18). There does not appear to be any dispute between the parties that the techniques disclosed could conceivably allow a person of ordinary skill in the art to make at least some

antibodies falling within the patent claims. Neither does there appear to be any dispute as to the level of skill in the art. A person of ordinary skill in the art would be familiar with the techniques disclosed in the patent: binning, alanine scanning, x-ray crystallography, immunizing mice, and making amino acid substitutions. (D.I. 864 at 347:9-12, 347:18-22, 348:16-24; D.I. 865 at 713:15-18).

d. Amount of Direction or Guidance Presented; Presence and Number of Working Examples

The record, taken in the light most favorable to Plaintiffs, indicates that there is no genuine dispute as to the amount of direction/guidance presented or the number of working examples present in the patent specifications.

Although the patent provides twenty-six working examples, the record indicates that there is no dispute that they do not teach a person of ordinary skill in the art how to predict from an antibody's sequence whether it will bind to specific PCKS9 residues. (D.I. 864 at 389:3-8; D.I. 865 at 779:10-14, 793:12-20, 794:11-16). Neither does the patent provide any direction or guidance on how to predict whether an antibody will bind. (D.I. 865 at 779:10-14, 794:11-16). Even for the suggested substitutions in the patent ('165 patent, table 1), a person of ordinary skill in the art would still be required to test the newly-generated antibody to see if it meets the functional limitations of the claims. (*Id.*). This is less guidance than was provided by the patent in *MorphoSys*, where the testimony indicated that "conservative variants of the disclosed [CD38] antibodies could be designed and would be 'reasonably expected' to be effective without screening." 358 F. Supp. 3d at 372.

The record also indicates that the specification and the examples do not improve a person of ordinary skill in the art's ability to discover non-disclosed antibodies within the scope of the

claims. Plaintiffs' expert, Dr. Rees, using claim 7 of the '741 patent as an example, testified that the patent teaches the following roadmap:

> Step 1: Make a known antibody binding D238;
> Step 2: Generate a pool of antibodies through super immunization procedure and test the pool of antibodies to see if they bind to PCSK9;
> Step 3: Run a binning assay against the known antibody to identify competing antibodies;
> Step 4: Run a blocking assay to determine whether the antibodies block the binding of PCSK9 to the LDL receptor; and
> Step 5: Verify the identity of the amino acids bound by alanine or arginine scanning.

(D.I. 865 at 737:17-738-10, 739:15-745:12). In comparison, the inventor, Dr. Jackson testified to the following methods ("the research plan") implemented in discovering the twenty-six disclosed antibodies:

> Step 1: Generate a pool of antibodies by super immunizing mice;
> Step 2: Test the pool of antibodies to see if they bind to PCSK9;
> Step 3: Test the pool of binders to determine whether and how much the antibodies block the binding of PCKS9 to the LDL receptor;
> Step 4: Attempt to characterize through a competition/binning assay; and
> Step 5: Generate amino acid sequences and identify the amino acid residues bound by the antibodies.

(D.I. 864 at 501:23-502:15, 503:7-504:9, 504:22-505:15, 507:1-508:23, 513:15-19). Dr. Jackson also testified that the patent describes "optimiz[ing]" the binding test by putting PCSK9 "in the right position so that [the binding] site was accessible to the antibodies." (*Id.* at 503:18-23). The significant similarity between the "research plan" used by Dr. Jackson and the "roadmap" disclosed in the patent demonstrates that a person of ordinary skill in the art attempting to obtain a claimed antibody that is not disclosed or is a variant of a disclosed antibody "would have to do essentially the same amount of work as the inventors of the patents-in-suit." *MorphoSys AG*, 358 F. Supp. 3d at 372; *see also Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013) (invalidating patent for lack of enablement where specification "disclose[d] only a starting

point for further iterative research in an unpredictable and poorly understood field."). As in *MorphoSys*, a person of ordinary skill in the art "would have to discover these [nonconservative variant] antibodies de novo through" super immunization or another technique. 358 F. Supp. 3d at 372. After considering the disclosed roadmap in light of the unpredictability of the art, any reasonable factfinder would conclude that the patent does not provide significant guidance or direction to a person of ordinary skill in the art. A person of ordinary skill in the art can only discover undisclosed claimed embodiments either (1) through trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties, or (2) by discovering the antibodies *de novo*.

e. The Quantity of Experimentation Necessary

Defendants argue,

> The quantity of experimentation required to make and use the full scope of the Claims is vast. . . . [because] a skilled artisan must either (1) randomly generate pools of antibodies, or (2) make substitutions to known antibodies, [and then] test those resulting antibodies to determine whether they satisfy the functional limitation of binding to specified PCSK9 residues.

(D.I. 888 at 17). More specifically, Defendants argue that a person of ordinary skill in the art may not be able to make a desired antibody using the patent's specification. As noted above, there is no dispute between the parties that a person of ordinary skill in the art would need either to follow the roadmap to generate a pool of antibodies for further testing, or to make substitutions to known antibodies and then to test the newly created antibodies.

The parties dispute how much experimentation is needed. Defendants assert that because of the unpredictability of the art and the need for functional testing, the experimentation required is an "iterative trial and error" process that will take substantial time and effort. (D.I. 888 at 18; D.I. 864 at 329:2-13, 329:16-24). In fact, Dr. Boyd testified that a person of ordinary skill in the

art might never know whether the entire claim scope had been discovered. (D.I. 864 at 330:18-22). Dr. Rees admitted that generating large pools of antibodies was impractical. (D.I. 865 at 779:23-780:3; 781:10-14). Plaintiffs argue that the quantity of experimentation required to make the full scope of the claims is low and points to Dr. Rees' testimony that "automated high-throughput techniques existed for testing a large number of antibodies" to determine whether they fall within the scope of the claims "quickly, efficiently, and cheaply." (D.I. 923 at 15; D.I. 865 at 761:6-762:4). However, Dr. Rees' testimony about the time and effort required was largely conclusory. (D.I. 865 at 761:6-13). Such conclusory expert testimony is insufficient to support a factual conclusion that the time and effort required to enable the full scope of the claims is minimal. In contrast, Dr. Boyd testified that "you could be immunizing mice for a hundred years. There might be kind of an antibody that you didn't come up with in that time period and no one else came up with but it might be still out there waiting to be found. . . ." (D.I. 864 at 330:18-22). Also, as noted above, the significant similarity between the "research plan" used by Dr. Jackson and the "roadmap" disclosed in the patent (as testified to by Dr. Rees) demonstrates that a person of ordinary skill in the art attempting to obtain a claimed antibody that is not disclosed or a variant of a disclosed antibody "would have to do essentially the same amount of work as the inventors of the patents-in-suit." *MorphoSys AG*, 358 F. Supp. 3d at 372.

Even taking the testimony in the light most favorable to Plaintiffs, the testimony of Plaintiffs' own experts indicates that the experimentation necessary to enable the full scope of the claims would take a substantial amount of time and effort. Dr. Rees' own testimony indicated that despite routine techniques and low cost, it would be impractical for a person of ordinary skill in the art to generate large pools of antibodies (as the patent's "roadmap" requires) and that the "roadmap" requires "essentially the same amount of work as the inventors of the patents-in-suit"

did to discover the invention. *MorphoSys AG*, 358 F. Supp. 3d at 372. Thus, a reasonable factfinder could only have determined that the experimentation necessary to enable the full scope of the claims would take a substantial amount of time and effort.

f. Summary of the *Wands* Factors

In light of the factual conclusions above, any reasonable factfinder would find that practicing the claims' full scope would require substantial experimentation. The remaining question is whether a reasonable factfinder could not fail to find that the experimentation required is "undue." Defendants assert that *MorphoSys AG v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354 (D. Del. 2019), should control my determination. Plaintiffs attempt to distinguish *MorphoSys* on the basis that the patentee in that case "did not establish that the claimed genus was small or that routine techniques could be employed to practice the full scope of the genus." (D.I. 923 at 17).

I agree with Defendants that *MorphoSys* is instructive. First, as I determined above, there does not appear to be a genuine dispute that the number of antibodies potentially falling within the claim scope is in the millions. Second, there does not appear to be a genuine dispute that substitution of amino acids in a sequence may have unpredictable effects on the function of the antibody. Third, the techniques employed to identify antibodies within the full scope of the genus are routine. Fourth, despite the routine techniques employed, it appears that a person of ordinary skill in the art would still be required "to do essentially the same amount of work as the inventors of the patents-in-suit," *MorphoSys AG.*, 358 F. Supp. 3d at 372, or engage in a trial-and-error process of amino acid substitution as even conservative substitutions may have unexpected results. Fifth, the specifications do not provide guidance on how to predict the effect of the sequence on the function of the antibody. The "roadmap" disclosed by the patents is almost exactly the same as the patentee's initial research process to discover the twenty-six disclosed antibodies. Finally,

a reasonable factfinder could only conclude that the amount of time and effort required to enable the full scope of the claims would be substantial. Therefore, I determine as a matter of law that undue experimentation would be needed to practice the full scope of the claimed invention.

Further comparison with precedent from the Federal Circuit and this Court supports these conclusions. As in *Wyeth*, there is "no genuine dispute that it would necessary to first synthesize and then screen *each* candidate [antibody] using the assays disclosed in the specification to determine whether it has" binding and blocking effects. 720 F.3d at 1385. Additionally, the art in *Wyeth* and the art here are unpredictable, and the specification "discloses only a starting point for further iterative research." *Id.* at 1386. As in *Idenix Pharms.*, where there was a broader class of compounds that required testing to determine if they met functional limitations, it is "only through experimentation, not prediction" that a person of ordinary skill in the art could conclude that a particular antibody would meet the binding and blocking requirements of the claim. 2018 WL 922125 at *23.[11]

Thus, the claims are not enabled, and I will grant Defendants' motion for judgment as a matter of law for lack of enablement.

C. New Trial

"If the court grants a renewed motion for judgment as a matter of law, it must also conditionally rule on any motion for a new trial by determining whether a new trial should be granted if the judgment is later vacated or reversed." Fed. R. Civ. P. 50(c)(1). Thus, I will now address Defendants' motion for a new trial.

[11] The Federal Circuit heard argument on the appeal from this decision on July 9, 2019.

1. Clear Weight of the Evidence

For the reasons stated above addressing the 50(b) motion, I do not find the jury verdict on written description to be against the clear weight of the evidence or require a new trial to prevent a miscarriage of justice.

On the issue of enablement, I must conditionally decide the motion for a new trial with the assumption that the appellate court reversed or vacated the grant of the renewed JMOL motion. It was Defendants' burden at trial to show that the asserted claims were not enabled by clear and convincing evidence. I determine that if the JMOL of no enablement is reversed, the jury verdict that the asserted claims were enabled was not against the clear weight of the evidence and a new trial need not be granted to prevent a miscarriage of justice.

2. Post-Priority Date Evidence

Defendants argue that a new trial should be granted because I erroneously excluded post-priority-date evidence. (D.I. 885 at 2). I disagree. The thrust of Defendants' argument seems to be that I disregarded the Federal Circuit's mandate from the first appeal in this suit and that the Federal Circuit therein said that post-priority-evidence is always relevant to demonstrating a lack of written description or enablement. (*Id.* at 2-3). Defendants misread the Federal Circuit's opinion.

The Federal Circuit held that "[i]t was [] legal error for the district court to *categorically* preclude all of [Defendants'] post-priority-date evidence of Praluent and other antibodies." *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1375 (Fed. Cir. 2017). More specifically, for written description purposes, the Federal Circuit distinguished between the prohibition on "post-priority-date evidence proffered to illuminate the post-priority-date state of the art, which is improper, [and] post-priority-date evidence proffered to show that a patent fails to disclose a representative number

of species," which it held to be proper. *Id.* at 1374-75. For purposes of enablement, the Federal Circuit stated that post-priority-date evidence showing lengthy and potentially undue experimentation to enable the full scope of the claims "*could have been* relevant to determining if the claims were enabled as of the priority date and should not have been excluded simply because it post-dated the claims' priority date." *Id.* at 1375 (emphasis added). However, the Federal Circuit did not state that post-priority-date evidence would always be admissible for these purposes.

In my second order on motions in limine, I excluded post-priority-date evidence related to Plaintiffs' research program for catabolic antibodies presented to show a lack of enablement under FRE 402 and 403. I determined that the evidence was irrelevant to the issue of enablement because the research program reflected a subsequent state of the art and therefore should be excluded under FRE 402. I also determined that to the extent there was any probative value, the evidence, if offered to prove enablement was likely to confuse the issues, mislead the jury, and waste time, such that the evidence's probative value was substantially outweighed by those concerns and should be excluded under FRE 403. (D.I. 693 at 3).

At trial, after further argument by the parties, I determined that certain documents could have been relevant to enablement, but only if Defendants could "first establish that [Dr. Jackson] was trying to make other antibodies within the scope of the patent." (D.I. 864 at 570). Defendants did not make this showing, and thus, I continued to exclude these documents for the reasons stated in the order on motions in limine.

Regarding enablement, Defendants argue that the excluded evidence would have shown that "Amgen continued to look for [antibodies similar to the Competitor Antibodies] for more than four years after the priority date and never found them." (D.I. 885 at 5). However, the documents they cite did not actually show that. Defendants submitted no evidence into the

record that Amgen was continuing to look for antibodies from 2008 to 2012. The only cited documents are from March 2012 to June 2012, a relatively short period of time. They do not show that the patentee "engaged in lengthy and potentially undue experimentation" over the four-year period to enable the claim scope. *Amgen*, 872 F.3d at 1375. Thus, the documents are irrelevant to the issue of enablement. To the extent the documents have any marginal relevance, the probative value was substantially outweighed by the likelihood of jury confusion because the documents arose in a subsequent state of the art and a subsequent research program into "catabolic" antibodies. (D.I. 763 at 3).

Regarding written description, I did not exclude documents when ruling on the motion in limine. (*Id.* at 2-3). However, when presented with specific documents and questions at trial, I did exclude a subset of documents that Defendants sought to introduce at trial. At trial, Defendants' attorneys asked, "Were there any documents from Amgen that you considered which confirm your opinion that you just gave that Amgen's claims fail to satisfy the written description requirement?" (D.I. 863 at 211:9-12). Plaintiffs objected, arguing that the question was designed to elicit irrelevant documents and conflate "actual" possession of a species with possession of a representative species. (*Id.* at 211:15-212:6, 212:18-23). Defendants responded that the documents they sought to admit demonstrated that "Amgen was aware . . . that EGFa mimics were a separate category of antibodies which they failed to have." (*Id.* at 213:1-5). Plaintiffs responded that the documents were related to a subsequent state of the art and did not serve the purpose of determining whether a person of ordinary skill in the art in 2008 would have found any disclosed antibody to be representative of the Competitor Antibodies. (*Id.* at 213:6-11). I sustained Plaintiffs' objection because the written description inquiry is an objective

inquiry and the experts could testify as to whether the disclosed antibodies were representative (or not) of the competitor antibodies. (*Id.* at 215:8-16).

The second instance related to written description at trial occurred as follows. Defendants asked Dr. Jackson if his team "monitored specifically Regeneron PCKS9 research?" (D.I. 864 at 542:11-13). Plaintiffs objected to the question as violating the MIL order. (*Id.* at 542:13). At sidebar, Defendants asserted the question should be allowed because of follow-up questioning as to whether Dr. Jackson found Praluent in the pre-patent work, reading from a specific document. (*Id.* at 542:20-543:6). I sustained the objection under the MIL because "whether or not they developed Praluent as part of the patent is actually irrelevant" to the issue of written description because a patentee does not have to describe every species in a genus to have adequately described the claims. (*Id.* at 543:22-24).

After the conclusion of testimony that day, I heard further argument from the parties on the documents Defendants sought to introduce with Dr. Jackson. I determined that for the purposes of Dr. Jackson's testimony, the documents would be excluded for the purposes of written description as "irrelevant to the written description issues" and that "to the extent there is any marginal relevance, [] the confusion would substantially outweigh the probative value." (*Id.* at 569:15-21).

Defendants argue that the excluded documents would have shown that (1) "Amgen monitored Regeneron/Sanofi, Pfizer, and Merck . . . and made the Competitor Antibodies based on published sequence information," (D.I. 885 at 6)[12], (2) Amgen "found the Amgen Antibodies different from the Competitor Antibodies in ways that were directly relevant to the claims,

[12] Defendants point to the following excluded documents for these points: Exs. 4-14 (DTX3137, DTX3147, DTX3155, DTX3156, DTX3170, DTX3171, DTX3188, DTX3141, DTX3173, DTX3190, and DTX3198).

including where they bind to PCSK9," (*id.*)[13] (3) Amgen had a "missing epitope" (*id.* at 7), and (4) Amgen did not have an EGFa mimic (*id.*).

First, whether Plaintiffs monitored their competitors and made the Competitor Antibodies based on published sequence information is irrelevant to the objective inquiry of written description. It is irrelevant to written description that Plaintiffs did not make the Competitor Antibodies until the sequence information was published; written description does not require actual reduction to practice. Rather, the specification must demonstrate possession. Whether an inventor actually made a specific embodiment before filing the patent is irrelevant.

Second, the documents Defendants cite for their second assertion are also irrelevant to the issue of written description. Exhibit 16 (DTX 3205) does not make any comparison between the Amgen antibodies and the competitor antibodies. Exhibit 5 states, "316P is a different PCKS9 antibody. We also did not get this one from PCSK9#1" in the context of a previous comparison of another Regeneron antibody to two Amgen antibodies (8A3 and 11F1). This statement is also irrelevant to the issue of written description because being a "different antibody" does not equate to being a non-representative antibody. Exhibit 15 is also irrelevant to the issue of written description because it does not compare the Rinat antibody to the antibodies disclosed in the patent. To the extent this document had any marginal relevance, its probative value was substantially outweighed by the likelihood of jury confusion due to these documents arising in research project at a subsequent state of the art.

Third, as to both the "missing epitope" and the "EGF-a mimic" that Defendants allege the excluded documents would show, the evidence is irrelevant to written description. As I stated at trial, merely saying the patentee didn't have "X" is irrelevant for written description because

[13] Ex. 5 (DTX3147, Ex. 15 (DTX3191), Ex. 16 (DTX3205).

"actual possession" is not required. Furthermore, written description is an objective inquiry into what a person of ordinary skill in the art would have understood at the time the patent application was filed. Defendants never established that a person of ordinary skill in the art in 2008 would have known or considered the EGF-a binding region or the missing epitope in determining whether the disclosed patents were representative of the Competitor Antibodies. Finally, even if there was error in excluding these documents, there was no prejudice to the Defendants. Defendants submitted significant expert testimony to the jury that the disclosed antibodies were not representative of the Competitor Antibodies because of the difference in the binding region and the "missing epitope."

Thus, I determine that the documents were properly excluded under FRE 402 and 403, and a new trial is thus unwarranted.

3. Representative Species Jury Instruction

Defendants assert that "a new trial should be granted because the Court failed to instruct the jury that the patent must describe antibodies representative of the infringing product." (D.I. 885 at 13). Defendants requested that I include the following statement in the jury instruction for written description:

> When a patent owner asserts that an antibody made by other companies like Defendants falls within the scope of its claimed genus of antibodies, the patent must at least describe some antibody or antibodies representative of antibodies that are structurally similar to the Defendants' antibody (and other third-party antibodies that fall within the scope of the claim) in order to meet the written description requirement.

(D.I. 791-1 at 12-13). Defendants also requested this jury instruction at the first trial. It was not given in the first trial. Defendants did not appeal the Court's decision not to give this instruction. Upon remand and reassignment of this case to me, I stated that the parties could "propose changes

to the . . . final jury instructions . . . from the first trial that reflect new developments in the law or the record at trial, and the reassignment of the case to [me]." (D.I. 458 at 12).

First, I note that Defendants' proposed inclusion of this language was not motivated by a new development in the law or the record at trial. The case Defendants rely on, *AbbVie*, was decided in 2014, well before the first trial. *AbbVie*, 759 F.3d 1285 (Fed. Cir. 2014) (decided on July 1, 2014; (D.I. 1 (filed Oct. 17, 2014)).

Second, I note that Defendants did not appeal the Court's decision not to include this language in the jury instructions. "An issue that falls within the scope of the judgment appealed from but is not raised by the appellant in its opening brief on appeal is necessarily waived." *Engel Indus., Inc. v. Lockformer Co.*, 166 F.3d 1379, 1383 (Fed. Cir. 1999). I determine that the jury instruction issue was thus waived by Defendants.

Third, even if the jury instruction issue were not waived, it was not error to not include this language. As I recognized, this language, while coming from *AbbVie*, was repetitive of the underlying principle stated in a more neutral fashion earlier on in the paragraph: "When there is a substantial variation within the claimed genus, the specifications must describe a sufficient variety of species to reflect the variation within the claimed genus." (D.I. 865 at 831:9-11; D.I. 812 at 14).

Thus, declining to include Defendants' specific language in the representative species jury instruction does not warrant the grant of a new trial.

4. Alleged Inherent Data / Improper Inherency Jury Instruction

Defendants argue that the admission of post-priority-date data was improper because the data was not included in the patents.

I disagree with Defendants. Data admission was proper to illuminate the state of the art at the priority date, show enablement, and to demonstrate inherent properties of antibodies that may be relevant to the representative species test. The Federal Circuit has held, "There is no requirement that an invention's properties and advantages were fully known before the patent application was filed . . . [n]or is it improper to conduct additional experiments and provide later-obtained data in support of patent validity." *Knoll Pharm Co. v. Teva Pharms. USA*, 367 F.3d 1381, 1385 (Fed. Cir. 2004). It is not contested that a person of ordinary skill in the art could have used the routine techniques of x-ray crystallography and alanine scanning at the time the patent application was filed to determine the binding properties of these antibodies. (D.I. 922 at 17-18; D.I. 982 at 9). Thus, the admission of post-priority-date data was proper.

Defendants also challenge the inclusion of a jury instruction regarding inherency. The jury instruction reads,

> Under the doctrine of inherent disclosure, when a specification describes an invention that has certain undisclosed yet inherent properties, those inherent properties may be relied upon for written description support. To be inherent, the feature that is alleged to have been inherent must necessarily have existed in the specification. The fact that the feature is likely to have existed is not sufficient. It is not required, however, that persons of ordinary skill recognize or appreciate the inherent disclosure at the time the January 9, 2008 application was filed.

(D.I. 812 at 13-14). Defendants cite *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998), for the proposition that the instruction was improper "because the allegedly 'inherent disclosure' was not 'necessarily . . . present' in all example provided in the specification." (D.I. 885 at 20). But *Tronzo* requires solely that "the missing descriptive matter must necessarily be present in the . . . specification such that one skilled in the art would recognize such a disclosure." 156 F.3d at 1159. Here, the structural data is necessarily present in the specification for antibodies that are disclosed by sequence; a person of ordinary skill in the art could make the antibodies and use

routine techniques to discover the data that Plaintiffs relied upon here. *See Ariad*, 598 F.3d at 1351 (enumerating a number of factors for evaluating adequacy of disclosure including existing knowledge in particular field). The facts here are analogous to those in *Kennecott Corp. v. Kyocera Intern., Inc.*, 835 F.2d 1419, 1423 (Fed. Cir. 1987), where "anyone with a microscope would see the microstructure of the product." Defendants attacks the applicability of *Kennecott* because in that case, every example produced a ceramic that had an equiaxed structure, whereas here, there were some examples that fell outside the claims. (D.I. 885 at 15-16). But *Kennecott* did not involve genus claims. 835 F.2d at 1420. Where the inquiry is whether the disclosed species are representative, the inherent disclosure need not be common to every species. Thus, *Kennecott* applies here. The instruction was not error.

IV. CONCLUSION

For the foregoing reasons, Defendants' Motion for Judgment as a Matter of Law is granted-in-part and denied-in-part. Defendants' Motion for a New Trial is conditionally denied. Plaintiffs' Motion for Permanent Injunction will be dismissed as moot. An accompanying order will be entered.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC., AMGEN MANUFACTURING, LIMITED, and AMGEN USA INC.,

Plaintiffs;

v.

SANOFI, SANOFI-AVENTIS U.S. LLC, AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., and REGENERON PHARMACEUTICALS, INC.,

Defendants.

Civil Action No. 14-1317-RGA

ORDER

For the reasons stated in the accompanying opinion, IT IS HEREBY ORDERED that Defendants' Motion for Judgment as a Matter of Law (D.I. 886) is GRANTED for lack of enablement and DENIED as to written description. Defendants' Motion for a New Trial (D.I. 883) is conditionally DENIED. Plaintiffs' Motion for Permanent Injunction (D.I. 871) is DISMISSED as moot.

Entered this 28 day of August, 2019.

Richard G. Andrews
United States District Judge

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC.; AMGEN MANUFACTURING, LIMITED; and AMGEN USA INC. Plaintiffs, v. SANOFI; SANOFI-AVENTIS U.S. LLC; AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., and REGENERON PHARMACEUTICALS, INC., Defendants.	C.A. No.: 14-1317-RGA (CONSOLIDATED) **JURY TRIAL DEMANDED**

~~[PROPOSED]~~ FINAL JUDGMENT

Pursuant to the Court's memorandum opinion (D.I. 1050) and order (D.I. 1051) entered on August 28, 2019, and all prior ~~[BY AMGEN: related or underlying]~~ rulings, orders, judgments and findings, IT IS ORDERED AND ADJUDGED that Judgment be and is hereby entered in favor of Defendants Sanofi, Sanofi-Aventis, U.S. LLC, Aventisub, LLC, and Regeneron Pharmaceuticals, Inc. and against Plaintiffs Amgen Inc., Amgen Manufacturing Limited, and Amgen USA, Inc.

SO ORDERED this 3 day of October, 2019

Richard G. Andrews
United States District Judge

01:23526794.1

CERTIFICATE OF SERVICE

I, Jeffrey A. Lamken, hereby certify that on February 21, 2020, I caused the foregoing Brief of Plaintiffs-Appellants Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc., to be filed using the court's CM/ECF system, which will send notification of such filing to all counsel of record.

/s/ Jeffrey A. Lamken
Jeffrey A. Lamken
MOLOLAMKEN LLP
The Watergate, Suite 500
600 New Hampshire Avenue, N.W.
Washington, D.C. 20037
(202) 556-2000 (telephone)
(202) 556-2001 (fax)
jlamken@mololamken.com

Counsel for Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc.

CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Fed. R. App. P. 32(a) because this brief contains 13,980 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f).

2. This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type-style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced typeface using Microsoft Word in Times New Roman 14-point font.

February 21, 2020

/s/ Jeffrey A. Lamken
Jeffrey A. Lamken

Counsel for Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc.