IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

IN RE: AFLIBERCEPT PATENT LITIGATION

MDL NO. 1:24-MD-3103-TSK

THIS DOCUMENT RELATES TO CASE NO. 1:23-CV-97

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

Pending before the Court is Plaintiff Regeneron's Motion for Preliminary Injunction [ECF No. 101]. The motion is fully briefed and ripe for decision. For the reasons set forth herein, the motions are **GRANTED.**

I. PRELIMINARY STATEMENT

Plaintiff Regeneron Pharmaceuticals, Inc. ("Regeneron") filed this patent infringement action. Therein, Defendant Formycon AG ("Formycon") disputes the infringement and validity of multiple patents owned by Regeneron. At issue in the preliminary injunction is one of those patents: U.S. Patent No. 11,084,865 (the "Product Patent"). The asserted patent claims are associated with Regeneron's product Eylea® and Formycon's filing of an abbreviated Biologics License Application ("aBLA") seeking to commercially manufacture, use, import, offer to sell, and/or sell "FYB203," a biosimilar version of Eylea.

II. FACTUAL BACKGROUND

A. Regeneron's Eylea Product

Regeneron invented and developed Eylea, which the U.S. Food and Drug Administration ("FDA") approved on November 18, 2011. The Court has previously addressed the pertinent background and development of Eylea. See Regeneron Pharm., Inc. v. Mylan Pharm. Inc., --- F. Supp. 3d ----, 2024 WL 382495, at *13-14 (N.D.W. Va. Jan. 31, 2024) ("Mylan") (discussing relevant background of Eylea). "Eylea is an ophthalmic drug product invented by Regeneron scientists that has been used to treat millions of patients suffering from diseases that can cause vision loss or even blindness." Id. at *13. The active ingredient in Eylea is the fusion protein now referred to as aflibercept. Aflibercept was initially developed as a cancer therapeutic and Regeneron later discovered that aflibercept could be used to treat angiogenic eye diseases — eye diseases caused by uncontrolled blood vessel growth in the retina — through intravitreal injections (injection into the vitreous of the eye). Id. at *13-14.

Only after more than a decade of development and multiple clinical trials did Regeneron discover an Eylea formulation that improved on the leading treatment for one angiogenic disease — wet Age-Related Macular Degeneration ("AMD"). Id. at *13 (quoting

Trial Tr. 172:16-24 (Yancopoulos)). The Eylea formulation contains 40 mg/ml aflibercept, 10 mM sodium phosphate, 40 mM sodium chloride, 0.03% polysorbate 20, and 5% sucrose, pH 6.2. Id. Following its initial FDA approval, Regeneron tested Eylea effectiveness in patients with other angiogenic eye disorders, ultimately obtaining approval for Eylea's use to treat those conditions as well. Id. Soon, Eylea "became the new gold standard of care" for treating such eye disorders. Mylan Trial Tr. at 172:19-20 (ECF No. 101-30, Sheridan Ex. 51).

Following the success of Regeneron's Eylea vial formulation, Regeneron developed and obtained approval in November 2011 for Eylea in a pre-filled syringe ("PFS"). See Sheridan Decl. ¶ 48 (ECF No. 101-24). Then in August 2023, Regeneron received approval to sell Eylea HD, an 8 mg formulation that requires less frequent injections and provides improved anatomical outcomes in the form of drier retinas. Id.; Clark Decl. ¶ 3 (ECF No. 101-37). Eylea HD is currently approved to treat wet AMD, Diabetic Macular Edema ("DME"), and Diabetic Retinopathy ("DR"). Clark Decl. ¶ 3.

B. Other Anti-VEGF Treatments

For the past five years, Eylea has maintained its place as the "category leader" in anti-VEGF treatments, [redacted]

[redacted] The second most popular anti-VEGF agent, Avastin (bevacizumab), [redacted] Clark Ex. 1 at 3-4. Avastin is an oncology drug for metastatic colorectal cancer (among other cancers), but ophthalmologists sometimes use it off-label (i.e., for diseases for which it does not have FDA approval) to treat angiogenic eye disorders. Sheridan Decl. ¶ 55. The third- and fourth-most popular anti-VEGF agents, Vabysmo (faricimab) and Lucentis (ranibizumab) are approved to treat angiogenic eye disorders. Id. ¶¶ 57-59. Genentech manufactures all three drugs. Id. ¶¶ 55, 57-59.

Eylea, Avastin, Vabysmo, and Lucentis make up more than 96% of anti-VEGF ophthalmic sales. Clark Decl. ¶ 6; Clark Ex. 1 at 3-4. Other products on the market such as Beovu are prescribed less frequently. Regeneron Pharms., Inc. v. Mylan Pharms. Inc., C.A. No. 1:22-cv-61, ECF No. 571 (Trial Tr.) at 861:6-862:4 (Albini). Overall, Eylea has maintained its category leadership due to its safety, efficacy, and dosing regimen advantage. Clark Decl. ¶ 7.

C. Aflibercept Biosimilars

At least [redacted] pharmaceutical companies are developing and seeking FDA approval for aflibercept biosimilars, each of which contains the same active ingredient as Eylea, also in a 2 mg vial

formulation and in some cases PFS formulation. Sheridan Decl. ¶ 49. Absent injunctive relief, Regeneron expects [redacted]

D. Formycon's aBLA and Proposed Biosimilar Product

Formycon is a German biopharmaceutical company headquartered in Planegg/Martinsried, Germany, and is the developer of a proposed biosimilar of Regeneron's Eylea® product. Plutat Decl. ¶¶ 1-2 (ECF No. 58-2). On June 28, 2023, Formycon filed aBLA No. 761378 ("Formycon's aBLA") with FDA seeking approval under the Biologics Price Competition and Innovation Act ("BPCIA"), 42 U.S.C. §§ 262(k)-(l), to market and distribute its biosimilar of Eylea, "FYB203," throughout the United States. See Formycon 356h Form (ECF No. 95-3); Trout Ex. F-3 (ECF No. 101-5). Formycon's aBLA [redacted]. See Formycon 356h Form.

Formycon's aBLA specifies that the FYB203 drug product is "an ophthalmic formulation suitable for intravitreal administration," Trout Decl. App. C ¶¶ 9-14 (ECF No. 101-4), [redacted]

[redacted] Id. ¶ 16 (internal quotations omitted); Trout Ex. F-3. Formycon's aBLA also specifies the composition of FYB203. Trout Decl. App. C ¶ 1; Trout Ex. F-3 at FYB203_00000026. Like Eylea, FYB203's active ingredient is aflibercept, at a concentration of 40mg/ml, and it comprises a buffer, a tonicity agent, a stabilizing agent, and an organic cosolvent. Trout Decl. App. C ¶¶ 2-3.

Formycon's aBLA also includes a proposed label to be packaged along with the marketed FYB203 product. See Trout Decl. App. C ¶¶ 12-13; Trout Ex. F-3. Like the Eylea label, Formycon's proposed label recommends that doctors use FYB203 to treat wet AMD, Macular Edema Following Retinal Vein Occlusion ("RVO"), DME, and DR. Trout Decl. App. C ¶¶ 12-13; Trout Ex. F-3.

In connection with Formycon's aBLA, [redacted] Plutat Decl. ¶¶ 7-10, 12. [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted] Plutat Decl. ¶¶ 9-10; Partner License Agreement (ECF No. 95-8). That Partner will market, sell, and distribute FYB203 in West Virginia. See Compl. ¶ 11 (ECF No. 1) ("Formycon and its respective . . . agents develop, manufacture, distribute, sell, and/or import drug products for the entire United States market . . . , including West Virginia, either directly or indirectly."); see also Plutat Tr. 20:9-13, 71:8-10 [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

Plutat Tr. 115:15-117:9

III. Procedural Background

Pursuant to 42 U.S.C. § 262(l)(8)(A), an applicant must provide notice to the reference product sponsor no later than 180 days before the date of the first commercial marketing of the applicant's product. On November 27, 2023, Formycon transmitted its Notice of Commercial Marketing ("NCM") to Regeneron, stating:

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted] Id. Subsequently, Regeneron filed this lawsuit against Formycon on November 29, 2023, asserting that Formycon's proposed FYB203 product would infringe at least 39 of its patents. ECF No. 1.

On December 28, 2023, Regeneron filed an emergency motion requesting either a schedule for preliminary injunction proceedings or an emergency status conference. ECF No. 33.

Following the Scheduling Conference in this matter on January 5, 2024, the Court issued an Order Setting the Briefing Schedule on Motions to Dismiss and Setting the Schedule for Preliminary Injunction Proceedings ("Scheduling Order"). ECF No. 45. The Court's Scheduling Order required Regeneron to identify no more than eight patents that may be included in a motion for preliminary injunction. Id. at 3. On January 11, 2024 and pursuant to the Scheduling Order, Regeneron provided Formycon a narrowed list of patents that may be included in a motion for preliminary injunction, see ECF No. 49, and on February 2, 2024, Regeneron

further narrowed that list of patents that may be included in a motion for preliminary injunction, see ECF No. 70.

On January 17, 2024, Formycon filed a motion to dismiss for lack of personal jurisdiction or alternatively to transfer venue. ECF No. 57. Regeneron filed its opposition to that motion on February 19, 2024, ECF No. 95, and Formycon filed a reply on February 26, 2024, ECF No. 105.

Pursuant to the Court's Scheduling Order, Regeneron filed a motion for preliminary injunction against Formycon on February 22, 2024 on the basis of four patents: the Product Patent, and U.S. Patent Nos. 11,104,715 ("'715 Patent"), 11,472,861 ("'861 Patent"), and 11,535,663 ("'663 Patent") (collectively, the "Manufacturing Patents"). ECF No. 101. Regeneron did so given that, pursuant to 42 U.S.C. § 262(k)(7)(A), approval of Formycon's aBLA may be made effective 180 days after the service of Formycon's NCM and as soon as Eylea's regulatory exclusivity expires on May 18, 2024. Id. Regeneron's motion asserted claims 4, 7, 9, 11, and 14-17 of the Product Patent (the "Asserted Product Patent Claims") and claims 6 and 12 of the '715 and '861 Patents and claims 3 and 6 of the '663 Patent ("Asserted Manufacturing Claims"). Id. Formycon filed its opposition to Regeneron's PI

motion on March 21, 2024, Opp. (ECF No. 155-2), and Regeneron filed a reply on April 18, 2024, Reply (ECF No. 206-2).

On May 13, 2024, the Court entered a stipulation under which Formycon agreed to maintain the marketplace status quo and not launch its FYB203 product before Regeneron's motion for preliminary injunction is resolved or June 28, 2024, whichever is earlier. ECF No. 226. On May 17, 2024, the Court held a scheduling conference. ECF No. 227.

To streamline the issues in dispute in the Preliminary Injunction motions, Regeneron moved to withdraw its Motions for Preliminary Injunction with respect to the Manufacturing Patents on May 21, 2024. ECF No. 232.

The Court has not held an evidentiary hearing on Regeneron's motion for injunctive relief, and one is not necessary here. The Court originally scheduled a hearing on Regeneron's motion for May 2, 2024. On April 23, 2024, the parties filed a joint motion requesting "a status conference to discuss the logistics of the injunction hearings scheduled for May 2, 2024, including the length of the time of the hearings, and the Court's preferences for the presentation of argument." Joint Mot. for Status Conf. (MDL No. 1:24-md-3103, ECF No. No. 9). The parties did not request or otherwise discuss the presentation of testimony or other evidence

during the May 2 hearing in their April 23 submission. Id. On April 24, 2024, the Court continued the May 2 hearing in view of the multi-district litigation consolidation of this and several related proceedings as well as the scheduling of a separate criminal trial. Order Continuing May 2, 2024 Preliminary and Permanent Injunction Hearings (MDL No. 1:24-md-3103, ECF No. No. 13). On May 17, the Court held a status conference in which all parties appeared, and no party objected to the cancellation of the preliminary injunction hearing, sought its reinstatement,[1] or otherwise objected to proceeding on the papers. To the extent any party now argues that a hearing was necessary, the Court finds that the parties waived request to a hearing. See Baxter Healthcare Corp. v. Med. Lab'y Automation, Inc., 1994 WL 695521, at *2 (N.D. Ill. Dec. 9, 1994) ("Baxter did not request an evidentiary hearing or suggest that an evidentiary hearing was needed or would be preferable. . . . A party that rests on affidavits and other written submissions waives an evidentiary hearing."); Sciele Pharma Inc. v. Lupin Ltd., 2012 WL 113004, at *3 (D. Del. Jan. 12, 2012). The Court thus resolves Regeneron's

[1] Even a cursory review of the docket in the MDL and individual member cases will quickly reveal the parties are no stranger to frequent and extensive motions practice. The lack of a motion to reschedule or convene an evidentiary hearing is telling here.

motion for a preliminary injunction based on the parties' written submissions and cited testimony. See Richmond Tenants Org., Inc. v. Kemp, 956 F.2d 1300, 1304 (4th Cir. 1992) (affirming preliminary injunction where "the district court issued a preliminary injunction prohibiting evictions without prior notice and a hearing and enjoining defendants").

IV. FACTUAL BACKGROUND

A. Expert Declarants

Regeneron filed declarations from two expert witnesses, Dr. Bernhardt Trout and Dr. Sean Sheridan, and two fact witnesses, Mr. Kevin Clark and Dr. Kenneth Graham, in support of Regeneron's preliminary injunction motion regarding the Product Patent. Formycon deposed three of Regeneron's witnesses but declined to take the deposition of Dr. Kenneth Graham, a fact witness. See Regeneron's Opp. to Samsung Bioepis's and Formycon's Mot. to Strike (ECF No. 215) at 5-6, 11, 21. Formycon presented declarations from three expert witnesses relevant to the Product Patent: Dr. Peter Tessier, Dr. Denis Boyle, Dr. Laird Forrest, and Mr. Arun Sharma. Regeneron deposed all of Formycon's witnesses.

1. Regeneron's Declarants

Dr. Bernhardt Trout, Ph.D., addressed the infringement and validity of the Product Patent. Dr. Trout also provided expert

testimony regarding infringement and validity of the Product Patent at the Mylan trial. Dr. Trout is a Professor of Chemical Engineering at the Massachusetts Institute of Technology and holds a Ph.D. in chemical engineering. Trout Decl. ¶¶ 16-17 (ECF No. 101-4). At MIT, Dr. Trout performs pharmaceutical development and manufacturing research on biopharmaceutical (e.g., protein-based) therapeutics and has worked on approximately fifty biologic therapeutics. Id. ¶¶ 19-20.

Dr. Sean Sheridan is a Vice President at Charles River Associates, an international business consulting firm, and has a Ph.D. in genetics as well as an MBA with concentrations in finance and economics from the University of Chicago. Sheridan Decl. ¶¶ 1-2. Dr. Sheridan's declaration addressed whether Regeneron would be irreparably harmed by market entry of Eylea biosimilars prior to expiry of the asserted patents. Dr. Sheridan's previous experience has included the quantification of economic damages, and he has experience in modeling and valuation in a variety of intellectual property matters. Id. ¶¶ 3-5.

Kevin Clark is Vice President of Regeneron's Ophthalmology Commercial Business Unit, a role he has held since 2020. Clark Decl. ¶ 1. Mr. Clark's focus at Regeneron has been on the commercialization of Eylea and Eylea HD. Id. ¶ 3. Mr. Clark's

declaration addressed the effect of biosimilar entry on Regeneron and its Eylea product.

Dr. Kenneth Graham, Ph.D., is a named inventor on the Product Patent. Dr. Graham has worked at Regeneron for over twenty-two years and is currently the Executive Director of Formulation Development at Regeneron. Graham Decl. ¶ 1. He joined Regeneron's Formulation Development group in 2005, when the group was engaged in aflibercept formulation stability studies. Id. ¶ 2. Dr. Graham's declaration addresses several internal stability studies Regeneron's scientists conducted on aflibercept.

2. Formycon's Declarants

Formycon filed an expert declaration from Peter M. Tessier, Ph.D. addressing the validity of the Product Patent. Dr. Tessier is a Professor in the Departments of Pharmaceutical Sciences and Chemical Engineering and Biomedical Engineering at the University of Michigan and holds a Ph.D. in chemical engineering. Tessier Decl. (ECF No. 157-1) ¶¶ 10-11. At the University of Michigan, Dr. Tessier performs research on the formulation of biologics, including research on formulations of protein-based biologics. Id. ¶ 10.

Formycon also filed an expert declaration from Denis M. Boyle, Ph.D., addressing whether Formycon's FYB203 product infringes the

Asserted Product Patent Claims. Dr. Boyle is the President and CEO of CMC BioPharma Consulting, LLC, a company that provides consulting services related to chemistry, manufacturing, and controls for biologics products. Boyle Decl. ¶ 7 (ECF No. 159-1). Dr. Boyle holds a Ph.D. in chemical pathology (medical biochemistry). Id. ¶ 8. Dr. Boyle's previous experience includes work in human biopharmaceuticals development and manufacturing of monoclonal antibodies. Id. ¶¶ 14, 18.

Formycon filed an additional expert declaration from Laird Forrest, Ph.D., addressing whether Formycon's FYB203 product infringes the Asserted Product Patent Claims. Dr. Forrest is a Professor in the Department of Pharmaceutical Chemistry, the Bioengineering Center, and the Department of Chemical and Petroleum Engineering at the University of Kansas, and holds a Ph.D. in chemical and biomolecular engineering. Forrest Decl. ¶¶ 3-4 (ECF No. 156).

Formycon also filed an expert declaration from Mr. Arun Sharma addressing whether Regeneron would be irreparably harmed by the launch of Formycon's biosimilar product. Mr. Sharma is a Partner at Bates White Economic Consulting, a professional services firm that conducts economic and statistical analyses. Sharma Decl. ¶ 1 (ECF No. 175-1).

B. Product Patent

The United States Patent and Trademark Office ("USPTO") issued U.S. Patent No. 11,084,865 (the "Product Patent"), titled "VEGF Antagonist Formulations Suitable for Intravitreal Administration," on August 10, 2021, to Regeneron Pharmaceuticals, Inc. upon assignment from inventors Eric Furfine, Daniel Dix, Kenneth Graham, and Kelly Frye. Product Patent, Cover Page (ECF No. 101-10, Trout Ex. 65). The Product Patent claims priority through continuation and divisional applications to Provisional Patent Application No. 60/814,484, filed June 16, 2006. Id.

This Court has previously addressed Regeneron's Eylea product and the Product Patent which Regeneron asserts in this preliminary injunction proceeding. In Regeneron v. Mylan, this Court previously held that the Product Patent was not invalid and that Mylan's Eylea biosimilar, "M710," infringed claims 4, 7, 9, 11, and 14-17 of the Product Patent. Mylan, 2024 WL 382495, at *25-33, 46-70. Since, the Court has also decided other of Regeneron's motions for preliminary injunction in related cases on nearly identical issues. See In re: Aflibercept Patent Litigation, 1:24-MD-3103, ECF No. 171 (addressing preliminary injunction motions in Regeneron v. Pharmaceuticals, Inc. v. Samsung Bioepis, Co., Ltd., 1:23-CV-94 and 1:23-CV-106).

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

The following table lists the claims Regeneron contends that Formycon infringes, as well as the claims from which they depend. Regeneron PI Br. at 5-8.

Claims of the Product Patent	
Claim 1 (*unasserted*)	1. A vial comprising an ophthalmic formulation suitable for intravitreal administration that comprises: a vascular endothelial growth factor (VEGF) antagonist, an organic co-solvent, a buffer, a stabilizing agent, wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4; and wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography.
Claim 2 (*unasserted*)	2. The vial of claim 1, wherein the concentration of said VEGF antagonist fusion protein is 40 mg/ml, and wherein said organic co-solvent comprises polysorbate.
Claim 4	4. The vial of claim 2, wherein said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20.
Claim 5 (*unasserted*)	5. The vial of claim 2, wherein said organic co-solvent comprises 0.01% to 3% polysorbate 20.
Claim 7	7. The vial of claim 5, wherein said buffer comprises 5-25 mM buffer.
Claim 9	9. The vial of claim 5, wherein said buffer comprises a pH about 6.2-6.3.
Claim 10 (*unasserted*)	10. The vial of claim 5, wherein said stabilizing agent comprises a sugar.
Claim 11	11. The vial of claim 10, wherein said sugar is selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol.

Claim 14	14. The vial of claim 5, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.
Claim 15	15. The vial of claim 5, wherein said formulation is capable of providing a turbidity of 0.01 or lower at OD405 after 2 month storage at 5° C.
Claim 16	16. The vial of claim 5, wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography.
Claim 17	17. The vial of claim 5, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.

The meaning and validity of a patent are evaluated from the perspective of a Person of Ordinary Skill in the Art ("POSA"). Neither party has advanced a definition of the POSA at this stage of litigation and the definition does not seem to be an issue of dispute at this time. As such, the Court adopts the definition of the POSA in this case that it adopted in Mylan:

> [T]he POSA 'would be a professional with a master's degree at least in a relevant field, so a technical field directly relevant to formulations here.' Tr. 2092:6-17 (Trout); PDX-9.002 (explaining that the POSA 'would have held an advanced degree, such as a Master's in a biopharmaceutical science, or a related discipline, such as chemical engineering, and several years of experience

> in the development of biologics products. Alternatively, the POSA could have a Ph.D. in such discipline and less experience. The POSA may collaborate with others, including a medical doctor with experience treating ophthalmic diseases.').

Mylan, 2024 WL 382495, at *22-23.

1. Prior Claim Constructions

This Court already construed two claim terms in the earlier Mylan litigation. In Mylan, "[t]he Court construed 'organic co-solvent' to mean 'an organic substance added to the primary solvent to increase the solubility of the solute, here a VEGF antagonist' . . . [and] construed 'native conformation' to mean 'the original intact form of the VEGF antagonist, which is a form that does not exhibit chemical or physical instability.'" Mylan, 2024 WL 382495, at *17 (quoting Mylan, C.A. No. 1:22-cv-61, ECF No. 427 at 20, 25-26). The parties have applied those constructions in these preliminary injunction proceedings, and the Court applies those constructions here as well.

2. Infringement

As detailed below, the Court finds that Formycon's FYB203 product meets each and every limitation of the Asserted Product Patent Claims; thus, Regeneron is likely to succeed on infringement of the Asserted Product Patent Claims.

Both sides submitted expert declarations on the topic of infringement of the Asserted Product Patent Claims. Regeneron submitted an expert declaration from Dr. Trout, who explained that Formycon's FYB203 product infringes all of the Asserted Product Patent Claims. Trout Decl. App. C. Formycon submitted an expert declaration from Dr. Forrest, who contended that the Asserted Product Patent Claims are not infringed because Formycon's FYB203 product does not contain a "buffer," Forrest Decl. ¶¶ 52-82, and Dr. Boyle, who contended that the Asserted Product Patent Claims are not infringed because the aflibercept in Formycon's FYB203 product is not present in at least 98% native conformation as measured by size exclusion chromatography ("SEC"), as construed by the Court, Boyle Decl. ¶¶ 54-99. As explained below, the Court credits the opinions of Dr. Trout over the opinions of Dr. Forrest and Dr. Boyle on issues involving infringement of the Asserted Product Patent Claims.

3. Validity

Formycon raises two grounds of invalidity with respect to the Product Patent: obviousness-type double patenting and written description. Opp. at 2-11. Both parties submitted expert declarations addressing validity. Dr. Trout submitted an expert declaration for Regeneron, and Dr. Tessier submitted an expert

declaration for Formycon. Again, this Court has already addressed similar challenges to the Product Patent in related cases. See In re:Aflibercept Patent Litigation, 1:24MD3103, ECF No. 171. For the same reasons, the Court rejects those challenges here.

4. Formycon May Launch FYB203 in Absence of an Injunction

[redacted] Regeneron has sought a preliminary injunction to prevent Formycon from producing, marketing, or selling their allegedly infringing product until after a decision after a trial on the merits.

5. FYB203's Launch Will Irreparably Harm Regeneron

As detailed below, the Court finds that Formycon's launch of FYB203 will irreparably harm Regeneron. Regeneron's expert, Dr. Sheridan, submitted a declaration setting forth the anticipated harms that Regeneron would face if a biosimilar such as FYB203 were to launch, including harm to market share, pricing, payor

relationships, reputation, and research and development funding. The Vice President of Regeneron's Ophthalmology Commercial Business, Mr. Clark, also submitted a declaration detailing these anticipated harms. As explained below, the Court credits the opinions of Dr. Sheridan and the testimony of Mr. Clark on issues involving irreparable harm.

Regeneron has demonstrated that it will suffer irreparable harm that a damages award could not fully remedy. A future damages award cannot compensate Regeneron adequately for the harm to its sales, price, relationships with payors, reputation, and research and development investments. These harms, while nearly certain to occur, are all but impossible to fully quantify. They are also generally impossible to reverse. The Court will analyze each type of harm in the discussion that follows.

V. ANALYSIS

A. Personal Jurisdiction

1. Regeneron's burden to establish a reasonable probability of success on the question of personal jurisdiction in the context of the Direct-File Defendants' jurisdictional challenges[2]

Generally speaking, a plaintiff need only make a prima facie showing of personal jurisdiction to survive a motion to dismiss for lack of personal jurisdiction pursuant to Federal Rule of Civil Procedure ("Rule") 12(b)(2). Combs v. Bakker, 886 F.2d 673, 676 (4th Cir. 1989); United Coals, Inc. v. Attijariwafa Bank, No. 1:19-cv-95, 2022 WL 4715695, at *3 (N.D.W. Va. Sept. 30, 2022) (Kleeh, C.J.). However, "a party cannot obtain injunctive relief against another without first obtaining in personam jurisdiction over that person." R.M.S. Titanic, Inc. v. Haver, 171 F.3d 943, 958 (4th Cir. 1999). Accordingly, when a challenge to jurisdiction is interposed upon an application for a preliminary injunction, the plaintiff must establish that there is "a reasonable probability of ultimate success upon the question of jurisdiction when the action is tried on the merits." Catalog Mktg. Servs., Ltd. v.

[2] "Direct-File Defendants" refers to those defendants against whom Regeneron filed suit in this Court – i.e., Samsung Bioepis Co., Ltd.; Celltrion, Inc.; and Formycon AG – and who have challenged the Court's exercise of personal jurisdiction by means of motions to dismiss for lack of personal jurisdiction.

Savitch, No. 88-3538, 1989 WL 42488, at *2 (4th Cir. Apr. 24, 1989) (quoting Visual Scis., Inc. v. Integrated Commc'ns, Inc., 660 F.2d 56, 58 (2d Cir. 1981)). "Reasonable probability" is something "less than a preponderance of the evidence." Buckner v. Polk, 453 F.3d 195, 203 (4th Cir. 2006).

2. Legal framework for determining whether the court may exercise personal jurisdiction over the Direct-File Defendants

Under Rule 4(k)(1)(A), a district court has personal jurisdiction over a defendant if the defendant "would be subject to the jurisdiction of a court of general jurisdiction in the state where the district court is located" — here, West Virginia. See Acorda Therapeutics Inc. v. Mylan Pharma. Inc., 817 F.3d 755, 759 (Fed. Cir. 2016) ("Acorda"). Because the West Virginia long-arm statute, W. Va. Code § 56-3-33, is coextensive with the full reach of due process, it is unnecessary to go through the traditional two-step process for determining the existence of personal jurisdiction. See Mey v. All Access Telecom, Inc., No. 5:19-cv-00237-JPB, 2021 WL 8892199, at *2 (N.D. W. Va. Apr. 23, 2021) (citing In re Celotex Corp., 124 F.3d 619, 627-28 (4th Cir. 1997)). Instead, the statutory inquiry merges with the Constitutional inquiry, and the district court must determine whether exercising

personal jurisdiction is consistent with the Due Process Clause. Id. at *2.

A court may exercise specific personal jurisdiction without violating the Due Process Clause where the defendant "ha[s] certain minimum contacts with [the forum] such that the maintenance of the suit does not offend traditional notions of fair play and substantial justice." Acorda, 817 F.3d at 759 (quoting Int'l Shoe Co. v. Washington, 326 U.S. 310, 316 (1945)). The Supreme Court has held that the minimum-contacts requirement is satisfied where the defendant "purposefully directed" activities at the forum "and the litigation results from alleged injuries that 'arise out of or relate to' those activities." Acorda, 817 F.3d at 759 (quoting Burger King v. Rudzewicz, 471 U.S. 462, 472-73 (1985)).

The Federal Circuit has held that "the minimum-contacts standard is satisfied" where a non-resident defendant files an abbreviated new drug application ("ANDA") "for the purpose of engaging in . . . allegedly wrongful marketing conduct in" the forum state. Id. at 760, 762-63; see also Valeant Pharms. N. Am. LLC v. Mylan Pharms. Inc., 978 F.3d 1374, 1384 (Fed. Cir. 2020) ("We held [in Acorda] that submission with an intent to distribute the generic product in a given state was sufficient for personal jurisdiction purposes."). The Federal Circuit further held that

the minimum-contacts requirement is satisfied even where the defendant "does not sell its drugs directly into" the forum state but rather contracts with a wholesaler or distributor to market the drugs in the state. Acorda, 817 F.3d at 763. The court reasoned that the defendant had "taken the costly, significant step" of applying to FDA for approval to market its generic drug in the forum state and elsewhere and that this intent to market was evidenced by distribution channels the defendant had established — i.e., a "network of independent wholesalers and distributors with which it [had] contract[ed] to market the drugs in" the forum state and elsewhere. Id. at 759-60, 763.

District courts have applied Acorda in the context of both Hatch-Waxman and BPCIA cases. See, e.g., AbbVie Inc. v. Alvotech Hf., No. 21-c-2258, 2021 WL 3737733, at *12-13 (N.D. Ill. Aug. 23, 2021) (denying defendant/aBLA-filer's motion to dismiss for lack of personal jurisdiction and rejecting defendant's argument that Acorda did not govern because defendant itself did not "sign" the aBLA); Apicore US LLC v. Beloteca, Inc., No. 2:19-CV-00077-JRG, 2019 WL 1746079, at *3-4 (E.D. Tex. Apr. 18, 2019) (denying motion to dismiss for lack of personal jurisdiction where defendant filed ANDA to market generic drug throughout the United States, even though defendant was "not licensed to do business in Texas, [did]

not have a registered agent in Texas, [did] not have a Texas Taxpayer Number, [was] not licensed as a distributor of prescription drugs sold in Texas," and had entered into an agreement with a Delaware company headquartered in Florida to market, sell, and distribute the generic drug throughout the United States, on the grounds that defendant's "ANDA filing and approval — in combination with its intent to market, distribute, and sell the [accused product] through [the distributor's] established distribution network, which includes Texas — constitute sufficient minimum contacts with Texas"); Helsinn Healthcare S.A. v. Hospira, Inc., No. 15-cv-2077, 2016 WL 1338601, at *6-7 (D.N.J. Apr. 5, 2016) (denying motion to dismiss for lack of personal jurisdiction where defendant filed an ANDA to market generic drug throughout the United States, stating that "[t]he facts in Acorda bear a strong similarity to this action," including the fact that defendant would utilize a distributor to market, sell, and distribute the generic in the United States).

3. Regeneron Has Established That It Has At Least a Reasonable Probability of Success on the Question of Jurisdiction When the Formycon Action Is Tried on the Merits

The relevant allegations of Regeneron's complaint; the Parties' motion papers, legal memoranda, and supporting affidavits; and the documents produced and deposition testimony

taken in connection with the limited jurisdictional discovery between the Parties demonstrate that Formycon has filed an aBLA with the intent to distribute FYB203 in West Virginia. Formycon, [redacted], has "taken the costly, significant step" of applying to the FDA for approval to market, sell, and distribute FYB203 in the United States, which of course includes West Virginia. See Acorda, 817 F.3d at 759. Formycon has served an NCM which explicitly communicates its intent to market FYB203 in the United States upon FDA approval of its aBLA. And Formycon has not disputed Regeneron's allegation that Formycon intends, either directly or indirectly (i.e., through a distributor), to market, sell, and distribute FYB203 in West Virginia. See Compl. ¶ 13. On the contrary, Formycon has admitted that its commercialization partner will "commercially market[], sell[], offer[] for sale, and distribut[e] FYB203 in the United States[.]" Plutat Decl. ¶ 9. These facts alone establish at least a reasonable probability of success on the question of jurisdiction under Acorda. See Acorda, 817 F.3d at 760, 762-63; see also Valeant Pharms. N. Am. LLC, 978 F.3d at 1384.

The record developed during the Parties' limited jurisdictional discovery only further evidences Formycon's intent to market, sell, and distribute FYB203 in West Virginia. As set

forth above, [redacted]. Plutat Decl. ¶¶ 7-10, 12. [redacted] See id. [redacted] See id. [redacted] See id.

Formycon asserts the Court may not exercise personal jurisdiction over it because [redacted] Formycon Mem. in Supp. of Mot. to Dismiss (ECF No. 58-3) ("MTD") at 1, 3. But the Federal Circuit in Acorda precluded such an argument when it held that minimum contacts exist where a non-resident defendant has "a network of independent wholesalers and

[3] Because these "factual allegations are not directly controverted, [they] are taken as true for purposes of determining jurisdiction." Nuance Commc'ns, Inc. v. Abbyy Software House, 626 F.3d 1222, 1231 (Fed. Cir. 2010).

distributors with which it contracts to market [its] drugs in" the forum state. Acorda, 817 F.3d at 763 ("Such directing of sales into [the forum state] is sufficient for minimum contacts."). Formycon attempts to distinguish Acorda by pointing out that, in that case, non-resident defendant Mylan Pharmaceuticals ("Mylan") had registered to do business in the forum state, appointed an agent for service of process in the forum state, and indicated in its certificate of registration that it intended to engage in manufacturing, distribution, and sales in the forum state. MTD at 7-9 (citing id.). These, however, were not the facts upon which the Federal Circuit relied in determining that the district court could exercise jurisdiction over Mylan. Valeant Pharms. N. Am. LLC, 978 F.3d at 1384; Millennium Pharms., Inc. v. Pharmascience Inc., No. 15-702-GMS, 2016 WL 3382131, at *3 (D. Del. June 10, 2016) ("The Acorda court noted that Mylan was incorporated in West Virginia, prepared its ANDA primarily in West Virginia, and filed its ANDA in Maryland. . . . The court also acknowledged that Mylan was registered to do business in Delaware . . . , however, the holding in the case was not based upon these facts."). Instead, the Acorda court focused on Mylan's ANDA submission and U.S. distribution channels — evidence of Mylan's intent to market its drug in the forum state. Acorda, 817 F.3d at 760, 762-63;

Valeant Pharms. N. Am. LLC, 978 F.3d at 1384; Millennium Pharms., Inc., 2016 WL 3382131, at *3. As discussed above, such evidence is present here.

The Court therefore concludes that Regeneron has established at least a reasonable probability of ultimate success on the question of personal jurisdiction when the Formycon action is tried on the merits and that it has authority to enter, at least, a preliminary injunction against Formycon here.

B. Preliminary Injunction

The Patent Act provides that in patent infringement cases, courts "may grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable." 35 U.S.C. § 283.

Indeed, patent owners have "a constitutional and statutory grant to exclude others from one's property. U.S. Const. art. I, § 8, cl. 8 ("by securing for limited times to . . . inventors the exclusive right to their respective . . . discoveries") (emphasis added); 35 U.S.C. § 154(a)(1) ("Every patent shall contain . . . a grant to the patentee . . . of the right to exclude others from making, using, offering for sale, or selling the invention . . . .") (emphasis added)." And "the axiomatic remedy for trespass on property rights is removal of the trespasser."

Presidio Components, Inc. v. Am. Tech. Ceramics Corp., 702 F.3d 1351, 1362 (Fed. Cir. 2012). A preliminary injunction thus "serve[s] to prevent ongoing trespasses during the pendency of an infringement case." See BlephEx, LLC v. Myco Indus., Inc., 24 F.4th 1391, 1404 (Fed. Cir. 2022).

Issuance of a preliminary injunction depends on four factors: whether (1) the plaintiff likely will succeed on the merits at trial; (2) the plaintiff will be irreparably injured if an injunction is not granted; (3) the balance of hardships favors the plaintiff; and (4) the public interest will be furthered by an injunction. See Winter v. NRDC, 555 U.S. 7, 20 (2008). Here, each factor favors entry of a preliminary injunction.

1. Patent Law Framework

a. Claim Construction

The Federal Circuit's leading authority on how to construe claims, Phillips v. AWH Corp., 415 F.3d 1303 (Fed. Cir. 2005) (en banc), explains that "the claims of a patent define the invention." Id. at 1312 (internal quotations and citation omitted). "[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms" and "the context in which a term is used in the asserted claim can be highly instructive." Id. at 1314. This is true for both the claim containing the disputed

term itself, as well as all other claims in the patent — whether asserted or unasserted. Id. Indeed, "an independent claim is broader than a claim that depends from it, so if a dependent claim reads on a particular embodiment of the claimed invention, the corresponding independent claim must cover that embodiment as well." Littelfuse, Inc. v. Mersen USA EP Corp., 29 F.4th 1376, 1380 (Fed. Cir. 2022); see Phillips, 415 F.3d at 1314 ("Differences among claims can also be a useful guide in understanding the meaning of particular claim terms."). Relatedly, "a dependent claim that adds a particular limitation gives rise to a presumption that the limitation . . . is not present in the independent claim." Phillips, 415 F.3d at 1314-15.

Together with the claim language, "the specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" Phillips, 415 F.3d at 1315 (citation omitted). The specification may define claim terms "expressly," or it may define them "by implication," i.e., "such that the meaning may be found in or ascertained by a reading of the patent." Id. at 1321 (internal quotation marks and citation omitted). But while the specification serves as a resource to understand the words used in the claims, courts must avoid the "cardinal sin[]"

of importing language from the specification into the claims. Id. at 1320. Indeed, even if every example described in the specification contains a particular element, such uniformity is not enough to justify importing that element into claims whose plain language does not expressly require it. See id. at 1323; Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 906-07 (Fed. Cir. 2004); AstraZeneca AB v. Mylan Pharm. Inc., No. 1:22-cv-35, 2022 WL 17178691, at *4-6 (N.D.W. Va. Nov. 23, 2022) ("Dependent claims . . . refer to at least one other claim, include all of the limitations of the claim to which they refer, and specify a further limitation on that claim.").

"[E]xtrinsic evidence in the form of expert testimony can be useful to a court for a variety of purposes, such as to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." Phillips, 415 F.3d at 1318. Conclusory, unsupported assertions as to the definition of a claim term are not useful to a court, however. Id. "Similarly, a court should discount any expert testimony that is clearly at odds with the claim construction

mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent." Id. (internal quotations omitted).

b. Infringement

Under 35 U.S.C. § 271(e)(2), the filing of an aBLA with the FDA "constitutes a technical" act of infringement. Sunovion Pharm., Inc. v. Teva Pharm. USA, Inc., 731 F.3d 1271, 1278 (Fed. Cir. 2013); Amgen Inc. v. Apotex Inc., 712 F. App'x 985, 991-992 (Fed. Cir. 2017) (applying Sunovion to aBLA filing). "[I]f a product that an . . . applicant is asking the FDA to approve . . . falls within the scope of an issued patent, a judgment of infringement must necessarily ensue." Sunovion Pharm., Inc., 731 F.3d at 1278.

Regeneron, as the "patentee seeking relief under § 271(e)(2)[,] bears the burden of proving infringement by a preponderance of the evidence" at trial. Eli Lilly & Co. v. Teva Parenteral Medicines, Inc., 845 F.3d 1357, 1364 (Fed. Cir. 2017).

c. Validity

1) Presumption of Validity

"A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other

claims." 35 U.S.C. § 282(a). This presumption of validity "exists at every stage of the litigation," Canon Comput. Sys., Inc. v. Nu-Kote Int'l, Inc., 134 F.3d 1085, 1088 (Fed. Cir. 1998), including the preliminary injunction stage. Titan Tire Corp. v. Case New Holland, Inc., 566 F.3d 1372, 1377 (Fed. Cir. 2009). Thus, if "the challenger fails to identify any persuasive evidence of invalidity, the very existence of the patent satisfies the patentee's burden on the validity issue." Canon Comput. Sys., 134 F.3d at 1088.

A patentee is never required to prove validity. See, e.g., Prometheus Labs., Inc. v. Roxane Labs., Inc., 805 F.3d 1092, 1101-02 (Fed. Cir. 2015) ("[A] patentee never must submit evidence to support . . . that a patent remains valid . . . ." (emphasis in original) (quoting Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1360 (Fed. Cir. 2007)); Ajinomoto Co. v. Archer-Daniels-Midland Co., 1996 WL 621830, at *5 (D. Del. Oct. 21, 1996) ("It is not necessary that the court hold a patent valid; it is only necessary that it hold that the patent challenger has failed to carry its burden.") (citing Jones v. Hardy, 727 F.2d 1524, 1529 n.3 (Fed. Cir. 1984)), aff'd, 228 F.3d 1338 (Fed. Cir. 2000).

Pursuant to the statutory presumption of 35 U.S.C. § 282(a), Defendants must prove invalidity at trial by clear and convincing

evidence. Microsoft Corp. v. i4i Ltd., 564 U.S. 91, 95 (2011). Under the clear and convincing standard, a party alleging invalidity must create "in the mind of the trier of fact 'an abiding conviction that the truth of [the] factual contention are highly probable.'" Buildex Inc. v. Kason Indus, Inc., 849 F.2d 1461, 1463 (Fed. Cir. 1988) (quoting Colorado v. New Mexico, 467 U.S. 310, 316 (1984)).

"[T]he evidentiary burdens at the preliminary injunction stage track the burdens at trial." Titan Tire, 566 F.3d at 1377; Gonzalez v. O Centro Espirita Beneficente Uniao do Vegetal, 546 U.S. 418, 429-430 (2006) (rejecting argument that plaintiff "should have borne the burden of disproving [affirmative defense] at the hearing on the preliminary injunction"). However, the patentee has the burden to "persuade the court that, despite the challenge presented to validity, the patentee nevertheless is likely to succeed at trial on the validity issue." Titan Tire, 566 F.3d at 1377. The Court "must determine whether it is more likely than not that [Defendants] will be able to prove at trial, by clear and convincing evidence, that the patent is invalid." Id. at 1379. In other words, after weighing the evidence for and against validity available at the preliminary injunction stage, the Court must determine whether Defendants have raised a

"'substantial question' concerning the validity of the patent." Id.

"Substantial weight may be given to a patent's litigation history in connection with a motion for relief pendente lite." H.H. Robertson, Co. v. United Steel Deck, Inc., 820 F.2d 384, 388 (Fed. Cir. 1987), abrogated on other grounds, Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed. Cir. 1995) (en banc); Leeds & Catlin Co. v. Victor Talking Mach. Co., 213 U.S. 301, 311 (1909) ("prior adjudications fortified the presumption of the validity of the patent in suit, and established its scope" and affirming preliminary injunction); see also, e.g., Fireball Gas Tank & Illuminating Co. v. Com. Acetylene Co., 198 F. 650, 653 (8th Cir. 1912) ("It is an incontrovertible rule of equity jurisprudence that where there has been a prior adjudication sustaining a patent . . . where the validity of the patent has been contested on full proofs, the Circuit Court should, upon a motion for a preliminary injunction, sustain the patent and leave the question of its validity to be determined upon the final hearing."), aff'd, 239 U.S. 156 (1915); Hybritech Inc. v. Abbott Labs., 849 F.2d 1446, 1452-53 (Fed. Cir. 1988) ("[T]he patent holder may use a prior adjudication of patent validity involving a different defendant as evidence supporting its burden of proving likelihood of success on

the merits."); Atlas Powder Co. v. Ireco Chem., 773 F.2d 1230, 1232 (Fed. Cir. 1985) (similar).

2) Obviousness-Type Double Patenting

Obviousness-type double patenting ("ODP") "is a judicially created doctrine" "that prevents the extension of the term of a patent . . . by prohibiting the issuance of the claims in a second patent not patentably distinct from the claims of the first patent." Otsuka Pharm. Co. v. Sandoz, Inc., 678 F.3d 1280, 1297 (Fed. Cir. 2012) (internal quotation omitted). There are two steps to the ODP analysis. "First, the court construes the claims in the earlier patent and the claims in the later patent and determines the differences. Second, the court determines whether those differences render the claims patentably distinct." AbbVie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Trust, 764 F.3d 1366, 1374 (Fed. Cir. 2014) (cleaned up). In order for a claim in the later patent to be invalid for ODP, it must either be anticipated by or obvious over the claims in the earlier patent. Id. ODP "turn[s] on a comparison between a patentee's earlier and later claims, with the earlier patent's written description considered only to the extent necessary to construe its claims." Eli Lilly & Co. v. Teva Parenteral Meds. Inc., 689 F.3d 1368, 1378-79 (Fed. Cir. 2012) (emphasis added). In other words, the

challenger cannot rely on the teachings of the reference patent's specification to show that a particular limitation was known in the art. Id.

For an earlier claim to anticipate a later claim, it must disclose "each and every limitation" of the later claim. See Ericsson, Inc. v. D-Link Sys., Inc., 773 F.3d 1201, 1224 (Fed. Cir. 2014). For an earlier claim to render a later claim obvious, "one of ordinary skill in the art would have had reason or motivation to modify the earlier claim[] to . . . the asserted claim with a reasonable expectation of success." Otsuka Pharm., 678 F.3d at 1298-99. Further, with regards to obviousness, the party asserting ODP bears the burden to prove that the POSA as of the patent's priority date would have been motivated to modify the "reference claims" of the earlier patent to obtain the asserted claims with a reasonable expectation of success. Otsuka, 678 F.3d at 1298-99; Eli Lilly, 689 F.3d at 1378.

As in the obviousness context, objective evidence of nonobviousness must be considered. Eli Lilly, 689 F.3d at 1381. Evidence of an invention's unexpected properties and that others have copied the invention (among other evidence) can serve as such objective indicia in support of non-obviousness. See, e.g., WBIP LLC v. Kohler Co., 829 F.3d 1317, 1332-37 (Fed. Cir. 2016); Mintz

v. Dietz & Watson, Inc., 679 F.3d 1372, 1379-80 (Fed. Cir. 2012). Likewise, "[e]vidence of industry skepticism weighs in favor of non-obviousness." WBIP, 829 F.3d at 1335 ("Doubt or disbelief by skilled artisans regarding the likely success of a combination or solution weighs against the notion that one would combine elements in references to achieve the claimed invention."). Objective indicia of nonobviousness also may consist of evidence that a prior art reference taught away from the claimed invention, i.e., that "person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." Millennium Pharms., Inc. v. Sandoz Inc., 862 F.3d 1356, 1366 (Fed. Cir. 2017) (quoting In re Urbanski, 809 F.3d 1237, 1244 (Fed. Cir. 2016)).

Such evidence can help to "guard against slipping into use of hindsight" and "the temptation to read into the prior art the teachings of the invention at issue." Apple Inc. v. Samsung Elecs. Co., 839 F.3d 1034, 1052 (Fed. Cir. 2016) (en banc) (quoting Graham v. John Deere Co., 383 U.S. 1, 36 (1966)); see also WBIP, 829 F.3d at 1328 ("[O]bjective indicia of non-obviousness play an important role as a guard against the statutorily proscribed hindsight reasoning in the obviousness analysis.").

3) Inherency

An earlier claim that does not expressly disclose every limitation of a later claim may still anticipate the later claim if the missing limitation is inherent in the earlier claim. See Allergan, Inc. v. Apotex Inc., 754 F.3d 952, 960 (Fed. Cir. 2014). An inherent limitation must be "necessarily present" in the prior art, id., and "may not be established by probabilities or possibilities," PAR Pharm., Inc. v. TWI Pharm., Inc., 773 F.3d 1186, 1195 (Fed. Cir. 2012) (internal quotation omitted); Cont'l Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269 (Fed. Cir. 1991). It is of no matter if the missing limitation often or usually would result from practice of the earlier claim — there is no inherent anticipation unless the missing limitation is present each and every time the earlier claim is practiced. See Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047 (Fed. Cir. 1995) (finding no inherent anticipation when the missing limitation was present in thirteen out of fifteen examples of the earlier claim being practiced).

In the obviousness context, the role of inherency is limited because inherent properties may not have been understood by the POSA and thus cannot support the POSA's motivation. As the Federal Circuit has explained, "the use of inherency in the context of

obviousness must be carefully circumscribed because '[t]hat which may be inherent is not necessarily known' and that which is unknown cannot be obvious." Honeywell Int'l Inc. v. Mexichem Amanco Holding, 865 F.3d 1348, 1354 (Fed. Cir. 2017) (quoting In re Rijckaert, 9 F.3d 1531, 1534 (Fed. Cir. 1993)).

4) Written Description

The written description requirement under 35 U.S.C. § 112 provides that a patent specification must "contain a written description of the invention, and of the manner and process of making and using it." 35 U.S.C. § 112 ¶ 1 (pre-AIA). This requirement is met when "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." Forest Labs., LLC v. Sigmapharm Labs., LLC, 918 F.3d 928, 937 (Fed. Cir. 2019) (quoting Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)).

The patent's specification is not required to have "'either examples or an actual reduction to practice'; rather, the critical inquiry is whether the patentee has provided a description that 'in a definite way identifies the claimed invention' in sufficient detail that a person of ordinary skill would understand that the inventor was in possession of it at the time of filing." Alcon

Rsch. Ltd. v. Barr Labs., Inc., 745 F.3d 1180, 1190-91 (Fed. Cir. 2014) (quoting Ariad, 598 F.3d at 1350).

"A patent satisfies the written description requirement if the specification 'allows [the POSA] to visualize or recognize the identity of the subject matter purportedly described'; the patent need not contain 'either examples or an actual reduction to practice.'" Mylan, 2024 WL 382495, at *63 (quoting Allergan, Inc. v. Sandoz, Inc., 796 F.3d 1293, 1308 (Fed. Cir. 2015)). "[T]he test for sufficiency [of written description] 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." Nalpropion Pharms. v. Actavis, 934 F.3d 1344, 1350 (Fed. Cir. 2019) (internal quotation omitted). There is no requirement, in the context of claim limitations that recite ranges, that the specification provide any examples at all, much less examples for all embodiments throughout the range. Id.; Alcon Rsch, 745 F.3d at 1190-91 (explaining that the specification is not required to have "either examples or an actual reduction to practice"). The specification need not describe "every conceivable and possible future embodiment of [the] invention" for the patent to satisfy the written description requirement. Cordis Corp. v. Medtronic AVE,

Inc., 339 F.3d 1352, 1365 (Fed. Cir. 2003). Further, "a patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed." Martek Biosciences Corps. v. Nutrinova, Inc., 579 F.3d 1363, 1371 (Fed. Cir. 2009).

B. Regeneron Is Likely to Succeed on the Merits of the Product Patent

1. Claim Construction

"Before deciding whether an accused device infringes asserted claims, a court must first construe the claim language to determine the meaning and scope of the claims." Rambus Inc. v. Infineon Techs. AG, 318 F.3d 1081, 1087 (Fed. Cir. 2003). As explained previously, the parties and the Court apply the construction of "native conformation" from Mylan, in which the Court "construed 'native conformation' to mean 'the original intact form of the VEGF antagonist, which is a form that does not exhibit chemical or physical instability.'" Mylan, 2024 WL 382495, at *17 (quoting Mylan, C.A. No. 1:22-cv-61, ECF No. 427 at 20, 25-26). Thus, the parties' principal claim construction dispute centers on the proper construction of the term "buffer" in claim 1. The Court addresses this term in "light of the claim language" and other pertinent evidence, "not in light of the accused device." Exigent Tech., Inc. v. Atrana Sols., Inc., 442 F.3d 1301, 1309

n.10 (Fed. Cir. 2006) (quoting SRI Int'l v. Matsushita Elec. Corp. of Am., 775 F.2d 1107, 1118 (Fed. Cir. 1985) (emphasis in original)).

Formycon proposes that the term be construed to refer "to a phosphate buffer, and not to any other type of buffer." Opp. 14-15. Regeneron proposes that the term be construed according to its ordinary meaning to the POSA: "a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, including, for example, histidine, phosphate, and proteins like aflibercept." See Trout Decl. ¶ 86.

The Court adopts Regeneron's construction of the term "buffer" because Regeneron's construction is consistent with the claim language, specification, and a POSA's understanding of the term. First, it is foundational claim construction law that "a dependent claim that adds a particular limitation gives rise to a presumption that the limitation . . . is not present in the independent claim." Phillips, 415 F.3d at 1315; see also Ortho-McNeil Pharm., Inc. v. Mylan Lab'ys., Inc., 520 F.3d 1358, 1362 (Fed. Cir. 2008) ("[T]his court strives to reach a claim construction that does not render claim language in dependent claims meaningless."). Here, independent claim 1 recites a

"buffer" and dependent claim 6 recites that "said buffer comprises a phosphate buffer." For this language in claim 6 to have any meaning, the term "buffer" in claim 1 must include more than just the phosphate buffer required by claim 6 — for example, buffers such as histidine or proteins like aflibercept that contain histidine residues. Regeneron's construction is the only construction that gives meaning to this dependent claim language. In contrast, Formycon's proposed construction would render claim 6 superfluous by reading its distinct limitation into claim 1. Moreover, dependent claim 18 recites that the "formulation does not contain phosphate," which is nonsensical under Formycon's construction of "buffer" in claim 1 (from which claim 18 depends) to require phosphate. When challenged in his deposition to explain these discrepancies under Formycon's construction, Formycon's expert, Dr. Forrest, was unable to reconcile the limitations of claims 6 and 18 with Formycon's construction of "buffer" in claim 1. Forrest Tr. 185:12-186:14, 191:3-15 (ECF No. 206-3, Patel Ex. 3).

Second, Regeneron's construction is also consistent with the specification, which does not limit a "buffer" to phosphate buffer, but rather states that "the buffering agent may be, for example, phosphate buffer." Product Patent, 2:45-46. The specification's

use of the phrase "for example" indicates that the specification necessarily contemplates buffers other than phosphate. Formycon's construction, in contrast, commits a "cardinal sin[] of patent law — reading a limitation from the written description into the claims." Phillips, 415 F.3d at 1320. Formycon argues that the term is limited to phosphate buffers because the only buffer expressly discussed in the specification of the Product Patent is a phosphate buffer. Opp. at 15. But to narrow a term's ordinary meaning, Formycon must establish that "the patentee disavow[ed] the full scope of a claim term," which requires "expressions of manifest exclusion or restriction." Thorner v. Sony Comput. Ent. Am. LLC, 669 F.3d 1362, 1365-66 (Fed. Cir. 2012). Formycon has failed to do so. Rather than disavow the full scope, the specification's open-ended statement that "the buffering agent may be, for example, phosphate buffer" (Product Patent, 2:45-46) embraces other buffers and plainly does not limit the "buffer" to a phosphate buffer. See Hill-Rom Servs., Inc. v. Stryker Corp., 755 F.3d 1367, 1371 (Fed. Cir. 2014) ("[W]e do not read limitations from the embodiments in the specification into the claims."). Formycon does not point to any statement in the Product Patent that restricts the meaning of "buffer" to a phosphate buffer. That the patent's examples use phosphate is not a disavowal of other

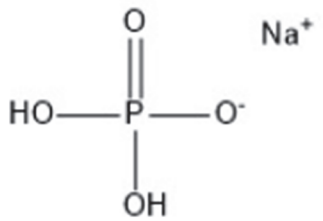
buffers, as it is "not enough that . . . all of the embodiments[] contain a particular limitation to limit a claim term beyond its ordinary meaning." Aventis Pharma S.A. v. Hospira, Inc., 675 F.3d 1324, 1330 (Fed. Cir. 2012) (internal quotation marks omitted); Phillips, 415 F.3d at 1310, 1326-27. Additionally, the Court notes that the aflibercept protein is also disclosed in the Product Patent (e.g., Product Patent, 6:35-36 ("the fusion protein comprises amino acids 27-457 of SEQ ID NO:4")), and as explained below, Dr. Trout explains that a POSA would have understood proteins like aflibercept to be buffers.

Finally, Regeneron's construction is consistent with how a POSA would understand the term. The Court credits Dr. Trout's opinion in this regard. Specifically, Dr. Trout explained that a POSA would have understood, within the context of the specification, that a buffer is used to resist changes to pH within a range of pH values. For example, as Dr. Trout explains, a given buffer might resist changes to pH within a range of 4.0-6.0 but not 7.0-9.0. Trout Decl. ¶ 81. According to the Oxford Dictionary of Biochemistry and Molecular Biology, "[a] substance is useful as a buffer over a range of about one pH unit either side of its pK, but is most effective at or near the pK." Id. ¶ 81; Oxford Dictionary of Biochemistry and Molecular Biology at 83 (ECF No.

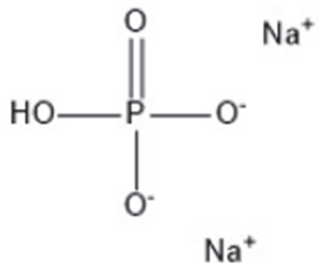
101-7, Trout Ex. F-18). Dr. Trout explains that the pK, or pKa, of a substance is called its acid dissociation constant and informs the pH at which the protonated and deprotonated forms of the substance are in equilibrium. Trout Decl. ¶ 81.

Dr. Trout further explained that several structures were known buffers as of 2006. First, as the specification of the Product Patent teaches, one example of a buffer is a "phosphate buffer." E.g., Product Patent, 2:46-48. The Product Patent teaches that "[u]nless stated otherwise, the phosphates employed are sodium phosphates and a desired buffering pH is achieved by mixing appropriate amounts of mono- and dibasic sodium phosphate." Product Patent, 6:55-58. Sodium phosphate was a known buffer as of 2006. See Handbook of Pharmaceutical Excipients ("HPE"), 4th ed. (2003) at 574 (ECF No. 101-15, Trout Ex. 115) ("Dibasic sodium phosphate is used in a wide variety of pharmaceutical formulations as a buffering agent and as a sequestering agent."); id. at 577 (same for monobasic sodium phosphate); Chang 2002 at 14 (ECF No. 101-8, Trout Ex. 11) (listing phosphate, acetate, histidine, and glutamate as buffers). Structurally, sodium phosphate can be protonated (meaning that it has accepted a proton) or deprotonated (meaning that it lost a proton) in solution. Trout Decl. ¶ 82.

This is evident from the well-known structures of sodium phosphate, depicted below:



sodium phosphate monobasic



sodium phosphate dibasic

Sodium phosphate resists changes to pH because it can be protonated at the negatively charged oxygen atoms. Id. The POSA would have understood that the relevant pKa of sodium phosphate (a mixture of sodium phosphate monobasic and sodium phosphate dibasic) is 7.2, resulting in a buffering pH range of approximately 6.2-8.2. See HPE at 575.

As Dr. Trout explains, a POSA would read the specification's statement that "the buffering agent may be, for example, phosphate buffer" as making explicit that phosphate is not the only buffer that may be used in practicing the claimed invention of intravitreal formulations of aflibercept, and that phosphate is only an example. Trout Decl. ¶¶ 82-86. Indeed, a POSA would have understood, in the context of the specification, that several molecules would be suitable for use as a buffer in the claimed

formulations. See Mylan Trial Tr. 2098:8-13 (ECF No. 101-13, Trout Ex. 97) (Dr. Trout explaining that succinate was a buffer); id. 1494:6-25 (Dr. MacMichael) (agreeing that succinate, citrate, phosphate, and histidine were buffers, and testifying that "other buffers out there . . . could have been considered").

Dr. Trout explained, without rebuttal, that histidine (like phosphate) has sites that can be protonated. Trout Decl. ¶ 84. Particular to histidine, the imidazole ring in the molecule's structure can accept protons. Id. And as Dr. Trout explained, that structure thus may act as a buffer either when histidine is present as a chemical added to a solution or when it is present as an amino acid making up a protein structure. Id. ¶¶ 84-86. Buffering by histidine through the imidazole ring was known to occur physiologically. As Dr. Trout explained, and the POSA understood, the imidazole groups of the histidine residues in proteins "are utilized as potent proton buffering constituents." Id. ¶ 84 (quoting H. Abe, Role of Histidine-Related Compounds as Intracellular Proton Buffering Constituents in Vertebrate Muscle, 65 Biochemistry (Moscow) 757 (2000) (ECF No. 101-7, Trout Ex. F-19). And more specifically, the prior art disclosed that "[t]he pKa of histidine in polypeptides ranges around 6.0." Trout Decl. ¶ 85; WO 2006/138181 ("Gokarn") at 38:21-22 (ECF No. 101-7, Trout

Ex. F-21). Thus, as Dr. Trout explains, the POSA would have understood in the context of the specification that both free histidine and certain proteins (polypeptides) containing histidine residues could act as buffers within a pH range of roughly 5-7.

Dr. Trout also relied on Gokarn, which is prior art and is directed to the relevant field here. Trout Decl. ¶¶ 84-85. Gokarn is entitled "Self-Buffering Protein Formulations" and describes "[h]ighly preferred proteins of the invention" to include "fusion proteins comprising an antibody or a moiety derived from an antibody or from an antibody fragment, which may be any of the foregoing or a modification or derivative thereof." Gokarn, at 1, 41:6-7, 41:14-18. As discussed previously, aflibercept undisputedly is a fusion protein. Mylan, 2024 WL 382495, at *13.

Because both the intrinsic and extrinsic evidence support Regeneron's construction, the Court adopts Regeneron's construction and finds that the term "buffer" is not limited to phosphate; rather, it means "a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, and thereby includes phosphate, histidine, and proteins like aflibercept." The POSA would not understand the claim term "buffer" to exclude those molecules and be limited to phosphate,

as Formycon urges, which would improperly read a limitation from the specification into the claims. The Court's construction is similarly consistent with its analysis in Mylan, 2024 WL 382495, at *18, *25, where Mylan also used a histidine buffer. And although Dr. Forrest disputed Dr. Trout's opinion that proteins like aflibercept could act as a buffer (Forrest Tr. 95:21-98:19) within the meaning of the Product Patent claims, the Court agrees with the persuasive analysis of Dr. Trout based on the disclosure of the specification and the prior art's teachings.

2. Regeneron Is Likely To Succeed on Infringement of the Product Patent

Regeneron is likely to succeed on infringement of the Product Patent. Formycon disputes infringement of only the "buffer" and the at least 98% and 99% native conformation by SEC limitations of the Product Patent, and offers declarations from Dr. Forrest and Dr. Boyle in support. Regeneron rebuts these points with evidence from Dr. Trout.

As explained below, the Court credits the declaration of Dr. Trout over the declarations of Dr. Forrest and Dr. Boyle for the disputed limitations and credits the unrebutted declaration of Dr. Trout for the undisputed limitations.

a. Undisputed Infringement Issues: FYB203 meets the limitations of the Asserted Product Patent Claims other than the limitations involving "a buffer" and the at least 98% and 99% native conformation by SEC limitations

Formycon, Dr. Forrest, and Dr. Boyle do not dispute that FYB203 meets every limitation of the Asserted Product Patent Claims other than the "buffer" and at least 98% and 99% native conformation by SEC limitations. Dr. Trout's declaration explaining that FYB203 meets all limitations of the Asserted Product Patent Claims is therefore unrebutted as to all limitations other than the "buffer" and at least 98% and 99% native conformation by SEC limitations.

Claim 1. Every Asserted Product Patent Claim ultimately depends from claim 1. The Court credits Dr. Trout's opinion that FYB203 meets each limitation of claim 1 of the Product Patent. As Dr. Trout explained, Formycon's aBLA states that "FYB203 drug product (DP) is a solution <u>for</u> <u>intravitreal</u> <u>(IVT)</u> <u>injection</u> in a vial," which meets the requirement of claim 1 of "[a] vial comprising an ophthalmic formulation suitable for intravitreal administration." Trout Decl. App. C. ¶¶ 9-14.

Dr. Trout also explained that the requirement of "a vascular endothelial growth factor (VEGF) antagonist . . . wherein said VEGF antagonist fusion protein is glycosylated and comprises amino

acids 27-457 of SEQ ID NO:4" refers to glycosylated aflibercept, which is described as "FYB203" in Formycon's aBLA. Id. ¶¶ 15-29. First, Dr. Trout explained that the aflibercept in FYB203 is a VEGF antagonist. Id. ¶¶ 15-16. Second, Dr. Trout explained that [redacted] Id. ¶¶ 17-24. Third, Dr. Trout explained that Formycon's aBLA contains explicit statements [redacted] Id. ¶¶ 25-28.

Dr. Trout explained that Formycon's FYB203 product meets the requirement of "an organic co-solvent" in claim 1. Id. ¶¶ 32-43. He explained that Formycon's aBLA submission states that the product contains polysorbate 20, which is an organic co-solvent under the Court's claim construction. Id. Specifically, Dr. Trout explained that Formycon's aBLA describes that polysorbate 20 in FYB203 is an organic substance that is "added to a primary solvent," which is water in Formycon's aBLA. Id. ¶¶ 34-35. In addition, Dr. Trout detailed that polysorbate 20 "increase[s] the solubility of said VEGF antagonist" by preventing the formation of insoluble aggregates. Id. ¶¶ 36-43. Dr. Trout explained that this conclusion is confirmed by Formycon's aBLA, which explicitly

states that "[p]olysorbate20 (PS20) acts as a solubilizing agent and prevents protein aggregation." Id. ¶ 42; FYB203_00000422, at -504 (ECF No. 101-5, Trout Ex. F-8).

Dr. Trout further explained that Formycon's FYB203 product meets the requirement of "a stabilizing agent" in claim 1. Trout Decl. App. C ¶ 48. He explained that Formycon's aBLA submission states that the product contains sucrose, which is a stabilizing agent. Id.

Formycon and its non-infringement experts, Dr. Forrest and Dr. Boyle, offered no argument or evidence that their accused FYB203 product does not meet the foregoing limitations of claim 1. The Court thus credits Regeneron's unrebutted evidence, including the declaration of Dr. Trout, that Formycon's FYB203 product meets each of the foregoing claim limitations.

Regarding the dependent claims, aside from the "buffer" and at least 98% native conformation by SEC limitations addressed below, Formycon did not dispute any limitations of any of the asserted dependent claims of the Product Patent. Regeneron, through its expert Dr. Trout, explained that Formycon's FYB203 product meets each of these claim limitations, as summarized below. The Court credits Dr. Trout's unrebutted opinions.

Claim 2. All of the Asserted Product Patent Claims also depend from claim 2. The Court credits Dr. Trout's opinion that Formycon's FYB203 product meets the requirement of claim 2 that "wherein the concentration of said VEGF antagonist fusion protein is 40 mg/mL." Id. ¶¶ 30-31. Dr. Trout explained that [redacted] which is confirmed by the labeled dose for FYB203, which is 2 mg of aflibercept in 0.05 mL. Id. ¶ 30.

Claims 2, 4, and 5. In addition to the "organic co-solvent" limitation of claim 1, the Court credits Dr. Trout's opinion that Formycon's FYB203 product meets the requirements of claims 2, 4, and 5: claim 2 specifies that "said organic co-solvent comprises polysorbate;" claim 4 specifies that "said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20;" and claim 5 specifies that "said organic co-solvent comprises 0.01% to 3% polysorbate 20." Id. ¶¶ 32-46, 69. Dr. Trout explained that Formycon's aBLA states that FYB203 contains 0.03% polysorbate 20, and thus FYB203 meets the requirements of claims 2, 4, and 5. Id. ¶¶ 44-46, 69.

Claims 10 and 11. Regarding claims 10 and 11, the Court credits Dr. Trout's opinion that Formycon's FYB203 product meets the limitations of these claims. Id. ¶¶ 75-76. He explained that

the sucrose stabilizing agent in FYB203 is a sugar, so FYB203 meets the requirement of claim 10 that "said stabilizing agent comprises a sugar." Id. ¶ 76. He further explained that the sucrose stabilizing agent in FYB203 is among the sugars expressly listed in claim 11, so FYB203 meets the requirement of claim 11 that "wherein said sugar is selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol." Id.

Claim 14. Regarding claim 14, the Court credits Dr. Trout's opinion that [redacted] Id. ¶¶ 77-78. Thus, FYB203 meets the requirement of claim 14 that "wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO:4."

Claim 15. Regarding claim 15, the Court credits Dr. Trout's opinion that Formycon's FYB203 product meets the additional limitation of this claim. Id. ¶¶ 79-92. Dr. Trout explained that [redacted] Id. ¶¶ 83-86. Dr. Trout explained [redacted] FYB203 meets the requirement of claim 15 that

"said formulation is capable of providing a turbidity of 0.01 or lower at OD405 after 2 month storage at 5° C." See id. ¶¶ 79-90. Further, Dr. Trout explained that [redacted], thus demonstrating infringement of this limitation. Id. ¶¶ 91-92.

b. Disputed Limitation: The histidine present in FYB203 is "a buffer."

Each Asserted Product Patent Claim requires "a buffer" — either expressly or by virtue of its dependency on another patent claim. Claim 1 recites "a buffer"; claim 7 recites "wherein said buffer comprises 5-25 mM buffer"; and claim 9 recites "wherein said buffer comprises a pH between about 5.8-7.0." Formycon disputes that FYB203 contains a "buffer." As described further above, the Court rejects Formycon's effort to read a limitation from the specification into the claims and construe "buffer" as limited to a phosphate buffer. The Court instead construes "buffer" in view of the intrinsic and extrinsic evidence to mean: "a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, and thereby includes phosphate, histidine, and proteins like

aflibercept." Under this construction, there is no dispute that FYB203 meets the "buffer" limitation because it includes 10 mM histidine. Opp. 14-16; Regeneron PI Br. 5-8; see Forrest Decl. ¶ 66; Trout Decl. App. C ¶ 1. There likewise is no dispute that Formycon's FYB203 product has a pH of 6.2. Trout Decl. App. C ¶ 1; see Trout Ex. F-8 at FYB203_00000503 [redacted]

The Court credits Dr. Trout's opinions, which Formycon does not dispute, that, under the Court's construction, at least the histidine buffer undisputedly present in Formycon's FYB203 product meets the "buffer" claim element. Trout Decl. ¶¶ 80-86; Trout Decl. App. C ¶ 47; see also Forrest Decl. ¶ 60, 63. Indeed, Formycon's aBLA explicitly describes histidine as a buffer. Trout Decl. App. C ¶ 47 [redacted] That histidine is a

buffer is also consistent with the Court's opinion in the Mylan case, where this Court found that the histidine in Mylan's M710 product infringed the same buffer limitation. Mylan, 2024 WL 382495, at *18, *25-26.

In sum, having considered the evidence regarding whether FYB203 contains "a buffer," the Court credits Dr. Trout's opinions over Dr. Forrest's opinions, and concludes that at least the histidine in Formycon's FYB203 product infringes the limitations of the Asserted Product Patent Claims requiring "buffer," "wherein said buffer comprises 5-25 mM buffer," and "wherein said buffer comprises a pH between about 5.8-7.0."

c. Disputed Limitations: The aflibercept in FYB203 satisfies the % native conformation by SEC limitations

Each Asserted Product Patent Claim requires the VEGF antagonist fusion protein be present in levels of at least 98% native conformation, as measured by SEC—either expressly or by virtue of its dependency on another patent claim. Claim 1 recites "wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography"; claim 16 recites "wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C, as measured by

size exclusion chromatography"; and claim 17 recites "wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C for 24 months as measured by size exclusion chromatography."

The parties dispute whether the aflibercept in the FYB203 product is present at levels of at least 98% or 99% native conformation as measured by SEC. This dispute centers on which analytical tests are required to measure the percentage of aflibercept present in native conformation as measured by SEC under the Court's construction of "native conformation." As mentioned above, the Court previously construed the term "native conformation" to mean "the original intact form of the VEGF antagonist, which is a form that does not exhibit chemical or physical instability." Mylan, 2024 WL 382495, at *17 (quoting Mylan, C.A. No. 1:22-cv-61, ECF No. 427 at 20, 25-26). Formycon contends that SEC is not the only analytical method required to determine the percentage of VEGF antagonist present in native conformation under the Court's construction, and that the claims require other analytical tests such as LC-MS and icIEF to determine whether the product meets the claimed percentage. Regeneron contends that measuring the percentage of aflibercept present in native conformation under the Court's construction requires

analysis by SEC. For the reasons explained below, the Court agrees with Regeneron.

This Court in Mylan construed the claim term "native conformation." Mylan, C.A. No. 1:22-cv-61, ECF No. 427 at 25 ("the claim language, 'native conformation' is construed"); id. (discussing "the term 'native conformation' itself"). The Court expressly declined to construe "other claim elements (e.g., . . . as measured by size exclusion chromatography)," which are "properly considered during the infringement and invalidity part of the case." Id. at 26. Thus, "as measured by size-exclusion chromatography" remains a requirement of the claims, and the Court's construction of "native conformation" did not eliminate the required "as measured by [SEC]" limitation from the claims of the Product Patent.

Formycon's interpretation of the Court's construction effectively omits the "as measured by [SEC]" claim term required by each Asserted Product Patent Claim. Digital-Vending Servs. Int'l, LLC v. Univ. of Phoenix, Inc., 672 F.3d 1270, 1275 (Fed. Cir. 2012) (underscoring "the importance of construing claim terms in light of the surrounding language" so "words in a claim are not rendered superfluous"). Indeed, [redacted]

[redacted] Boyle Tr. 140:17-144:15 (ECF No. 206-3, Patel Ex. 4). There is only one analytical test recited in the Asserted Product Patent Claims for measuring percent native conformation: size-exclusion chromatography. Formycon's attempt to read additional analytical test requirements into the claims is improper. Phillips, 415 F.3d at 1320.

Moreover, neither Dr. Trout nor Dr. Boyle dispute that SEC measures aggregation, which is a form of chemical and physical instability. Boyle Tr. 46:9-58:12. Consistent with the view that SEC alone can measure chemical and physical instability, this Court in the Mylan case found that the Product Patent's examples, which provide SEC data, meet the "native conformation" limitation as construed by the Court. Mylan, 2024 WL 382495, at *67-68.

Further, the Court finds Dr. Trout's testimony to be more credible than Dr. Boyle's. Dr. Trout's opinions were consistent with the Product Patent's claims, the Court's claim construction, [redacted]. By contrast, Dr. Boyle's opinions [redacted] he improperly based his analysis on two analytical tests that are neither recited in nor required by the Asserted Product Patent Claims. He insisted on reading the Court's

construction in a vacuum, and, as a result, his opinion directly conflicts with the Court's finding in Mylan that the patent's examples (which provide SEC data) meet the "native conformation" limitations. Boyle Tr. 84:17-85:3, 34:12-20, 38:19-39:1, 39:9-41:2, 72:13-19; Mylan, 2024 WL 382495, at *64. The Court observes that Formycon's position on infringement of this limitation is inconsistent with its position that the "stable" limitation of the '594 patent is patentably indistinct from the native conformation limitation in the Product Patent. Formycon attempts to have it both ways by having its experts apply opposing interpretations of the Court's claim construction depending on whether they are arguing non-infringement or invalidity, which is improper. TVIIM, LLC v. McAfee, Inc., 851 F.3d 1356, 1362 (Fed. Cir. 2017) ("Claim terms must be construed the same way for the purpose of determining invalidity and infringement."). For purposes of infringement, Dr. Boyle interprets the Court's construction to require two analytical tests that are not recited in the claim in concluding that FYB203 contains less than 98% native conformation, whereas for purposes of invalidity, Dr. Tessier assumes the limitation requires less — i.e., only SEC data—and that the Product Patent's and Regeneron's internal data tables reporting only SEC data suffice to meet 98% native conformation. Thus, consistent with

its findings in related cases, see In re: Aflibercept Patent Litigation, 1:24-MD-3103, ECF No. 171, the Court agrees with Regeneron that measuring the percentage of aflibercept present in native conformation under the Court's construction of the Asserted Product Patent Claims requires analysis by SEC.

The proper question for infringement is whether at least 98% (or, for purposes of asserted claim 16, 99%) of FYB203's aflibercept is present in "native conformation," as that term was construed by the Court, as measured by SEC. This Court credits the opinions of Dr. Trout and finds that at least 98% and 99% of the aflibercept in FYB203 is present in native conformation, as measured by SEC and at the claimed storage conditions. As Dr. Trout explained, [redacted]

[4] [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

In sum, having considered the evidence regarding whether at least 98% of the aflibercept in FYB203 "is present in native conformation," the Court credits Dr. Trout's opinion [redacted] demonstrate that Formycon's FYB203 product meets the requirements of the Asserted Product Patent Claims.

3. Regeneron Is Likely to Succeed on the Validity of the Product Patent

Formycon advances two invalidity defenses to the Product Patent: obviousness-type double patenting, and lack of written description. Opp. 2-11. For the following reasons, Formycon's arguments do not raise a "substantial question" of validity of the Product Patent, and Regeneron has established a likelihood of success on the merits regarding the Product Patent's validity. See Titan Tire, 566 F.3d at 1380. This conclusion is, again, consistent with the Court's prior holdings. See In re: Aflibercept

---

[redacted].

Patent Litigation, 1:24-MD-3103, ECF No. 171.

a. Obviousness-Type Double Patenting

Formycon argues that the Product Patent is invalid for nonstatutory obviousness-type double patenting over claim 5 of U.S. Patent No. 9,340,594 (the "'594 patent," (Dkt. 101-10, Trout Ex. 74). Regeneron responds that the'594 patent is not a proper reference patent for ODP against the Product Patent. And even if the '594 patent were an ODP reference patent, Regeneron contends that the asserted claims of the Product Patent are patentably distinct over claim 5 of the '594 patent ("'594 claim 5") for multiple reasons.

There is no dispute that the asserted claims of the Product Patent and '594 claim 5 differ in several respects. First, all asserted claims of the Product Patent require that the VEGF antagonist "is glycosylated," while '594 claim 5 is silent as to glycosylation. Second, the asserted claims of the Product Patent recite that "at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography," while '594 claim 5 does not recite such level of native conformation. Third, asserted claims 4, 7, 9, 11, and 14-17 of the Product Patent recite a "vial" while '594 claim 5 requires a "pre-filled syringe."

Regeneron argues that each of these differences independently constitutes a patentable distinction over '594 claim 5 that forecloses ODP. Regeneron further argues that objective evidence of nonobviousness further rebuts ODP.

The Court agrees with Regeneron that Formycon has not met its burden of showing a substantial question of ODP. As discussed further below, the Court concludes that the '594 patent is not a proper ODP reference patent to the Product Patent. Furthermore, the Court concludes that each of the differences between the asserted claims of the Product Patent and '594 claim 5 constitutes a patentable distinction that precludes ODP.

1) The '594 patent is not a proper ODP reference.

The '594 Patent is a Regeneron patent directed to "[o]phthalmic formulations of a vascular endothelial growth factor (VEGF)-specific fusion protein antagonist . . . suitable for intravitreal administration to the eye." '594 Patent at Abstract. The '594 Patent was filed on June 14, 2014 and granted on May 17, 2016. Like the Product Patent, the '594 Patent is a continuation of U.S. Pat. Appl. No. 11/818,463, which was filed on June 14, 2007. Both the '594 Patent and the Product Patent share the same specification, priority date, and statutory term.

During the '594 patent prosecution, the Examiner rejected the

claims on the ground of nonstatutory obviousness-type double patenting. July 14, 2014 Final Office Action, U.S. Pat. Appl. No. 14/330,096, at 6 (ECF No.157-6, Tessier Ex. 51). In the rejection letter, the PTO informed Regeneron that "[a] timely filed terminal disclaimer in compliance with 37 CPR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground." Id. at 5. Regeneron then filed a terminal disclaimer to another patent that expired in 2021 (via yet another terminal disclaimer) "[s]olely in the interest of promoting prosecution and reserving the right to pursue the subject matter in another application." Response to Final Office Action, Appl. No. 14/330,096 (Filed July 14, 2014) (ECF No.157-6, Tessier Ex. 51). The application that became the '594 patent was then granted.

As explained in detail below, because the Product Patent and the '594 Patent share the same parent patent and have the same statutory term, the '594 Patent cannot be an ODP reference for the Product Patent simply because the '594 patent expired after a terminal disclaimer.

"Nonstatutory double patenting is a judicially created doctrine grounded in public policy that prevents the extension of the term of a patent . . . ." Otsuka Pharm., 678 F.3d at 1297

(cleaned up). "Since the inception of our patent laws," it has been recognized that an individual cannot "obtain[] more than one patent on the same invention." AbbVie, 764 F.3d at 1372. As Justice Story explained in 1819, "if [a patentee] can successively take out at different times new patents for the same invention . . . it would completely destroy the whole consideration derived by the public for the grant of the patent, the right to use the invention at the expiration of the term specified in the original grant." Id. (citing Odiorne v. Amesbury Nail Factory, 18 F. Cas. 578, 579 (C.C.D.Mass.1819)). In other words, "[t]he ban on double patenting ensures that the public gets the benefit of the invention after the original period of monopoly expires." Id.

If there is no extension of the original monopoly period, i.e., the statutory term of the patent grant, there cannot be ODP. Because both the '594 patent and the Product Patent are continuations of application No. 11/818,463, filed on June 14, 2007, both patents share the same specification, priority date, and statutory term — i.e., "20 years" from the date "such application was filed," June 14, 2027. 35 U.S.C. § 154(a)(2). The original monopoly period of the entire patent family runs from June 14, 2007 to June 14, 2027. Therefore, the '594 patent cannot

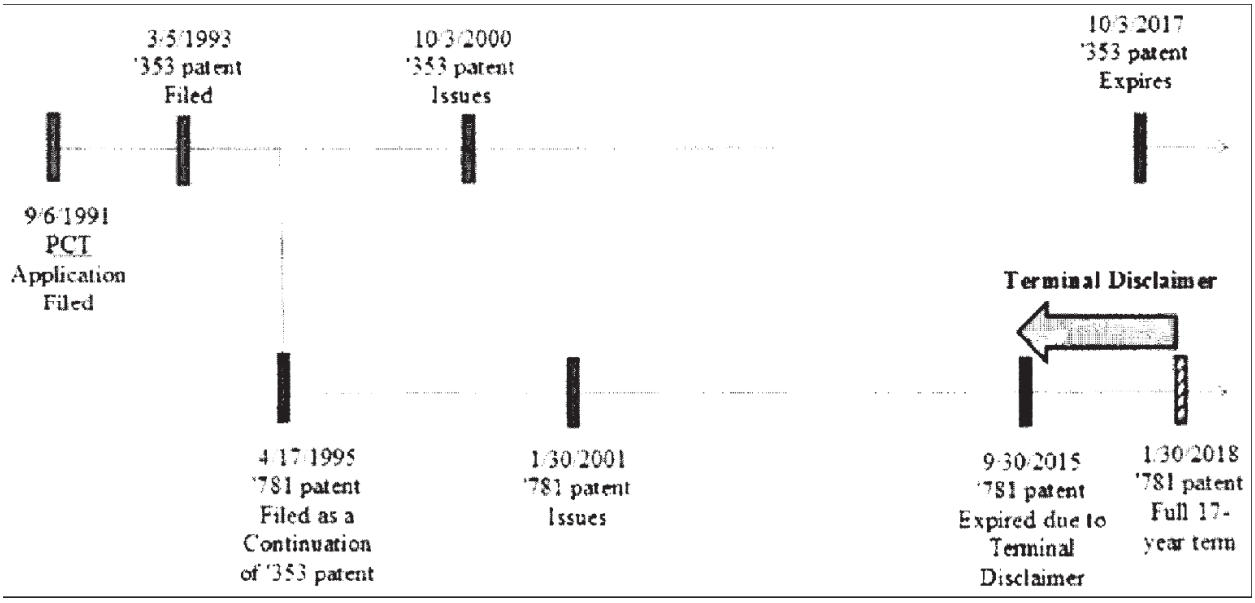
be an ODP reference for the Product Patent because the Product Patent does not and cannot extend the original monopoly period of any patent in its family.[5]

The fact that, during the '594 patent prosecution, Regeneron filed a "terminal disclaimer" to another patent that expired in 2021 does not change this conclusion. The '594 patent was rendered unenforceable before the end of its statutory 20-year term, and before the statutory term of the Product Patent, solely due to this terminal disclaimer. Regeneron filed the terminal disclaimer "[s]olely in the interest of promoting prosecution and reserving the right to pursue the subject matter in another application." Response to Final Office Action, Appl. No. 14/330,096 (Filed July 14, 2014). As the Federal Circuit has held, "the filing of a terminal disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither presumption nor estoppel on the merits of the rejection." Quad Env't. Techs. Corp. v. Union Sanitary Dist., 946 F.2d 870, 874 (Fed. Cir. 1991); see Motionless Keyboard Co. v. Microsoft Corp.,

[5] As noted in In re Cellect, LLC, the original monopoly period does not include any extension granted pursuant to Patent Term Adjustment under 35 U.S.C. § 154(b). 81 F.4th 1216 (Fed. Cir. 2023). No such extension is present in connection with the Product Patent, which expires after its statutory 20-year term on June 14, 2027.

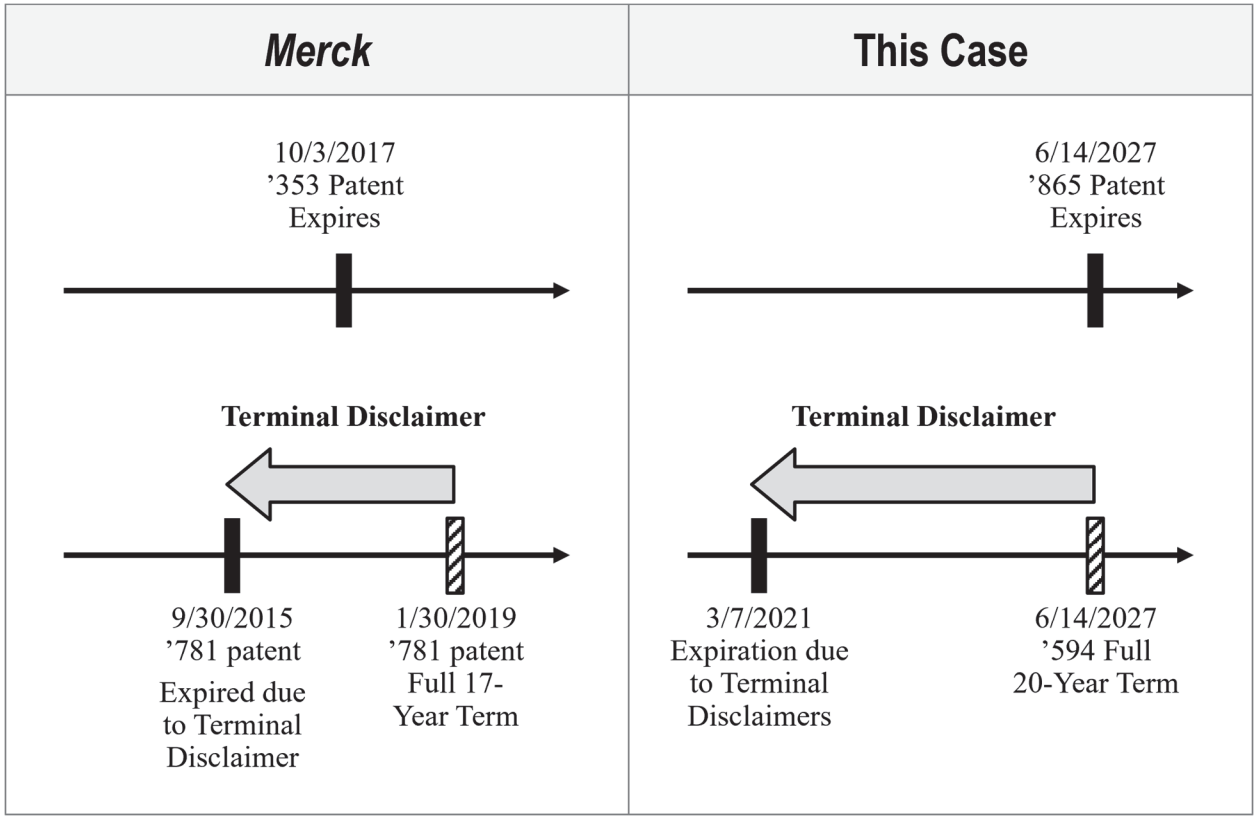
486 F.3d 1376, 1385 (Fed. Cir. 2007) ("A terminal disclaimer simply is not an admission that a later-filed invention is obvious."); Ortho Pharm. Corp. v. Smith, 959 F.2d 936, 941 (Fed. Cir. 1992) (rejecting argument that patent applicant admitted to obviousness-type double patenting by filing terminal disclaimer). Instead, a terminal disclaimer is a voluntary filing by a patentee that "dedicate[s] to the public" part of the patent's term. 35 U.S.C. § 253(b).

Formycon has cited no authority for the proposition that the filing of a terminal disclaimer in one patent can invalidate a related patent for ODP. In contrast, the only case cited by the parties that addressed whether one patent's terminal disclaimer can invalidate a related patent for ODP held that it could not. See Merck Sharp & Dohme Corp. v. Teva Pharms. USA, Inc., 217 F. Supp. 3d 782, 787-88 (D. Del. 2016). Specifically, in Merck the defendant alleged that a terminal disclaimer caused a patent to expire earlier than the asserted patent and thus rendered it invalid for ODP. Id. at 787. The court's illustration of the various expiration dates in Merck is shown below:



Id. As the depiction shows, the alleged '781 reference patent expired before the asserted ('353) patent solely due to a terminal disclaimer. And Merck held that the '781 patent "from the same family" could not serve as an ODP reference patent: "[u]nder the particular circumstances, the oddity of using the '781 patent as a reference patent to cut short the '353 patent's (the first issued parent patent) term of exclusivity is rejected. This is not an instance of a patentee seeking to extend the patent term with 'sequential' applications." Id. The Court agrees with the analysis in Merck; just as in that case, Regeneron does not seek any "extension of the term of a patent" contrary to the equitable principles underlying ODP. Otsuka Pharm., 678 F.3d at 1297. It seeks only the 20-year statutory term afforded under the statute.

35 U.S.C. § 154(a)(2). As illustrated below, the facts here are not meaningfully distinguishable from Merck:



The Court has considered In re Yamazaki, where the Federal Circuit held that "[w]hen a patent issues subject to a terminal disclaimer, the patentee . . . reduced the [patent] term itself by effectively eliminating the disclaimed portion from the original patent." In re Yamazaki, 702 F.3d 1327, 1333 (Fed. Cir. 2012). Yamazaki, however, did not address the ODP doctrine, and no court has extended it to that context to hold that the filing of a terminal disclaimer in one patent can invalidate a related patent

for ODP. In contrast, the mere fact that two patents have different expiry dates does not automatically give rise to ODP. For example, in Hoffmann-La Roche Inc. v. Orchid Chems. & Pharms. Ltd., 2011 WL 4433575, at *3 (D.N.J. Mar. 17, 2011), the court held there was no ODP where an alleged reference patent expired before its statutory term due to nonpayment of maintenance fees, "since it does nothing to effectuate the prohibition against double patenting." Id.; see also Novartis AG v. Ezra Ventures LLC, 909 F.3d 1367, 1374-75 (Fed. Cir. 2018) (rejecting ODP challenge even though related patents expired on different dates as a result of patent term extension under 35 U.S.C. § 156). Here too, the Court finds that "it does nothing to effectuate the prohibition against double patenting" to essentially propagate a terminal disclaimer from one patent in the family to another. Roche, 2011 WL 4433575, at *3. Indeed, the Federal Circuit has rejected ODP challenges premised on extending terminal disclaimers throughout a family. See Ortho Pharm Corp., 959 F.2d at 941.

The Court has also considered Federal Circuit precedent explicitly speaking to the issue of when a patent can serve as an ODP reference and have found them to be distinguishable. In Gilead Sciences, Inc. v. Natco Pharma Ltd., "[d]espite the[] similarities in content" between two patents (the '375 patent and '483 patent),

the patentee filed the '375 patent and then "crafted a separate 'chain' of applications having a later priority date than the '375 patent family" that "resulted in the issuance of the '483 patent." 753 F.3d 1208, 1210 (Fed. Cir. 2014). Thus, the asserted patent and the reference patent had different statutory terms. The specific question at issue in Gilead was "whether a later-issued patent can serve as a double patenting reference for an earlier-issued patent if the later one expires first." Id. at 1214. The Federal Circuit held that it could. Id. at 1217. But that is irrelevant to the question of the effect of terminal disclaimer on the ODP analysis here; regardless of the respective issuance dates of the Product Patent and the '594 patents, the patents undisputedly share the same priority date and 20-year term, but for the '594 patent's terminal disclaimers.

Gilead is further distinguishable from this case because, as the Federal Circuit later explained in Novartis, the Gilead decision was driven by the court's concern about the potential "gamesmanship issue" that could arise if ODP were based solely on a patent's issue date. Novartis, 909 F.3d at 1374. Gilead prevented "a situation where 'inventors could routinely orchestrate' longer patent-exclusivity periods by (1) filing serial patent applications on obvious modifications of an

invention, (2) claiming different priority dates in each, and then (3) strategically responding to prosecution deadlines such that the application claiming the latest filing date issues first, without triggering a terminal disclaimer for the earlier filed applications." Id. at 1375 (quoting Gilead, F.3d at 1215). This potential for gamesmanship is not at issue in a case, like the one here, where the two patents claim the same priority date and thus share the same 20-year term. Merck similarly found Gilead to be inapplicable when the putative reference patent only expired before the asserted patent because of a terminal disclaimer because it "is not an instance of a patentee seeking to extend the patent term with 'sequential' applications." Merck, 217 F. Supp. 3d at 787-88.

Similar gamesmanship was at play in AbbVie, 764 F.3d 1366. There, the patentee "claimed a priority date of October 8, 1992 (the filing date of an earlier application), for the '766 patent" and "claimed a later priority date [for the '442 patent], August 1, 1996 (the filing date of the application that issued as the '766 patent), so that the '442 patent would expire after the '766 patent." Id. at 1373 n.2. The Court held that the patentee "is not entitled to an extra six years of monopoly solely because it filed a separate application unless the two inventions are

patentably distinct." Id. at 1374. As in Gilead, AbbVie did not and could not address the effect of terminal disclaimer of the putative reference patent on the ODP analysis. Unlike the patentees in Gilead and AbbVie, Regeneron did not attempt to circumvent the expiration of the '594 patent by creating a different priority chain for the Product Patent to extend its term.

As discussed above, In re Cellect stands for the proposition that "for a patent that has received PTA, regardless whether or not a terminal disclaimer is required or has been filed, [ODP] must be based on the expiration date of the patent after [Patent Term Adjustment ("PTA")][6] has been added." 81 F.4th 1216, 1229 (Fed. Cir. 2023) (footnote added). In other words, a patent that expired after an asserted patent's original expiration date but before the asserted patent's expiration date with PTA could serve as a proper ODP reference. But here, the Product Patent was not extended by PTA or otherwise; Regeneron seeks only the Product Patent's ordinary 20-year statutory term, and so Cellect does not apply here.

Finally, the additional authority Formycon cited does not

[6] PTA grants a patent term extension beyond the normal 20-year statutory term if the issuance of a patent is delayed due to bureaucratic delays of the USPTO. In re Cellect, 81 F.4th at 1223.

compel a different conclusion. In Eli Lilly & Co. v. Barr Labs., Inc., the reference patent was unrelated to and expired earlier than the asserted patent. 251 F.3d 955, 959 (Fed. Cir. 2001). The patentee attempted to circumvent this typical ODP scenario by disclaiming the reference patent during the course of the litigation. Id. The Court explained that "[a] patent owner cannot avoid double patenting by disclaiming the earlier patent" and that "double patenting precludes [the asserted patent] from extending beyond the termination date of the [reference patent], whether that termination date is at the end of its normal term or, as in this case, is the date it is terminated via disclaimer." Id. at 967 n.5. Thus, in Barr the Court held that a statutory disclaimer of a proper reference patent could not be used to "avoid" ODP, id., but here the question is whether a terminal disclaimer in the '594 patent (filed years before this lawsuit) creates ODP between related patents that otherwise share the same statutory term. Barr (unlike Merck, discussed above) did not address that question and thus fails to support Formycon's ODP theory.

The terminal disclaimer of the '594 patent does not change the fact that both patents have the same priority date, and the Product Patent's term never has been extended. Accordingly, the '594 patent cannot be an ODP reference for the Product Patent.

Therefore, because Formycon's ODP theory of invalidity relies on an improper ODP reference patent, Regeneron has established a likelihood that it will succeed on Formycon's ODP defense.

2) The Product Patent claims are patentably distinct from Formycon's asserted reference claim.

The Court further concludes that even if the '594 patent were a proper reference patent, Formycon has not raised a substantial question that the Product Patent is invalid for ODP.

Unlike Formycon's asserted ODP reference claim, '594 claim 5, the asserted claims of the Product Patent recite a "glycosylated" protein and 98% native conformation. As explained in more detail below, because '594 claim 5 does not disclose each and every limitation in the asserted claims, either expressly or inherently, '594 claim 5 does not anticipate the asserted claims. With regards to obviousness, this Court finds that (1) the POSA lacked motivation to use glycosylated aflibercept, a requirement of the Product Patent but not '594 claim 5;[7] (2) the Product Patent's "98% native conformation" claim limitation is not inherent in claim 5 of the '594 patent; (3) the POSA lacked motivation to change '594 claim 5's PFS to the Product Patent's vial; and (4) objective

[7] This finding is consistent with this Court's identical finding in Mylan. 2024 WL 382495, at *55.

evidence strongly supports nonobviousness of the Product Patent's asserted claims.[8] The only ODP reference claim asserted by Formycon is '594 claim 5, and as explained below, Formycon has not met its burden to show a substantial question that the Product Patent's asserted claims are anticipated or obvious over '594 claim 5; accordingly, the Court holds that Regeneron is likely to succeed on ODP.

a) Claim Construction

The first step in the ODP analysis requires construing the disputed terms of the relevant claims. AbbVie, 764 F.3d at 1374. Formycon's ODP reference claim, claim 5 of the '594 patent, is set forth below along with the pertinent claims from which claim 5 depends:

> 3. The pre-filled syringe according to claim 2, wherein the VEGF trap is stable for at least 4 months.
>
> 4. The pre-filled syringe according to claim 3, wherein the VEGF trap consists of amino acids 27-457 of SEQ ID NO:4.
>
> 5. The pre-filled syringe according to claim 4, wherein the stable ophthalmic formulation comprises 40 mg/mL of the VEGF trap, 10 mM phosphate, 40 mM NaCI, 0.03% polysorbate 20, 5% sucrose, at pH 6.2-6.4.

[8] This finding is also consistent with the Court's Mylan decision. Mylan, 2024 WL 382495, at *59.

The parties dispute the construction of two terms: "stable" and "VEGF trap consists of amino acids 27-457 of SEQ ID NO:4."

(i) "Stable"

Formycon argues that "stable" should be construed to require the VEGF trap protein to be in at least 98% native conformation as measured by SEC after 2-month storage at 5 degrees C, the requirement recited in the asserted claims of the Product Patent. Opp. 7. Regeneron argues that "stable" does not have the limited meaning that Formycon urges and that the term carries its plain and ordinary meaning in view of the specification of the '594 patent. Reply 8. For the following reasons, the Court agrees with Regeneron.

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [which] is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (cleaned up). The POSA "is deemed to read the claim term . . . in the context of the entire patent, including the specification." Id. at 1313.

The specification of the '594 patent makes clear that a POSA would not understand "stable" as limited to "98% native conformation as measured by SEC." The specification of the '594

patent has numerous descriptions of stability beyond simply 98% native conformation as measured by SEC. First, the '594 patent specification teaches that "at least 90%" non-aggregated protein is preferred, thereby confirming that levels of non-aggregation below 98% in the patent's formulations are not only permissible, but desirable. '594 patent 6:15-25. Second, the patent describes multiple aspects of stability, including aggregation, deamination, and precipitation. Id., 5:27-34 ("Proteins possess unique chemical and physical properties that present stability problems: a variety of degradation pathways exist for proteins, implicating both chemical and physical instability. Chemical instability includes deamination, aggregation, clipping of the peptide backbone, and oxidation of methionine residues. Physical instability encompasses many phenomena, including, for example, aggregation and/or precipitation."). Third, the patent describes multiple ways to determine stability, including visual inspection of color and appearance, SDS-PAGE, isoelectric focusing, and SEC. Id., 6:42-48 ("Stability is determined in a number of ways at specified time points, including determination of pH, visual inspection of color and appearance, determination of total protein content by methods known in the art, e.g., UV spectroscopy, and purity is determined by, for example, SDS-PAGE, size-exclusion

HPLC, bioassay determination of activity, isoelectric focusing, and isoaspartate quantification."). These disclosures confirm that "stable" has a broader meaning than the particular SEC measurements of aggregation to which Formycon attempts to limit the term.

Experts from both sides agree that the term "stable" in claim 5 of the '594 patent is not limited to 98% native conformation as measured by SEC. As Regeneron's expert, Dr. Trout, explained in his declaration, a POSA would not understand the meaning of "stable" as being limited to percent native conformation as measured by SEC. Trout Decl. ¶ 385. He further explained that if stability is measured by percent native conformation by SEC, then the POSA would understand that the fusion protein can be stable despite having less than 98% native conformation by SEC. Trout Decl. ¶¶ 386-387. Dr. Trout explained that both the specification and the ordinary meaning of the term to practitioners in the field supported this broader understanding of "stable" as encompassing less than 98% and types of stability other than those measured by SEC. Trout Decl. ¶¶ 385-87. Formycon's expert, Dr. Tessier, agreed. In his declaration, he did not dispute Dr. Trout's evidence or conclusions that the ordinary understanding of "stable" to the POSA includes percentages below 98%. Tessier Decl. ¶¶ 154-55, 160. Dr. Tessier testified at his deposition that "It's

my understanding that the term stable in claim 5 would include the stability, for example, in example 4, but it's not necessarily limited to it." Tessier Tr. 15:1-9 (ECF No. 206-3, Patel Ex. 6) (emphasis added). The undisputed ordinary meaning of "stable" as including stability below 98% controls. Thorner v. Sony Comput. Entmt. Am. LLC, 669 F.3d 1362, 1365 (Fed. Cir. 2012) ("The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history," unless either of the "only two exceptions" apply, lexicography or disavowal).

The Court's conclusion is bolstered by the fact that another patent in the same family as the Product Patent and the '594 patent claims a "stable ophthalmic formulation" "wherein 90% or more of the weight of the fusion protein is not present as an aggregate" — thus indicating that the meaning of "stable" does not implicitly require 98% native conformation by SEC. Specifically, claims 1 and 2 of U.S. Patent 9,914,763 (the "'763 patent"), which shares the same specification as the '594 patent, read as follows:

> 1. A prefilled glass syringe suitable for intravitreal administration containing a stable ophthalmic formulation, comprising:

> a vascular endothelial growth factor (VEGF) antagonist,
>
> an organic co-solvent,
>
> a buffer, and
>
> a stabilizing agent,
>
> wherein the VEGF antagonist is a fusion protein produced in a Chinese Hamster Ovary (CHO) cell, the fusion protein comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor and Ig domain 3 of a second VEGF receptor, and a multimerizing component.
>
> 2. The prefilled glass syringe of claim 1, wherein 90% or more of the weight of the fusion protein is not present as an aggregate.

'763 patent (ECF No. 108-11, Trout Ex. 76) (emphases added). Thus, because claim 2 depends from claim 1, it must "specify a further limitation of the subject matter claimed" in the independent claim from which it depends, 35 U.S.C. § 112(d), and "stable" in claim 1 must be broader than the "90% or more" limitation in claim 2. Consistent with the statute, the Federal Circuit has held that it is improper for courts to construe claims such that a dependent claim would "have no scope and thus be meaningless." Littelfuse, 29 F.4th at 1380. Yet that is precisely what Formycon's proposed construction does. Under Formycon's construction, claim 2 of the '763 patent is meaningless because "stable" would already require a higher level of non-aggregates (98% native conformation) than

specified in dependent claim 2. In other words, Formycon's construction not only reads in an unwritten numerical aggregate limitation into "stable," it also reads in a stricter threshold than what claim 2 recites expressly. Such a construction would render claim 2 of the '763 patent a nullity, inconsistent with the Federal Circuit's clear precedent. That court likewise has dictated that claim terms appearing in multiple patents in a family, such as "stable" in the '763 and '594 patents here, must be construed consistently between across those patents. See SightSound Techs., LLC v. Apple Inc., 809 F.3d 1307, 1316 (Fed. Cir. 2015) ("[W]here multiple patents derive from the same parent application and share many common terms, we must interpret the claims consistently across all asserted patents." (internal quotation omitted)); Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1334 (Fed. Cir. 2003) (noting that claim terms in related patents should be construed consistently). Applying Formycon's proposed construction to the '763 patent, claim 2 would improperly "have no scope and thus be meaningless," as "stable" in claim 1 would require a more stringent stability limitation than the one set forth in dependent claim 2.

The prosecution history also reinforces that "stable" does not imply 98% native conformation. The Examiner reviewing the

Product Patent concluded that the 98% native conformation limitation in the Product Patent was patentably distinct over — i.e. not inherent in, and different from — the '594 patent's claims to a "stable" formulation. During Prosecution of the Product Patent, the Examiner initially entered an ODP rejection based on the '594 patent. Product Patent File History at RGN-EYLEA-BIOSIM-00016064 (ECF No. 101-11, Trout Ex. 66). Regeneron explained that the Product Patent claims were patentably distinct, explaining that the claims that ultimately issued in the Product Patent recited "the stability of the protein conformation in storage over a period of time" (i.e., the 98% native conformation limitation), whereas the '594 claims did not. Id. at -085-086. The Examiner then allowed the claims. Id. at -109-110. This further supports that the 98% native conformation by SEC limitation is distinct from "stable" as recited in the claims of the '594 patent. The Court is not persuaded by Formycon's construction of "stable" to make those distinct concepts the same.

Thus, properly understood, "stable" as required in '594 claim 5 is broader than, and not limited to, "at least 98% . . . native conformation . . . as measured by size exclusion chromatography." Having concluded that "stable for at least 4 months" is not limited to 98% native conformation as measured by SEC, the Court need not

further construe that term in the '594 patent to resolve the parties' dispute. See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co., 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[Courts] need only construe terms . . . to the extent necessary to resolve the [parties'] controversy.") (internal quotation omitted).

(ii) "VEGF Trap"

Formycon argues that the term "VEGF trap consists of amino acids 27-457 of SEQ ID NO:4"[9] in claim 5 of the '594 patent should be construed to require glycosylation at five specific residues in the protein's amino acid sequence. Opp. 5. Regeneron responds that the term "VEGF trap" should not be construed as including Formycon's proposed glycosylation requirement, given that this term (like the rest of claim 5 of the '594 patent) does not recite any glycosylation requirement. Reply 5.

The Court agrees with Regeneron. Neither '594 claim 5 nor any claim from which it depends recites any limitation with respect to glycosylation. It is black letter law that courts cannot "read limitations from the specification into the claims." Thorner, 669 F.3d at 1366; see also Markman v. Westview Instruments, Inc., 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc) ("The written description part of the specification itself does not delimit the right to

[9] For readability, this term will be referred to as "VEGF trap."

exclude. That is the function and purpose of claims."); Phillips, 415 F.3d at 1319-20 (explaining that "one of the cardinal sins of patent law" is to "read[] a limitation from the written description into the claims" (internal quotation omitted)). Formycon provides no basis in either the claim language or the specification for such a glycosylation limitation in '594 claim 5.

Formycon's construction, moreover, would render meaningless the express glycosylation limitations in the Product Patent claims. As the Federal Circuit has explained, "[i]t is highly disfavored to construe [claim] terms in a way that renders them void, meaningless, or superfluous," but that is what Formycon's proposed construction does. Intel Corp. v. Qualcomm Inc., 21 F.4th 801, 810 (Fed. Cir. 2021) (quoting Wasica Finance GmbH v. Continental Automotive Systems, Inc., 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017)); see Littelfuse, 29 F.4th at 1380. The "VEGF trap" recited in claim 5 of the '594 patent possesses the identical amino acid sequence as that recited in claim 1 of the Product Patent. Compare '594 patent, claim 4 (claiming a "VEGF trap consists of amino acids 27-457 of SEQID NO:4," upon which claim 5 depends); with Product Patent, claim 1 ("wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4"). Regeneron drafted claim 5 of the

'594 patent not to include any glycosylation requirement. By contrast, Regeneron drafted claim 1 of the Product Patent expressly to require glycosylation. See Product Patent, claim 1 ("wherein said VEGF antagonist fusion protein is glycosylated") & claim 14 ("wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4").

The differences in the claims of these related patents indicate that claim 5 of the '594 patent should not be construed to require glycosylation. Claim terms in related patents must be interpreted consistently. SightSound, 809 F.3d at 1316 ("[W]here multiple patents derive from the same parent application and share many common terms, we must interpret the claims consistently across all asserted patents." (internal quotation omitted)). Doing so here, under Formycon's construction, would render both the "is glycosylated" limitation of claim 1 (required by all asserted Product Patent claims) and the entirety of claim 14 (which requires glycosylation at specified sites) nullities—a "highly disfavored" result. Intel, 21 F.4th at 810.

Further, Formycon's proposed construction, which implies that the claimed aflibercept is necessarily glycosylated, contradicts undisputed evidence that aflibercept is not necessarily

glycosylated. Neither '594 claim 5 nor the Asserted Product Patent Claims limit the type of cell that may be used to produce the claimed protein. As explained by experts on both sides, aflibercept (having the amino acid sequence 27-457 of SEQ ID NO:4 set forth in the Product Patent) can be produced from different cells, only some of which result in glycosylation of aflibercept. See Trout Decl. ¶¶ 107, 380 (explaining if E. Coli cells are used to produce aflibercept, then the resulting aflibercept would not be glycosylated); id. ¶ 381 (stating that producing aflibercept in a CHO cell "would not inevitably result in glycosylated aflibercept"); Tessier Tr. 138:15-21 (agreeing that Daly, a prior art reference, disclosed that glycosylation can be eliminated by producing a protein in mutant CHO cell lines). Thus, contrary to the implication of Formycon's construction, both side's experts agree that aflibercept is not necessarily glycosylated. That conclusion is consistent with the prior-art reference Daly (U.S. Patent Application Publication 2006/0058234), which explains that mutant CHO cell lines can eliminate glycosylation in a VEGF antagonist fusion protein. Daly ¶ 38 (ECF No. 101-11, Trout Ex. 61). It is also consistent with this Court's identical finding in the Mylan post-trial decision. Mylan, 2024 WL 382495, at *55 ("[E]ven if a protein contains amino acid sequences that may be

glycosylated, a given protein may not be glycosylated." (citing Dr. Trout's testimony)).

In sum, the Court agrees with Regeneron that "VEGF trap" should not be construed to mean "glycosylated VEGF trap."

b) No motivation to use glycosylated aflibercept.

The second step of an ODP analysis requires comparing the construed reference patent claims with the asserted claims. AbbVie, 764 F.3d at 1374, 1378. As explained above, the parties agree that asserted reference claim 5 of the '594 patent differs in multiple respects from the asserted claims of the Product Patent. If any of those differences are not obvious or anticipated, Formycon cannot prove ODP. The Court analyzes each of those differences in turn and concludes that Formycon is not likely to succeed in proving that the Asserted Product Patent Claims are anticipated or rendered obvious by claim 5 of the '594 patent, thereby foreclosing a finding of ODP. Otsuka, 678 F.3d at 1298.

The Product Patent's asserted claims, unlike '594 claim 5, recite a "glycosylated" VEGF antagonist. Formycon argues that (1) '594 claim 5 requires glycosylation and therefore anticipates the asserted claims, and (2) the POSA would have been motivated to use glycosylated aflibercept and therefore '594 claim 5 renders the

asserted claims obvious. The Court disagrees with both of Formycon's assertions and, based on the present record, finds that this difference between the reference claims and the Asserted Product Patent Claims is not indistinct.

Formycon argues that '594 claim 5 anticipates the asserted claims of the Product Patent because '594 claim 5 covers a genus that includes only two species, glycosylated and unglycosylated aflibercept. Opp. 5-6. "It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus." Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 999 (Fed. Cir. 2006). However, "a very small genus can be a disclosure of each species within the genus." Id. Contrary to Formycon's assertions, even considering only glycosylation, the genus claimed in '594 claim 5 encompasses more than just two species. Because aflibercept has five distinct glycosylation sites, Formycon's expert, Dr. Tessier, agreed that there are at least thirty possible glycosylated forms of aflibercept, Tessier Tr. 130:21-131:8, in addition to the nonglycosylated form. This is not a "very small genus" for purposes of a finding of anticipation. Atofina, 441 F.3d at 999.

Moreover, for anticipation, a single reference must not only

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 97 of 203

"disclose all elements of the claim within [its] four corners," but "all elements of a claimed invention arranged as in the claim." Net MoneyIN, Inc. v. Verisign, Inc., 545 F.3d 1359, 1369 (Fed. Cir. 2008) (emphasis added) (internal quotation omitted). But in addition to encompassing every glycosylation profile, '594 claim 5 recites a range of pH values from 6.2-6.4, and does not recite the 98% native conformation limitation recited in claim 1. Thus, the POSA would need to select not only a particular glycosylation profile, but also a specific pH value that results in 98% native conformation as recited in the Product Patent claims. But Formycon has cited no evidence that any other glycosylation profile than the one described in the patent (which may not be considered as prior art, see Eli Lilly, 689 F.3d at 1379-80), or a formulation at a pH of 6.4, would achieve 98% native conformation. Dr. Tessier clarified that he did not "have an opinion about that sequence without glycosylation at the five sites" and that there was no native conformation data (even in the non-prior-art patent) at pH 6.4. Tessier Tr. 117:12-20, 132:15-20, 133:18-19. Accordingly, Formycon has not made a showing that the genus recited in '594 claim 5 is "very small" or that it recites every element of claim 1 of the Product Patent "as arranged in the claim," and thus has not shown a substantial question of anticipation. Atofina, 441

F.3d at 999; Net MoneyIN, 545 F.3d at 1369; Mylan, 2024 WL 382495, at *47-48 (rejecting similar anticipation argument).

Formycon also argues that glycosylation would have been obvious because the POSA would have been motivated to use a glycosylated form of aflibercept as recited in the claimed ophthalmic formulations. However, the evidence shows that the POSA would not have been motivated to use glycosylated aflibercept for an ophthalmic formulation.

Obviousness addresses what is, "on balance, desirable," not what is "feasible." Winner Intern. Royalty Corp. v. Wang, 202 F.3d 1340, 1349 (Fed. Cir. 2000); see Orexo AB v. Actavis, 903 F.3d 1265, 1272-73 (Fed. Cir. 2018). The prior art taught that VEGF Trap proteins could be made in CHO cells and glycosylated (Papadopoulos at 26:5-10 (ECF No. 101-11, Trout Ex. 84); Tessier Decl. ¶¶ 99-102) or made in E. coli or mutant CHO cells and not glycosylated (Trout Decl. ¶ 107; Tessier Tr. 138:15-21; Daly ¶¶ 38, 43). And for an ophthalmic formulation like that claimed in Product Patent, the prior art's teachings would have motivated the POSA against using glycosylated aflibercept. More specifically, the art showed that a POSA would avoid glycosylation because it would increase the size of aflibercept, thereby reducing retinal penetration, and because it would undesirably increase systemic

exposure and the risk of inflammation. Trout Decl. ¶¶ 376-82.

First, Daly taught that mini-Traps — substantially smaller VEGF Trap molecules than aflibercept — including a "smaller, non-glycosylated mini-trap expressed in E. coli . . . has optimized characteristics for local, intravitreal delivery, i.e. a shorter serum half life for faster clearance and minimizing unwanted systemic exposure." Daly ¶¶ 38, 43. As this Court previously found, because aflibercept is larger when glycosylated, the POSA expected reduced retinal penetration and would thus "have sought to use nonglycosylated aflibercept because glycosylation increases size and thus decreases retinal penetration." Mylan, 2024 WL 382495, at *55 (citing Dr. Trout). As the Court has previously recognized, numerous prior art references taught that larger molecules would have inferior retinal penetration. Id. at *14, 54 (citing Gaudreault, Jackson, Ghate); Ghate at 281 (ECF No. 101-9, Trout Ex. 26) (the retina's "internal limiting membrane" was "impermeable to . . . globular molecules > 70 kDa"); Jackson at 2141 (ECF No. 101-9, Trout Ex. 28) ("The [retinal exclusion limit] in human tissue was 76.5 ± 1.5 kDa."); Gaudreault at 726, 731 (ECF No. 101-9, Trout Ex. 24) ("[P]enetration of ranibizumab into the retina is critical for its clinical use" and ranibizumab's "ability [to penetrate the retina] has been attributed to [its] small

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 100 of 203

molecule size.”). Regeneron cites the same prior-art evidence here. Trout Decl. ¶¶ 308, 364, 377. Consistent with its prior decision in the Mylan case, the Court finds here that the POSA would have been motivated to avoid increasing the molecular size of aflibercept by using its glycosylated form.

To argue to the contrary, Formycon cites Dr. Tessier’s discussion of Rosenfeld (ECF No. 157-2, Tessier Ex. 18), where researchers investigated in early clinical studies the use of intravitreal bevacizumab (a molecule with a larger molecular weight than aflibercept) and Regeneron’s phase 1 aflibercept data. Opp. 6-7. However, a reference introduced by Regeneron, Ferrara 2006 (ECF No. 101-9, Trout Ex. 21), comprehensively reviewed the ranibizumab, bevacizumab, and VEGF Trap literature, including Rosenfeld’s research, and reported “skepticism specifically directed at intravitreal compositions comprising high molecular weight proteins such as VEGF Trap fusion proteins.” Mylan, 2024 WL 382495, at *60; Trout Decl. ¶¶ 308, 364, 377; Ferrara 2006 at 862-63. Ferrara 2006 specifically cautioned against overreliance on the early findings reported in Rosenfeld, explaining that “[a]lthough intriguing, these early findings are difficult to compare with data from rigorous, double-masked, controlled phase 3 trials of verteporfin photodynamic therapy, pegaptanib, and,

more recently, ranibizumab." Ferrara 2006 at 866. Ferrara 2006 further noted the problem with early-phase clinical study data, observing that "it is noteworthy that initial, uncontrolled phase 1 or 2 studies with pegaptanib or verteporfin photodynamic therapy suggested a considerably greater benefit in AMD patients than that eventually demonstrated in randomized phase 3 studies, further emphasizing the difficulty of interpreting early clinical results." Id. Thus, Formycon does not overcome the repeated teachings in the prior art motivating the POSA against using a larger molecule for an ophthalmic formulation, which would have dissuaded the POSA from using glycosylated aflibercept. See Henny Penny Corp. v. Frymaster LLC, 938 F.3d 1324, 1331-32 (Fed. Cir. 2019) (the cited prior art "must be considered for all its teachings, not selectively").

Second, Formycon argues that the fact that glycosylation could increase serum half-life would not deter a POSA because "the volume of drug being injected was too small to cause harm." Opp. 7. That argument also runs contrary to the prior art's teachings. The pharmacokinetics of glycosylated aflibercept that provide a longer half-life were only disclosed as favorable to treat cancer, by "extending in vivo half life" in the bloodstream. Holash at 11393-94 (ECF No. 101-9, Trout Ex. 27); Trout Decl. ¶ 379. By

contrast, the prior art relating both to VEGF Traps and ranibizumab taught that, for ophthalmic use, "shorter serum half life" was desirable. Daly ¶ 43 (emphasis added); see also Mylan, 2024 WL 382495, at *6; Gaudreault at 731 ("The low circulating concentrations of ranibizumab after [intravitreal] administration may be important in the clinical setting, because VEGF is necessary for normal physiological functions such as tissue repair and reproduction."). Both Regeneron's and Formycon's expert witnesses agree that glycosylation lengthens serum half-life in the bloodstream. Trout Decl. ¶ 379, Tessier Tr. 198:7-14. Thus, the Court finds that the prior art would motivate a POSA against using glycosylated aflibercept in formulations for ophthalmic use.

The Court notes that its finding in Mylan that a longer half-life was advantageous since it allowed for smaller doses and less-frequent dosing, Mylan, 2024 WL 382495, at *59, was based on Regeneron's discovery that Eylea's long half-life unexpectedly facilitated extended dosing, not on any document that could properly be considered prior art in the obviousness analysis, see 35 U.S.C. § 103(a) (pre-AIA) ("Patentability shall not be negatived by the manner in which the invention was made."); Otsuka, 678 F.3d at 1296 ("The inventor's own path itself never leads to a conclusion of obviousness; that is hindsight."). Indeed, this

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 103 of 203

Court previously explained that "the law does not require the inventors to have appreciated that the Eylea composition they invented would become the success it is; 'understanding of the full range of an invention is not always achieved at the time of filing the patent application,' and unexpected properties need not be appreciated at the time of the invention." Mylan, 2024 WL 382495, at *60 (quoting Knoll Pharm. Co. v. Teva Pharm. USA, Inc., 367 F.3d 1381, 1384-85 (Fed. Cir. 2004)).

Third, Formycon argues that glycosylation may contribute to "binding activity," see Opp. 6, but it cites no prior art analyzing VEGF traps to support this assumption. Daly taught that "[a]ffinity measurements showed that the non-glycosylated fusion polypeptides expressed in E. coli or the glycosylated polypeptides expressed in CHO cells had comparable binding affinity for VEGF as the full-sized parent trap." Daly ¶ 63. Dr. Trout examined this data, which was the only data comparing glycosylated and nonglycosylated VEGF traps, and came to the unrebutted conclusion that glycosylated and nonglycosylated aflibercept have comparable affinity. Trout Decl. ¶ 377. Dr. Tessier offered no contrary testimony and did not address these data. So, a POSA would not have been motivated to use glycosylated aflibercept on the basis of its comparative binding affinity.

Fourth, Dr. Tessier explained that glycosylation of aflibercept's "Fc" portion activates "effector functions," including immune-mediated toxicities. See Tessier Decl. ¶ 101 ("[G]lycosylation of the Fc region is important for IgG and Fc-fusion protein binding to FcgRs, which results in various effector functions, such as antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC)."); Tessier Tr. 148:17-22; cf. Trout Decl. ¶¶ 362-63. In the context of ophthalmic use, Daly taught that the "Fc" portion "may be modified to reduce effector functions" by "eliminat[ing] glycosylation." Daly ¶ 38. Dr. Tessier did not dispute that, for ophthalmic use, an immune response via glycosylation is undesirable, but did "not believe" this concern "would outweigh the benefits of using a glycosylated molecule." Tessier Tr. 155:18-156:10, 169:22-170:12. Dr. Tessier is not a physician, and he did not consult a physician to arrive at his conclusion. Id. 170:7-12, 171:4-6 (agreeing that "it would be logical to discuss with a medical professional" risks of effector functions but noting that he had not had such a discussion). As such, the Court does not credit Dr. Tessier's testimony on this point. It is also inconsistent with this Court's prior finding in its obviousness analysis that "'moderate to severe' inflammation was an extremely concerning phenomenon for

any intravitreal drug product to exhibit." Mylan, 2024 WL 382495, at *52. These immunological concerns would further motivate the POSA against using glycosylated aflibercept.

Finally, Formycon argues that the POSA would have used glycosylated aflibercept for stability reasons. Opp. 6. Dr. Tessier identified no prior art that compared the stability of glycosylated and nonglycosylated aflibercept. Tessier Tr. 202:10-205:19. Moreover, Formycon has not produced any prior art that teaches that glycosylation improves aflibercept's stability in the presence of a stabilizing agent and organic co-solvent, as required by '594 claim 5. Id. Further, '594 claim 5 depends from claim 3, which recites that "the VEGF trap is stable for at least 4 months" irrespective of glycosylation. Formycon fails to provide a persuasive reason why stability concerns would motivate the POSA, beginning with a stable formulation from claim 5 of the '594 patent, to glycosylate aflibercept.

Cumulatively, the evidence sufficiently points against a motivation to glycosylate the VEGF trap claimed in '594 claim 5. Thus, it would not have been obvious to the POSA to modify '594 claim 5 to arrive at the asserted claims of the Product Patent.

c) The Product Patent's "98% native conformation" claim limitation is not inherent in claim 5 of the '594 patent

Another difference between the asserted claims of the Product Patent and '594 claim 5 is that the former requires "at least 98% (or 99% in claim 16) of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography" whereas the latter recites that "the VEGF trap is stable for at least 4 months." As explained below, the Court concludes that the 98% native conformation claim limitation is not inherent in the subject matter claimed in '594 claim 5.

A missing claim limitation can be met for purposes of anticipation or obviousness by showing that the limitation is inherent in the reference claim. See PAR Pharm, 773 F.3d at 1194-95. An inherent limitation, however, must be "necessarily present," Apotex, 754 F.3d at 960, and "may not be established by probabilities or possibilities," Mylan, 2024 WL 382495, at *55 (quoting PAR Pharm., 773 F.3d at 1194). And in the context of obviousness in particular, the Federal Circuit has explained that the role of inherency is limited: "the use of inherency in the context of obviousness must be carefully circumscribed because '[t]hat which may be inherent is not necessarily known' and that

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 107 of 203

which is unknown cannot be obvious." Honeywell, 865 F.3d at 1354 (quoting Rijckaert, 9 F.3d at 1534). Thus, in order for the 98% native conformation claim limitation to be inherent in '594 claim 5, '594 claim 5 must necessarily and always meet the Product Patent's 98% native conformation claim limitation. Apotex, 754 F.3d at 960; Glaxo Inc., 52 F.3d at 1047.

Neither '594 claim 5 nor the shared specification of the '594 patent and the Product Patent discloses that a "stable" ophthalmic formulation within '594 claim 5 necessarily has 98% native conformation. As described above, the patent describes that the "fusion protein is preferably substantially free of aggregates . . . [which] means that at least 90% of the weight of fusion protein is not present in an aggregate at the time the fusion protein is used to prepare the pharmaceutically effective formulation." Product Patent, 6:50-55 (emphasis added). As Dr. Tessier agreed, the patent thus teaches preparing a preferred formulation that has at least 90% protein in non-aggregated form. Tessier Tr. 35:20-36:14. And because there is no dispute that the level of aggregation would not decrease after "the time the fusion protein is used to prepare the . . . formulation" (as described further below), a "stable" ophthalmic formulation does not necessarily possess 98% native conformation as measured by size

exclusion chromatography after two months storage. Apotex, 754 F.3d at 960-61 (finding no inherency when the claimed property is sometimes, but not always, present in the anticipating reference); PAR Pharm., 773 F.3d at 1195-96 (noting the same rule applies to an obviousness reference). This disclosure from the patents' common specification, together with the admission from Formycon's expert, is sufficient for the Court to find that the 98% native conformation limitation is not inherent in the subject matter of '594 claim 5.

In its opposition to Regeneron's preliminary injunction motion, Formycon relied on internal Regeneron data as evidence of inherency.[10] In response, Regeneron pointed to other internal data showing that a specific aflibercept formulation did not have 98% native conformation even at time zero and before storage, and therefore would not meet the Product Patent claim limitation requiring at least 98% native conformation as measured by SEC after 2 months. Although not necessary to the Court's finding, this "SS195" data confirms that the 98% native conformation limitation is not inherent in '594 claim 5. See Reply 9; Graham Decl. ¶11;

[10] The parties do not dispute that such data may be considered in evaluating inherency. See Hospira, Inc. v. Fresenius Kabi USA, LLC, 946 F.3d 1322, 1329-30 (Fed. Cir. 2020).

SS-195 Stability Data (ECF No. 113-3, Trout Ex. 106 (corrected)). The SS195 data corresponds to an internal stability study performed by Regeneron on a formulation that falls within the scope of '594 claim 5 (40 mg/mL of aflibercept, 10 mM phosphate, 0.03% polysorbate 20, 5% sucrose, and 40 mM NaCl at pH 6.25), a fact that Formycon does not dispute. See Tessier Tr. 84:4-6 (agreeing that '594 claim 5 is not limited to any particular lot of aflibercept); Graham Decl. ¶ 10. The formulation tested in the SS195 study possessed less than 98% native conformation by SEC even at time zero, before any storage. Graham Decl. ¶ 11 (showing percent native conformation at time zero of 97.3, 97.7, and a value in between); SS-195 Stability Data. This data comports with the common disclosure in the Product Patent and the '594 patent stating that "preferably . . . at least 90% of the weight of fusion protein is not present in an aggregate at the time the fusion protein is used to prepare the pharmaceutically effective formulation." Product Patent, 6:50-55. And it also demonstrates that not every formulation falling within the scope of '594 claim 5 "necessarily" achieves 98% native conformation, as required for a finding of inherency. See Glaxo, 52 F.3d at 1047-48; PAR Pharm., 773 F.3d at 1195-96.

In Formycon's reply in support of its motion to strike Dr.

Graham's testimony, Formycon argues that the SS195 composition is not within '594 claim 5 because the study does not report 4-month storage data and thus has not been proven to meet the "stable" limitation. Reply re Mot. to Strike at 1-2 (No. 24-md-3103, ECF No. 41). That is inconsistent with Formycon's prior argument that the 98% native conformation limitation is inherent based on the specification's disclosure, which also does not contain 4-month data for Examples 3 and 4 on which Formycon relies. Opp. 7. Regardless, as the Court described above, "stable" as required in '594 claim 5 is a lower requirement than the 98% native conformation limitation in the Product Patent, and Formycon bears the burden on invalidity and inherency. BlephEx, 24 F.4th at 1399. The data in SS195 demonstrates that formulations containing the structures recited in '594 claim 5 do not necessarily contain 98% native conformation, even before any storage, and nor does "stable" as required in '594 claim 5 require 98% native conformation. The data thus supports that "stable" formulations need not possess 98% native conformation, consistent with the patent's teachings.

Formycon does not dispute that a formulation starting with less than 98% native conformation could not possess 98% native conformation after 2 months' storage. The evidence demonstrates that the process of protein aggregation is irreversible, so that

the percent native conformation will be the same or lower after two months' storage, as compared to time zero. Formycon's expert, Dr. Tessier, did not dispute this proposition, Tessier Tr. 31:16-32:9; and in fact he relied upon it in his declaration, Tessier Decl. ¶ 52 n.2 ("[D]ata for 1 and 3 months of 99.2 and 99.1 % monomer, respectively, would imply that at 2 months, the % monomer would be between these values."). Regeneron's expert, Dr. Trout, likewise explained that aggregation is irreversible. Trout Decl. App. A ¶ 61 ("[I]f the percentage native conformation is greater than 98% at 3 months, then it must necessarily have been greater than 98% after 2 months."). This finding is consistent with the Court's prior finding that the process of aggregation is irreversible. Mylan, 2024 WL 382495, at *32. Thus, because the SS195 data, consistent with the '594 and Product Patent specification, demonstrates that a formulation falling within the scope of '594 claim 5 can have less than 98% native conformation by SEC at time zero, it also demonstrates that a formulation falling within the scope of '594 claim 5 can have less than 98% native conformation by SEC following storage for 2 months at 5°C. These data confirm the Court's finding that the 98% native conformation limitation of the Product Patent claims is not inherent in '594 claim 5, because formulations falling within the

scope of '594 claim 5 do not necessarily meet the at least 98% native conformation claim limitation. Glaxo, 52 F.3d at 1047-48; PAR Pharm., 773 F.3d at 1195-96.

Formycon points to other data, from Examples 3 and 4 of the '594 patent, in which a composition falling within the scope of '594 claim 5 exhibited at least 98% native conformation. Opp. 7. As an initial matter, Formycon incorrectly equates Examples 3 and 4 with '594 claim 5. Opp. 7. Examples 3 and 4, as well as Eylea itself, are specific compositions that are not prior art. See Eli Lilly, 689 F.3d at 1380 (explaining that the "double patenting analysis . . . turns on an evaluation of what [the patentee] has claimed, not what it has disclosed" and requires "[p]utting aside the teachings in the [] patent's specification"). There is no dispute that Eylea was not sold until well after the 2006 priority date of the Product Patent and is not prior art. And while these Examples (and Eylea) are embodiments of '594 claim 5, that claim is not limited to those embodiments. To the contrary, "although the specification often describes very specific embodiments of the invention, [the Federal Circuit] ha[s] repeatedly warned against confining the claims to those embodiments." Phillips, 415 F.3d at 1319-20. Notably, '594 claim 5 is not limited to any lot of aflibercept, or any particular glycosylation pattern of

aflibercept, and recites a range of pH values, and Formycon has failed to present persuasive evidence how or why the POSA would be motivated to obtain the specific examples in the patent specification or Eylea, which are not prior art.

For example, '594 claim 5 recites a pH range of "pH 6.2-6.4," whereas Examples 3 and 4 are limited to "pH 6.3." Compare '594 Patent at claim 5 with id. at 8:55-63, 9:15-24. Formycon's own expert could not identify a reason that the POSA would select the pH of 6.3 recited in Examples 3 and 4 from the broader genus of pH 6.2-6.4 that is recited in '594 claim 5. Tessier Tr. 116:5-11. Thus, although Examples 3 and 4 both meet the 98% native conformation limitation, both examples are limited to formulations having a pH of 6.3; these examples do not correspond to formulations with "pH 6.2-6.4" as recited in '594 claim 5. Formycon cites no percent native conformation data for formulations at pH 6.4 and provides no evidence that a '594 claim 5 formulation at pH 6.4 necessarily has 98% native conformation. Nor does Formycon identify a reason why the POSA practicing '594 claim 5 would select any particular pH within the claimed range or exclude formulations at pH 6.4, which is expressly recited in '594 claim 5. Dr. Tessier admitted that he did not "consider the pH sensitivity of aflibercept as part of this matter." Id., 117:21-

118:7. Dr. Tessier also refused repeatedly to testify that practice of '594 claim 5 at pH 6.4 necessarily would have 98% native conformation, asserting instead that he had no reason to doubt that it would. Id., 118:8-124:21. This probabilistic evidence cannot prove inherency. Apotex, 754 F.3d at 960-61.

Because the pH of 6.3 in the patent's examples is not prior art, it cannot be relied upon for obviousness — both because "[o]bviousness cannot be predicated on what is unknown," In re Rijckaert, 9 F.3d at 1534, and because the '594 patent's specification "does not qualify as prior art" in ODP, Eli Lilly, 689 F.3d at 1379. Without any prior art basis to select the pH in the examples to meet the Product Patent claims, Formycon's ODP defense fails. In re Kaplan, 789 F.2d 1574, 1580 (Fed. Cir. 1986).

In any event, Formycon's reliance on the native conformation data in Examples 3 and 4 is legally inadequate to prove inherency. That the practice of '594 claim 5 sometimes results in 98% native conformation is insufficient; inherency requires that the 98% native conformation limitation be present necessarily, not just possibly or probably. The Federal Circuit's Glaxo v. Novopharm precedent is instructive. Glaxo, 52 F.3d at 1043. There, the patent challenger argued that a claimed crystal was inherent from a prior art process because "experts performed the process

disclosed in [the prior art] thirteen times and each time they made" the claimed crystal ("Form 2"). Id. at 1047. But the Court held that was not sufficient to show inherency because two other times the prior art process was performed and the claimed crystal did not form. Id. at 1047-48 ("Glaxo's David Collin originally made Form 1 by practicing [the prior art process], and that Glaxo's expert, Nicholas Crouch, did too."); see also Apotex, 754 F.3d at 960-61 (finding no inherent anticipation when "it was at least possible" to perform the prior art process in a way that does not result in the asserted claim) (emphasis in original); PersonalWeb Techs., LLC v. Apple, Inc., 917 F.3d 1376, 1382 (Fed. Cir. 2019) ("[M]ere possibility is not enough" for inherency). The facts of Glaxo are materially indistinguishable from the ones here, as the evidence demonstrates that '594 claim 5 compositions may well achieve the 98% native conformation limitation (as in Example 4 of the patent) but they also may not (as in SS195) and the formulations referenced in the specification having 90% or less than 90% protein in non-aggregate form at the time of preparation), and in other instances there is simply no evidence one way or the other whether compositions would necessarily achieve 98% native conformation (as with a pH of 6.4). The same result as Glaxo thus applies here as well: 98% native conformation as claimed in the

Product Patent is not inherent.

The Court has also considered the Federal Circuit's decision in Hospira, Inc. v. Fresenius Kabi USA, LLC, 946 F.3d 1322 (Fed. Cir. 2020), and concludes that it does not support a finding of inherency. There, the Federal Circuit upheld an enablement finding where it "relied on fact and expert testimony regarding the stability data for more than 20 tested samples . . . , all of which met the [claim limitation]." Id. at 1327, 1330-31. Here, in contrast, all of the formulations within the scope of the reference claim do not meet the 98% native conformation limitation, as demonstrated by both the specification itself and the internal Regeneron data. Formycon therefore has failed to establish evidence that compositions within claim 5 necessarily possess the 98% native conformation limitation.

Finally, the Court notes that a patent challenger like Formycon who argues invalidity on a basis already addressed during prosecution bears "the added burden of overcoming the deference that is due to a qualified government agency presumed to have properly done its job." See PowerOasis, Inc. v. T-Mobile USA, Inc., 522 F.3d 1299, 1304 (Fed. Cir. 2008) (internal quotation omitted). The Court's conclusion that the 98% native conformation claim limitation is not inherent in the subject matter claimed in

'594 claim 5 is consistent with the Examiner's prior determination of this issue, and Formycon has not met its burden of demonstrating a substantial question of invalidity.

The Court further notes that patent office issued interim decisions as to a related patent, U.S. Patent 10,464,992 (ECF No. 108-11, Trout Ex. 64), to institute reexamination and inter partes review. See Celltrion, Inc. v. Regeneron Pharms., Inc., 2023 WL 5166828 (P.T.A.B. July 20, 2023). It is undisputed that Regeneron later disclaimed the '992 patent. However, Regeneron does not assert the '992 patent here and the Court does not find that the interim patent office decisions as to the '992 patent undermine the Product Patent asserted here. Notably, the '992 patent claims do not require 40 mg/mL of aflibercept and are silent as to whether aflibercept is glycosylated. The significant differences in the scope of the '992 patent and Product Patent claims and the preliminary nature of the decisions render them at most tangentially relevant and insufficient to support inherency or undermine the Examiner's conclusions regarding the Product Patent.

For all of these reasons, the Court finds that the 98% native conformation limitation of the Product Patent claims is not inherent in '594 claim 5.

Formycon has not provided any argument to rebut Regeneron's

position that the 98% native conformation limit would not have been obvious. Dr. Trout has provided testimony that the POSA beginning with claim 5 of the ’594 patent would not have been motivated to achieve the 98% native conformation limitation and would not have had a reasonable expectation of achieving that level of native conformation after two-months’ storage. Trout Decl. ¶¶ 339-40, 385-87, 390. Formycon did not rebut that evidence. Dr. Trout further explained that no prior art relevant to obviousness taught native conformation levels of aflibercept (Trout Decl. ¶¶ 339-40), that the POSA would not have been motivated to obtain such a high level of native conformation as lower levels would have been considered acceptable (Trout Decl. ¶¶ 385-87), and that even if the POSA did possess such motivation, the POSA would not have reasonably expected to obtain 98% native conformation after two-months’ storage given the absence of any relevant prior art teachings as to aflibercept’s stability, Trout Decl. ¶¶ 339-40, 390; see Mylan, 2024 WL 382495, at *56 (“Dr. Trout explained that because fusion proteins are synthetic ‘Frankenstein’ molecules that, unlike antibodies, did not evolve to possess inherent stability, the POSA would expect fusion proteins like aflibercept to have lower stability than antibodies. . . .”). There does not appear to be any dispute that “[j]ust because one protein has a

given native conformation at a specific condition, the [POSA] wouldn't expect that a different protein will have the same native conformation at that condition," consistent with the Court's prior finding. Mylan, 2024 WL 382495, at *56 (alterations in original) (emphasis removed). The Court thus credits Dr. Trout's opinion that the 98% native conformation limitation would not have been obvious.

d) Formycon's motion to strike portions of Regeneron's reply brief and the Graham declarations is DENIED [ECF No. 210]

Formycon moved to strike portions of Regeneron's reply brief and the accompanying Graham declaration as untimely. ECF No. 210. The Court previously denied a similar motion in the Samsung cases, 1:24-MD-3103, ECF No. 170, and, for the same reasons, **DENIES** Formycon's motion here.

It is well-settled that new evidence and new arguments are not permitted on reply. Mew Sporting Goods, LLC v. Johansen, 992 F. Supp. 2d 665, 671 n.2 (N.D.W. Va. 2014), aff'd, 594 Fed. App'x 143 (4th Cir. 2015) ("[T]he ordinary rule in federal courts is that an argument raised for the first time in a reply brief or memorandum will not be considered."). Still, the "entire purpose of a reply" is to "reply to counter-points made by [the party] in the opposition." Alston v. United Collections Bureau, Inc., No.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 120 of 203

DKC-13-0913, 2014 WL 859013, at *14 (D. Md. Mar. 4, 2014). Accordingly, the Federal Rules do "not preclude affidavits supporting a reply brief when they respond to evidence supporting an opposition brief." Amazon.com, Inc. v. WDC Holdings LLC, No. 20-1743, 2021 WL 3878403, at *3 n.1 (4th Cir. Aug. 31, 2021) (unpublished).

The issue here surrounds the evidence with respect to inherency. According to Formycon, via the Graham Declaration, Regeneron indicates, for the first time, that a formulation may or may not satisfy the 98% native conformation claim element, depending on the lot of aflibercept used to make the formulation, regardless of its composition. Thus, Formycon's position is that through the Graham Declaration, Regeneron alleges for the first time that the stability limitations of the '865 patent are not inherent. Regeneron, of course, claims that the Graham Declaration was submitted to counter Formycon's response.

After considering all of the parties' arguments and the governing law, the Court is convinced that Regeneron's position is correct. Formycon bears the burden to "present[] a substantial question of validity" at the preliminary injunction stage. BlephEx, LLC v. Myco Indus., Inc., 24 F.4th 1391, 1398-99 (Fed. Cir. 2022). In the context of a preliminary injunction, "the

patentee need not address invalidity as an initial matter in filing for a preliminary injunction." Gaymar Indus., Inc. v. Cincinnati Sub-Zero Prods., Inc., 790 F.3d 1369, 1375 n.7 (Fed. Cir. 2015). Prior to the filing of Formycon's response, Regeneron was not on notice that Formycon would rely on inherency as part of its obviousness-type double patenting defense, let alone the specific arguments and evidence that would support inherency. Accordingly, it was proper for Regeneron to address the issue in its reply brief with the Graham Declaration, and there is no good cause to grant the motion to strike. To the extent that there are any inconsistencies among the different declarations submitted by Regeneron, the Court will take them into consideration and afford the declarations their appropriate weight as detailed herein.

Even if Formycon's motion to strike were granted, the Court would come to the same conclusion that the 98% limitation in not inherent in '594 claim 5. Formycon had the burden to present a substantial question of ODP based on its assertion that the 98% limitation is inherent in '594 claim 5, BlephEx, 24 F.4th at 1399, contrary to the Examiner's finding. Trout ¶ 235. The SS195 formulation and data were in the record independent of Regeneron's reply brief or the Graham declaration. Trout Decl. ¶ 235. While Formycon focuses exclusively on the internal data where a '594

claim 5 formulation met the 98% limitation, the Court may not cherrypick that data while ignoring the same type of data in SS195 for a formulation that did not achieve 98% native conformation. See Glaxo, 52 F.3d at 1047-48.

Even if the challenged evidence was not considered, Formycon still does not present a substantial question that '594 claim 5 necessarily meets the 98% native conformation limitation. As discussed above, Formycon's reliance on limited examples from the patent specification that meet the 98% native conformation limitation is not sufficient to show that practicing '594 claim 5 results in the 98% native conformation limitation being met each and every time, as inherency requires. The patent specification makes clear that less than 98% native conformation is acceptable, and in fact preferable, for the "stable" formulation of '594 claim 5. See Product Patent, 6:50-55 ("[The] fusion protein is preferably substantially free of aggregates . . . [which] means that at least 90% of the weight of fusion protein is not present in an aggregate at the time the fusion protein is used to prepare the pharmaceutically effective formulation."). And as discussed above, Formycon provides no evidence that a '594 claim 5 formulation at pH 6.4 and irrespective of glycosylation necessarily has 98% native conformation. Thus, Formycon's

inherency argument does not raise a substantial question of validity of the Product Patent.

e) No motivation to change a PFS to a vial.

Formycon argues that a POSA would be motivated to replace the pre-filled syringe (PFS) of '594 claim 5 with the vial recited in asserted claims 4, 7, 9, 11, and 14-17 of the Product Patent. Opp. 8-9. Here too, Formycon does not meet its burden to show a substantial question of validity.

As stated previously, obviousness addresses what is, "on balance, desirable," not what is "feasible." Winner, 202 F.3d at 1349; Orexo AB, 903 F.3d at 1272-73. The evidence need not rise to the level of teaching away to defeat the showing of motivation to modify the claim. Arctic Cat Inc. v. Bombardier Recreational Prods. Inc., 876 F.3d 1350, 1363 (Fed. Cir. 2017). Formycon cites evidence that the prior art disclosed that biologics were available in both vial and PFS formats. Opp. 8 (citing Tessier ¶¶ 226-32). However, merely showing that a modification is possible does not show that such a modification is desirable and is thus insufficient to prove obviousness. Formycon even admits that "PFS is often considered a more convenient way to administer a formulation" but argues that a vial has other advantages, namely "more stability and has fewer surfaces that can cause problems such as

aggregation." Id. at 9. Formycon, however, cites no prior art to support this assertion and that fact that both a PFS and a vial may be useful does not support replacing a PFS with a vial. Dr. Trout cited the prior art's teaching that the "most preferred" dosage form for a therapeutic protein product was "a solution formulation that is typically stored in the refrigerator and preferably in a pre-filled syringe." Trout Decl. ¶ 393 (citing Trout Ex. 40 (Nayar 2002) at 183-184). Dr. Tessier did not dispute this or address the teaching in Nayar 2002. Thus, Formycon has not presented sufficient evidence to raise a substantial question of ODP based on the POSA's motivation to modify the PFS of '594 claim 5 to the vial claimed in the Product Patent, and thus has not raised a substantial question that the vial recited in asserted claims 4, 7, 9, 11, and 14-17 of the Product Patent is obvious over the PFS of '594 claim 5.

Formycon also argues in passing that a vial would have been "obvious to try." Opp. 8. However, Formycon does not meet its burden to identify a "finite number of identified, predictable solutions" in the field of intravitreal injection. Sanofi-Aventis Deutschland GmbH v. Glenmark Pharm. Inc., 748 F.3d 1354, 1358-61 (Fed. Cir. 2014). Thus, Formycon's cursory argument cannot substitute for its failure to identify a motivation to modify a

PFS to a vial.

f) Objective evidence supports nonobviousness.

Objective evidence must be considered before concluding that a claim is obvious. In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig., 676 F.3d 1063, 1079 (Fed. Cir. 2012). Objective evidence supports the Court's holding that Formycon has failed to raise a substantial question that the asserted claims of the Product Patent are obvious over '594 claim 5. Dr. Trout explained in his declaration that "[t]here was significant industry skepticism both towards VEGF Trap molecules and using VEGF Trap molecules in the eye," "[t]he efficacy of EYLEA as an intravitreal injection demonstrated unexpected properties," and that "evidence of copying supports the nonobviousness of the [Product Patent's] Asserted claims." Trout Decl. ¶ 361-69, 416. The Court credits Dr. Trout's opinion, relying on the same evidence addressed at Mylan, and concludes, as in Mylan, that objective evidence strongly supports nonobviousness here as well. See Mylan, 2024 WL 382495, at *59-60.

It is of no matter that Dr. Trout did not consider whether the secondary evidence had a nexus to the differences between '594 claim 5 and asserted claims of the Product Patent. The Federal Circuit has held that objective evidence may be "probative of

nonobviousness even if it was not precisely limited to the point of novelty of the claimed combination." Henny Penny, 938 F.3d at 1334. While "the identified objective indicia must be directed to what was not known in the prior art, . . . 'what was not known in the prior art . . . may well be the novel combination or arrangement of known individual elements.'" Id. at 1333 (quoting Novartis AG v. Torrent Pharm. Ltd., 853 F.3d 1316, 1331 (Fed. Cir. 2017)). Dr. Trout explained, and the parties do not appear to dispute, that Eylea is an embodiment of the asserted claims. Accordingly, "there is a presumption of nexus for objective considerations when the patentee shows that the asserted objective evidence is tied to a specific product and that product is the invention disclosed and claimed in the patent." WBIP, 829 F.3d at 1329 (internal quotation omitted); see also Immunex Corp. v. Sandoz Inc., 964 F.3d 1049, 1067 (Fed. Cir. 2020) ("Nexus is appropriately presumed in this case where the court concluded that the claims are directed to the active ingredient in [the patentee's biologic product] and its method of manufacture."). Nexus can be presumed in this case because Regeneron has shown that the objective evidence is tied to Eylea and Eylea is an embodiment of the asserted claims in the Product Patent.

Moreover, even if the specific differences between the claims

of the Product Patent and '594 claim 5 were relevant, the Court still finds that the objective evidence would weigh in favor of nonobviousness. Unlike the claims of the '594 patent, the Product Patent claims require that aflibercept is glycosylated (as in Eylea) and that the composition meets the 98% native conformation limitation. As this Court found in Mylan, and as the current record reflects, "the stability of the claimed compositions, including the required 98% native conformation, indicated to the POSA that the 'there's a relatively lower risk of inflammation'" as compared to a formulation with lower native conformation (and thus more protein aggregates). Mylan, 2024 WL 382495, at *60; Trout Decl. ¶ 369.

Even without objective evidence of nonobviousness, the Court would find that Formycon has not raised a substantial question that the Product Patent is invalid for ODP. See AstraZeneca AB v. Aurobindo Pharma Ltd., 232 F. Supp. 3d 636, 649 n.8 (D. Del. 2017) ("Because Aurobindo has failed to establish a prima facie case of obviousness, the court does not address AstraZeneca's secondary considerations."); Takeda Pharm. Co. v. Handa Pharm., 2013 WL 9853725, at *66 (N.D. Cal. Oct. 17, 2013) ("[T]he absence of secondary considerations does not prove obviousness."). Nevertheless, as explained, the available objective evidence,

taken together with the other evidence of record, supports the Court's conclusion that Formycon has failed to raise a substantial question that the asserted claims of the Product Patent are obvious over '594 claim 5.

b. Written Description

Formycon argues that the Product Patent's asserted claims are invalid for lack of written description because the claim language "at least 98%" denotes a range of 98%-100% and "at least 99%" denotes a range from 99%-100%, but the highest percent native conformation disclosed in the Product Patent's specification is 99.2%. Opp. 10-11. The Court disagrees and concludes that Formycon fails to demonstrate a substantial question of invalidity based on lack of written description. This holding is consistent with the Court's holding in Mylan. See Mylan, 2024 WL 382495, at *64, 66 (crediting Dr. Trout's analysis and conclusion that "all of the Product Patent's examples have 'at least 98 percent native conformation as measured by SEC after two months'" and that the Product Patent provided "adequate written description for the asserted claims").

The specification need not describe "every conceivable and possible future embodiment of [the] invention." Cordis Corp., 339 F.3d at 1365. Open-ended claims, such as the "at least" claim

here, "may be supported if there is an inherent, albeit not precisely known, upper limit and the specification enables one of skill in the art to approach that limit." Andersen Corp. v. Fiber Composites, LLC, 474 F.3d 1361, 1376-77 (Fed. Cir. 2007) (quoting Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1572 (Fed. Cir. 1991)). "At least" claims are ubiquitous in pharmaceutical patents.[11] Formycon's expert Dr. Tessier stated that the absolute upper limit of the "at least" limitation at issue here is, at most, 100%. See Tessier ¶ 339 ("[I]n my opinion, the language 'at least' denotes a range starting at the recited value and going as high as 100%"). Dr. Tessier also testified that

[11] Patents with "at least" claims related to purity have frequently been litigated without a finding that the patent is invalid or requiring examples that reach 100% purity. See Glaxo Grp. Ltd. v. Apotex, Inc., 376 F.3d 1339, 1343 (Fed. Cir. 2004) ("Cefuroxime axetil in amorphous form essentially free from crystalline material, and having a purity of at least 95% aside from residual solvents."); Cipla Ltd. v. Sunovion Pharms. Inc., 174 F. Supp. 3d 869, 871 (D. Del. 2016) ("[p]ure and isolated Levalbuterol L-tartrate having an enantiomeric excess of at least 95%"); United Cannabis Corp. v. Pure Hemp Collective Inc., 2019 WL 1651846, at *2 (D. Colo. Apr. 17, 2019) ("[E]very independent claim describes '[a] liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is' a specified cannabinoid or combination of them."); Mylan Institutional LLC v. Aurobindo Pharma Ltd., 2016 WL 7587325, at *7 (E.D. Tex. 2016) ("A compound N-[4-[[4-(diethyl amino) phenyl] (2,5-disulfophenyl) methylene]-2,5-cyclohexadien-1-ylidene]-N-ethylethanaminium, sodium salt having a purity of at least 99.0% by HPLC.").

practically, "most proteins are not purified to [100%]." Tessier Tr. 210:21-22. Thus, the maximum percent native conformation "would be limited by what a person skilled in the art would understand to be workable," which here would be somewhat less than 100% (the theoretical maximum). Ralston Purina Co. v. Far-Mar-Co., 772 F.2d 1570, 1576 (Fed. Cir. 1985); see also FS.com Inc. v. Int'l Trade Comm., 65 F.4th 1373, 1376 (Fed. Cir. 2023) (finding the inherent upper limit to be the limit of what was technologically feasible). As stated in Andersen, the inherent upper limit need not be precisely known provided it can be shown that an inherent upper limit exists. 474 F.3d at 1376-77.

Open-ended claims, such as the "at least" claim here, need not be supported by an embodiment at that upper limit; the patent need only "enable[] [the POSA] to approach that limit." Andersen, 474 F.3d at 1377. For example, in Anderson, the patent recited an open-ended claim — "a Young's modulus rating of greater than 500,000." Id. at 1376. At trial, the evidence showed that "the inventors did not obtain results with a modulus value of greater than 1.2 million." Id. However, the Court held that there was adequate written description because "a person of skill in the art would recognize that the upper limit of the Young's modulus of the structural member would lie somewhere between the Young's modulus

of the wood fiber and that of the polymer used in the composition." Id. Thus, although the results did not reach the upper limit (which was not numerically defined), the Court held that written description was satisfied because the disclosure allowed the POSA "to approach that limit." Id. The Federal Circuit's other relevant precedent is consistent. For example, in Nalpropion Pharms. v. Actavis Labs. FL, Inc., the claims recited "at least 99%" dissolution within a certain time, and the Federal Circuit upheld written description despite citing no results between 99-100%. 934 F.3d at 1349, 1351; see also Ralston Purina, 772 F.2d at 1576 (finding written description support for claims of "at least 25% by weight" despite no disclosure of 100% by weight); FS.com, 65 F.4th at 1375-77 ("at least [98] fiber optic connections per U space" enabled despite no disclosures between 98 and upper limit of 144 connections per U space).

Under the Federal Circuit's standard, the Court finds that the Product Patent's specification amply supports the claim reciting "at least 98%" native conformation. In his declaration, Dr. Trout explained that the Product Patent includes eight examples representative of the genus, each of which "achieved 98% or greater native conformation over two months storage as measured by size exclusion chromatography." Trout Decl. ¶¶ 450-51. More

specifically, the results in the patent show between 98.5 and 99.2% native conformation for the liquid formulations tested after storage for 2-3 months. Id.; Product Patent, Tables 1-6. This led Dr. Trout to the conclusion that "the specification teaches the POSA representative formulations with the claimed elements and possession of the claimed genus." Trout Decl. ¶ 451. The Court credits Dr. Trout's analysis and conclusion, as it did in Mylan. Mylan, 2024 WL 382495, at *64. The Product Patent's multiple disclosures of native conformations less than 1% shy of 100% (the absolute upper limit for the claim term, which "in general" is not met for proteins, Tessier Tr. 210:4-211:2) meets the Federal Circuit's standard. See Product Patent Table 3 (99.2% native conformation at two months), Table 4 (99.1% native conformation at two months); Andersen, 474 F.3d at 1377.

Indivior UK Ltd. v. Dr. Reddy's Labs. S.A., 18 F.4th 1323 (Fed. Cir. 2021), the case Formycon relies on, is inapposite. In Indivior, the patent claimed a range of "about 40 wt % to about 60 wt %," but the specification disclosed neither endpoint. 18 F.4th at 1328. The only disclosures in the specification that explicitly fell within the claimed range were a disclosure of "at least 25%," which the Court notes is "quite out of the [claimed] range," and a disclosure of "at least 50%," which the Court found to be "hardly

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 133 of 203

clear support in light of other inconsistent language." Id. at 1329. The Court also rejected the post hoc attempt to "select several components [in the example tables], add up the individual values, determine the aggregate percentages, and then couple those aggregate percentages with other examples" to arrive at the claimed range. Id. at 1329. But no such post-hoc rationalization is necessary here: the Product Patent claims "at least 98%" native conformation, and 98% is simply the highest whole number achieved in each example (all of which met the claim limitation).

The Court has also considered the Federal Circuit's nonprecedential decision in Columbia Ins. Co. v. Simpson Strong-Tie Inc., 2023 WL 2733427 (Fed. Cir. Mar. 31, 2023), where the patent at issue had the opposite problem as the patent in Indivior. The patent in Columbia claimed a range, but the specification only disclosed the lower bound of the range. 2023 WL 2733427 at *4-5. There was no disclosure of any other number within the range and there was nothing in the specification to suggest to a POSA that the inventors possessed anything other than the exact lower bound of their invention. Id. As previously noted, the Product Patent contained multiple disclosures of native conformations throughout the range of 98% to 100%. Unlike in Columbia, it is clear to a POSA reading the Product Patent that inventors possessed the

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 134 of 203

entirety of the claimed subject matter as required under Andersen.

In sum, the Court holds that Formycon has not raised a substantial question of invalidity due to a lack of written description with respect to any asserted claim of the Product Patent. Because Formycon does not raise any arguments addressed to any limitation other than the 98% native conformation limitation recited in claims 1 and 26, there is no substantial question as to the Asserted Product Patent Claims (which all depend from claims 1 or 26 and are thus narrower than those claims).

C. Irreparable Harm

Regeneron "must make a clear showing that [they are] at risk of irreparable harm, . . . which entails showing a likelihood of substantial and immediate irreparable injury." See Apple, Inc. v. Samsung Elecs. Co., 678 F.3d 1314, 1325 (Fed. Cir. 2012) (Apple I) (internal quotation marks omitted). The patentee must also establish that the harm is related to the infringement, a requirement referred to as the "causal nexus" requirement. Id. at 1324.

"Irreparable injury encompasses different types of losses that are often difficult to quantify." Douglas Dynamics, LLC v. Buyers Prods. Co., 717 F.3d 1336, 1344 (Fed. Cir. 2013). Accordingly, courts recognize multiple types of irreparable harm.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 135 of 203

See, e.g., Celsis In Vitro, Inc. v. CellzDirect, Inc., 664 F.3d 922, 930-31 (Fed. Cir. 2012) ("Price erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm.").

The evidence shows that Regeneron would experience irreparable injury if Formycon launches FYB203. See infra. Harm from the infringing product's competition for the same customers "is not speculative." Trebro Mfg., Inc. v. Firefly Equip., LLC, 748 F.3d 1159, 1170 (Fed. Cir. 2014).

1. Loss of Sales and Market Share

A showing of lost market share and sales can support a finding of irreparable harm. See Robert Bosch LLC v. Pylon Mfg. Corp., 659 F.3d 1142, 1154 (Fed. Cir. 2011).

In particular, the prospect of direct competition from an infringing competitor "strongly shows a probability for irreparable harm." See Trebro Mfg., 748 F.3d at 1170-71 (recognizing a strong "probability for irreparable harm" where an alleged infringer "is a direct competitor" and explaining that "[t]he district court's blanket dismissal of evidence showing likely loss of market share and loss of access to customers was an error of law") (internal quotation marks omitted). "Loss of market share constitutes irreparable injury because market share is so

difficult to recover. . . . Moreover, [t]he right to exclude direct competition in a limited sphere, a right inherent in the grant of a patent, is irreparably harmed by the loss of sales and the competitive foothold that the infringer will gain." Indivior Inc. v. Dr. Reddy's Lab'ys S.A., 2018 WL 3496643, at *12 (D.N.J. July 20, 2018) (internal quotation marks omitted), vacated on other grounds, 752 F. App'x 1024 (Fed. Cir. 2018); see also Abbott Lab'ys v. Sandoz, Inc., 544 F.3d 1341, 1361-62 (Fed. Cir. 2008) (holding that "precedent supports" recognizing "market share and revenue loss" as irreparable harms if the infringer enters the market "while the litigation proceeds").

"Where two companies are in competition against one another, the patentee suffers the harm — often irreparable — of being forced to compete against products that incorporate and infringe its own patented inventions." Douglas Dynamics, 717 F.3d at 1345 (reversing denial of permanent injunction); see also Presidio Components, 702 F.3d at 1363 ("Direct competition in the same market is certainly one factor suggesting strongly the potential for irreparable harm without enforcement of the right to exclude.").

The likelihood of irreparable harm increases in cases involving markets with few competitors. See Lonza Walkersville,

Inc. v. Adva Biotech., Ltd., 581 F. Supp. 3d 736, 750 (D. Md. 2022) ("Given the size and nature of the relevant market . . . a sale of [the infringing product] would quite likely be a lost sale for [the patentee]."), appeal dismissed, 2022 WL 1634221 (Fed. Cir. May 24, 2022). But irreparable harm from direct competition often exists even when there are multiple competing products. See, e.g., ePlus, Inc. v. Lawson Software, Inc., 2011 WL 2119410, at *7, 9 (E.D. Va. May 23, 2011) (finding irreparable harm when there are at least eight "companies that compete in the market"), modified, 946 F. Supp. 2d 459 (E.D. Va. 2013), vacated on other grounds, 760 F.3d 1350 (Fed. Cir. 2014); SynQor, Inc. v. Artesyn Techs., Inc., 2011 WL 238645, at *1, *3 (E.D. Tex. Jan. 24, 2011) (finding irreparable harm when there were 11 competitors); Callaway Golf Co. v. Acushnet Co., 585 F. Supp. 2d 600, 619-21 & n.22 (D. Del. 2008) (finding irreparable harm when there were 17 competitors), aff'd in part, vacated in part on other grounds, 576 F.3d 1331 (Fed. Cir. 2009).

Harm from competition is not limited to harm to products that practice the patent. It exists whenever products are "competing for the same customers in the same markets," Presidio Components, 702 F.3d at 1363, or when products "meet the same needs," Broadcom Corp. v. Emulex Corp., 2012 WL 13036855, at *3 (C.D. Cal. Mar. 16,

2012), aff'd, 732 F.3d 1325 (Fed. Cir. 2013). Indeed, a patentee can establish irreparable harm even if "it does not currently practice the claimed inventions" at all. Broadcom Corp. v. Qualcomm, Inc., 543 F.3d 683, 703 (Fed. Cir. 2008); see also Presidio Components, 702 F.3d at 1363 ("Even without practicing the claimed invention, the patentee can suffer irreparable injury.").

There are only a handful of anti-VEGF medications currently on the market to treat angiogenic eye disorders, Clark Decl. ¶ 6, and Formycon does not dispute that Regeneron's Eylea products, including the vial variety, are the only anti-VEGF medications with aflibercept. Sharma Decl. ¶ 25 Fig. 2 (identifying Eylea and Eylea HD as the only "competitor drugs" with an "aflibercept" molecule). While other medications exist that treat the same conditions as Eylea, Regeneron has presented testimony that those medications are clinically inferior to Eylea in certain respects. Clark Decl. ¶ 7; Mylan Trial Tr. 172:16-21 (Yancopoulos), Regeneron Pharms., Inc. v. Mylan Pharms., Inc., No. 22-cv-61-TSK (N.D.W. Va. June 12, 2023), ECF No. 558; id. at 309:13-20 (Csaky) ("[Ophthalmologists] all kind of believe that Eylea still is the best anti-VEGF agent out there."); id. at 861:24-862:4 (Albini) (discussing the safety issues with Beovu).

For example, Lucentis, the leading treatment for angiogenic eye disorders before Eylea's launch, must be dosed monthly, compared to Eylea's extended dosing interval of every eight weeks. Mylan Trial Tr. 123:15-124:5 (Yancopoulos). Other medications come with safety concerns or result in patients gaining less visual acuity than similarly situated patients taking Eylea. Clark Decl. ¶ 7. Eylea is thus the preferred treatment of many ophthalmologists. See e.g., id.; Mylan Trial Tr. 1917:12-1918:2 (Csaky), Regeneron Pharms., Inc. v. Mylan Pharms., Inc., No. 22-cv-61-TSK (N.D.W. Va. June 22, 2023), ECF No. 568; see also id. at 172:169-210 (Yancopoulos) (Eylea viewed as the "gold standard").

The evidence shows that if an aflibercept biosimilar launches, healthcare providers are likely to view it as interchangeable with Eylea. Sheridan Decl. ¶¶ 32-33 ("[B]iosimilars are known as interchangeable products."). Thus, while other anti-VEGF medications such as Lucentis and Avastin have not been viewed by clinicians as comparable to Eylea, FYB203 is nearly identical to Eylea, with the same vial formulation, indications, and effectiveness. Sheridan Ex. F-1 at -042 (ECF No. 101-24). Indeed, the sample label information produced by Formycon anticipates a formal statement of interchangeability from FDA. Id. The Court finds that providers are likely to treat it as such

and could choose to use FYB203 instead of Eylea.

Additionally, Formycon's documents show that part of their sales strategy is to compete on price. [redacted] Sheridan Ex. F-2 at -654. [redacted] See Sheridan Ex. F-4.

The Court also finds that, if FYB203 is permitted to launch, it will compete with all of Regeneron's Eylea products — Eylea sold in a vial, Eylea PFS, and Eylea HD. Because a patient only needs to take one anti-VEGF drug at any given time, a sale for Defendants is likely a lost sale of one of these products for Regeneron. Sheridan Decl. ¶ 62; Clark Decl. ¶ 8. Thus, if FYB203 launches, Regeneron will likely lose sales and market share for all three of its Eylea products.

Starting with Regeneron's original product, the parties agree that [redacted] Formycon's documents [redacted] Sheridan Ex. F-4 (ECF No. 101-24). As Formycon's expert, Arun Sharma acknowledges, roughly [redacted] of Regeneron's Eylea unit sales come through the 2mg vial presentation. Sharma Decl. ¶ 47; Clark Tr. 201:2-6. Accordingly, [redacted].

[redacted] Sharma Decl. ¶ 47. He also asserts that "the impact of FYB203's launch on Eylea® HD is likely to be minimal, if any." Id. ¶ 49.

The evidence, though, demonstrates that FYB203 is likely to compete with Eylea's PFS product and Eylea HD as well.

Formycon's documents show [redacted] Sheridan Ex. F-3, at -269

[redacted] Sharma Tr. 155:12-156:19.

Formycon similarly disputes that sales of Eylea HD will be harmed by the launch of FYB203, calling such claims "speculative." Opp. 19. But here, too, [redacted]. Sheridan Ex. F-2 at -657 [redacted].

Moreover, the introduction of aflibercept biosimilars so soon after the launch of Eylea HD "threatens to permanently and adversely impact the uptake, perception, and long-term adoption" of Eylea HD. Sheridan Decl. ¶ 72; Clark Decl. ¶ 12. Mr. Sharma apparently agreed, acknowledging in his deposition that the launch of a new molecule would "play a role in the uptake of a product," specifically Eylea HD. Sharma Tr. 149:4-20. Regeneron's evidence demonstrates that "most payors" are likely to implement policies

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 143 of 203

preferencing a less expensive biosimilar over Eylea HD, an effect which Mr. Sharma does not dispute but rather argues is "further down the road." Sharma Tr. 226:21-227:21. In light of the evidence presented, the Court finds that FYB203 is likely to compete with Eylea PFS and Eylea HD as well as Eylea 2 mg vial presentation.

Regeneron presented evidence that it will lose approximately [redacted] in net sales across all three Eylea products in 2024 alone if biosimilars, including FYB203, are permitted to launch. Sheridan Decl. ¶ 66. Regeneron anticipates it would lose [redacted] Id. ¶¶ 67, 69; Sheridan Ex. 99 at -480-81 (ECF No. 101-34). Regeneron's Vice President of the Ophthalmology Commercial Business Unit predicts that "the launch of one or more infringing EYLEA® biosimilars would all but certainly reduce EYLEA®'s and EYLEA® HD's sales and market share in each and every market in which our products compete." Clark Decl. ¶ 8; id. (estimating the loss of [redacted]

Regeneron has submitted several independent investment analyst reports forecasting [redacted] Sheridan Ex. 99 at -480-81; Sheridan Decl. ¶ 69 (collecting analyst reports

identifying a "gradual decline in Eylea franchise unit market share from ~48% in 2022 to roughly ~30% in 2032 (about 37.5% erosion) as increased competition from 2 mg Eylea biosimilars will start from as early as 2024"; an "approximately 37% market erosion from biosimilars (of Eylea) in medium-term"; and that "27% (3/11) of [RBC Capital Markets's] respondents expect to switch wAMD/DME [patients] to biosimilar Eylea regardless of discount").

The Court concludes that Regeneron will likely be irreparably harmed by the entry of the FYB203 biosimilar because Regeneron will be "forced to compete against products that incorporate and infringe its own patented inventions." Douglas Dynamics, 717 F.3d at 1345; see also Abbott Lab'ys, 544 F.3d at 1361-62.

One matter requires clarification – what defines the universe of potential irreparable harm to Regeneron. Regeneron urges the Court to consider FYB203's alleged potential impact on Regeneron's entire suite of Eylea product offerings – vial, PFS and Eylea HD. This Court declined that invitation in Mylan and in the Samsung cases. It does so again here for the same reasons. As noted in Mylan, the claims resolved in the Court's Trial Decision were not directed to the aflibercept molecule generally, but to a vial deli very mechanism specifically. See In re: Aflibercept Patent Litigation, ECF No. 794, at 16-24.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 145 of 203

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

The Second Circuit explained the difference in the market between anti-VEGF medications presented in the form of a vial and those presented in the form of a PFS:

> For several years after they were first introduced, anti-VEGF medications [like aflibercept] were packaged into vials and administered in a two-step process. A doctor would first fill a syringe with medicine from an anti-VEGF vial and then inject the drug into a patient's eye. The newer versions of the medications are sold in prefilled syringes ("PFSs") and administered in one step. PFSs contain the same medication as vials but are injected directly into the patient's eye. This simpler process carries a significantly lower risk of complications and infections and is now the preferred way of administering anti-VEGF medications.

Regeneron Pharms., Inc. v. Novartis Pharma AG, 96 F.4th 327, 332 (2d Cir. 2024). [redacted]

[redacted]

Given the above and other record evidence considered, the 2 mg aflibercept vials, 2 mg aflibercept PFS, and the 8 mg Eylea HD products represent distinct products and markets for purposes of assessing irreparable harm.

The Court concludes, however, that Regeneron will likely be irreparably harmed by the entry of the biosimilar FYB203 because Regeneron will be "forced to compete against products that incorporate and infringe its own patented inventions." Douglas Dynamics, 717 F.3d at 1345; see also Abbott Lab'ys, 544 F.3d at 1361-62.

Formycon argues that Regeneron will not suffer irreparable harm in the form of lost sales because "Regeneron's losses during the short-term period pertinent to its motion are likely to be . . . limited" and because "Formycon's biosimilar would only account for a fraction of that erosion, and likely a small fraction." Opp. 20. Neither of these arguments is compelling.

First, the launch of a biosimilar would fundamentally alter the dynamics of the anti-VEGF landscape. As noted, Regeneron's Eylea vial product competes with a few different anti-VEGF medicines. But the treatment landscape is still relatively small. And competition from these other products is irrelevant because

none of these products use aflibercept or Regeneron's patented technology. The dispositive finding for this Court's analysis is that, if FYB203 launches, Regeneron would be forced to compete with a product that incorporates its own patented technology.

The Court further concludes that the harm from competition with an infringing product is all the more acute here because the infringing product will be marketed as a biosimilar. By its nature, a biosimilar is a near-exact clinical substitute for its reference product. If FYB203 enters the market it will appear, not merely as a direct competitor, but as a purported replacement for Eylea. And physicians are in fact likely to directly substitute it for Eylea. Sheridan Ex. F-1 at -042 (identifying the same vial formulation, indications, and effectiveness as Eylea and a statement of interchangeability from FDA); [redacted]

Formycon's argument that its biosimilar would only account for a "fraction" of the market share erosion is unavailing. Opp.

20. "Given the size and nature of [the anti-VEGF patient population] . . . a sale of [FYB203] would quite likely be a lost sale for [Regeneron]." Lonza Walkersville, 581 F. Supp. 3d at 750. "Loss of market share constitutes irreparable injury because market share is so difficult to recover. . . . Moreover, [t]he right to exclude direct competition in a limited sphere, a right inherent in the grant of a patent, is irreparably harmed by the loss of sales and the competitive foothold that the infringer will gain." Indivior Inc., 2018 WL 3496643, at *12 (internal quotation marks omitted). In light of this evidence, the Court concludes that Regeneron has demonstrated irreparable harm from FYB203 competition with the Eylea vial product.

Leaving aside Regeneron's Eylea 2 mg's PFS presentation and Eylea HD, the direct competition between FYB203 and Regeneron's Eylea 2 mg vial supports a finding of irreparable harm. [redacted] Sheridan Ex. 4. Even if the rest of Regeneron's sales were somehow immune from harm, Regeneron continues to sell Eylea 2mg vials, [redacted].

Formycon asserts that Regeneron's lost market share is quantifiable and that legal remedies are adequate to compensate

Regeneron. Opp. 21; Sharma Decl. ¶¶ 56-57. This Court disagrees. Courts regularly recognize that being forced to "compete against products that incorporate and infringe [one's] own patented inventions" creates irreparable harm. Douglas Dynamics, 717 F.3d at 1345. Formycon's cases are not to the contrary.

In Takeda Pharmaceuticals U.S.A., Inc. v. Mylan Pharmaceuticals Inc., the plaintiff had made "a bare assertion of irreparable harm" consisting of "nonspecific and unsupported assertion[s]" that the infringer's sales "likely will cause" irreparable harm. 967 F.3d 1339, 1349-50 (Fed. Cir. 2020) (internal quotation marks omitted). That is not the case here, in which Regeneron has presented documentary evidence and witness testimony supporting such a finding. Formycon also cites to Biogen Inc. v. Sandoz Inc., 2023 WL 7130655 (D. Del. June 29, 2023). That case, though, simply confirms the general rule that "the availability of adequate monetary damages belies a claim of irreparable injury." Id. at *4 (quoting Takeda, 967 F.3d at 1349). There is no way to know how many patients Regeneron will lose, permanently, due to the disruption caused by FYB203 and those losses are likely to be permanent. Sheridan Decl. ¶¶ 75-76. This Court concludes that Regeneron has shown its likely harm due to lost market share and sales is not addressable through legal

remedies.

2. Price Erosion

When a competing product launches, the patented product often has to drop its price to remain competitive. This drop in price is consistently recognized as a source of irreparable harm. See, e.g., Celsis In Vitro, 664 F.3d at 930 (affirming price erosion as source of irreparable harm); Sanofi-Synthelabo v. Apotex, Inc., 470 F.3d 1368, 1383 n.9 (Fed. Cir. 2006) (same); Abbott Lab'ys, 544 F.3d at 1362 (same).

"The phenomenon of price erosion in the pharmaceutical industry is well known." Hoffmann-La Roche Inc. v. Cobalt Pharms. Inc., 2010 WL 4687839, at *12 (D.N.J. Nov. 10, 2010), modified, 2012 WL 458435 (D.N.J. Feb. 9, 2012). And "[p]rice erosion is most likely to occur in cases . . . in which no generic competitors have yet entered the marketplace, placing the patentee in an exclusive position." Id.

Price erosion is typically irreversible even if the infringing product exits the market because returning prices to pre-infringement levels risks loss of goodwill and reputation with payors and customers. Sanofi-Synthelabo v. Apotex Inc., 488 F. Supp. 2d 317, 343 (S.D.N.Y. 2006) (patentee would be "harmed by loss of consumer good will by customers who will have grown

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 151 of 203

accustomed to lower prices" if it restored pre-infringement pricing), aff'd, 470 F.3d 1368 (Fed. Cir. 2006); Celsis In Vitro, 664 F.3d at 930 (same).

Regeneron has also shown that Formycon's launch will force Regeneron to reduce the prices of its Eylea products. Clark Decl. ¶¶ 8-10; Sheridan Decl. ¶ 62. [redacted]

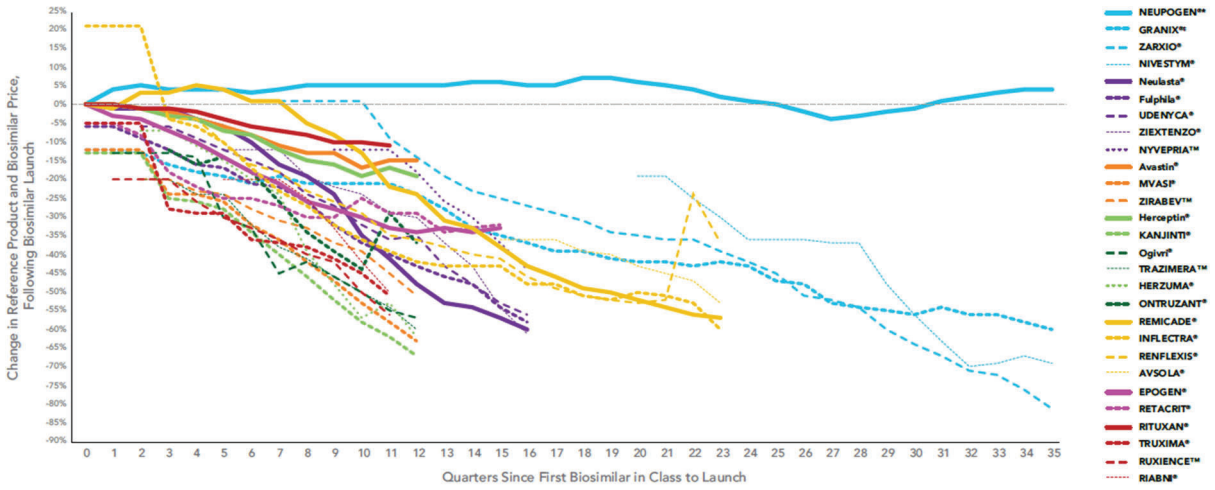
a. The launch of a biosimilar typically causes price erosion

[redacted] The WAC is the price a drug manufacturer lists, not including any discounts, rebates, or negotiated price reductions. Id. ¶ 35. And biosimilars launch at an average ASP — the average price that manufacturers charge purchasers after discounts and rebates — that is half that of the branded drug. Id. ¶¶ 35, 38. [redacted]

Samsung Bioepis's Biosimilar Market Report for Q1 2024 states

that "[b]iosimilar launches have led to significant price decreases over time," and "[o]n average, ASP declined by 41% three years . . . post first biosimilar launch with more mature markets demonstrating increasing price concessions." Sheridan Ex. 33 at 12 (ECF No. 101-28).

Amgen has observed the same trend, stating in its 2022 Biosimilars Trend Report that the ASP "for both reference products and biosimilars" "is declining, due to competition." Sheridan Ex. 52 at 6 (ECF No. 101-30); Sheridan Decl. ¶ 39. This same report shows that biosimilar prices "have decreased at a negative compound annual growth rate . . . of -9% to -24%," and "[t]he prices of most reference products have decreased at a negative [compound annual growth rate] of -4% to -21%." Sheridan Ex. 52 at 6. Amgen's 2022 Report contains a graph illustrating the trend in reference products' declining ASP following the launch of biosimilars:

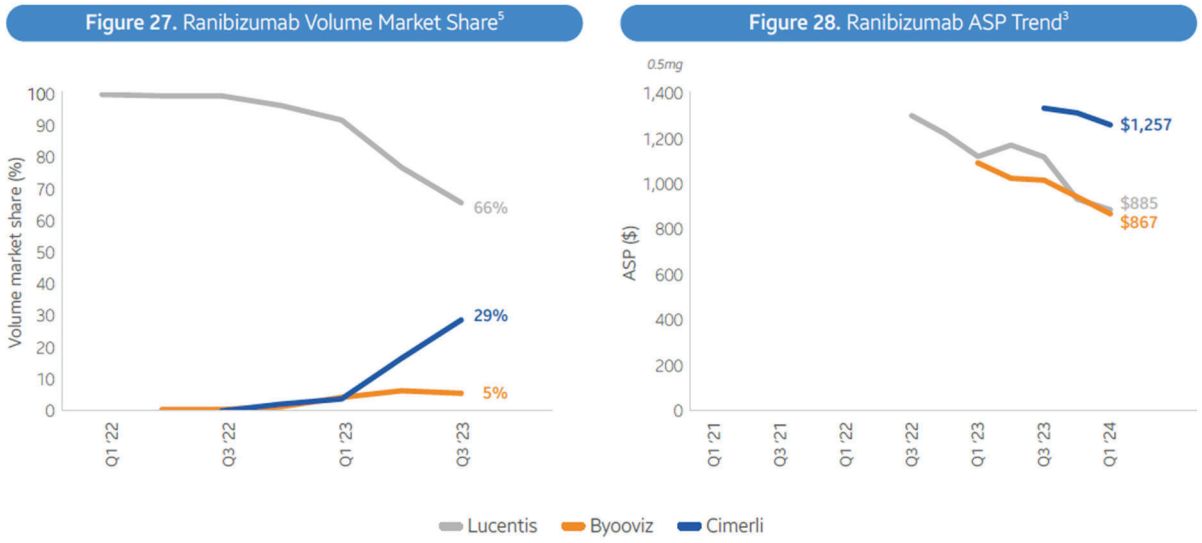


Id. 13 (Fig. 5); Sheridan Decl. ¶ 39.

Ophthalmic drugs are not immune from this trend, as the launch of ranibizumab biosimilars has shown. Sheridan Decl. ¶ 41; Sheridan Ex. 33 at 9 ("Recent ranibizumab biosimilar launches have already led to lower reference product ASP costs."). When these biosimilars entered the market, Genentech, the maker of the branded biologic Lucentis, was forced to reduce its ASP to or below the ASPs of the competing biosimilars. Sheridan Decl. ¶ 41. As of Q1 2024, the ASP of all ranibizumab products has declined 23% since the biosimilars' launch. Sheridan Ex. 33 at 22. Despite these price reductions, Lucentis continued to lose significant market share to ranibizumab biosimilars; as of Q3 2023 the two ranibizumab biosimilars hold a combined market share of 34%. Id.

The figures below, featured in Samsung Bioepis's 2024 Market

Report, illustrate the decline in Lucentis's ASP and market share that ranibizumab biosimilars caused:



Id. (Figs. 27 and 28).

However, although biosimilars often launch at a discount to the reference products price (on average at an ASP that is half the cost of the reference product), price erosion from a biosimilar launch can occur regardless of the launch price. Sheridan Decl. ¶ 38.

b. Regeneron will likely experience price erosion if FYB203 launches

The downward pricing pressure Eylea will face after FYB203's launch is different in kind from ordinary, non-biosimilar competition with other anti-VEGF medications. Almost across the board, biosimilars lead to permanent price erosion of the reference

drug. That is because their launch causes the reference drug to compete for the first time with its own formulation. The same will happen with Eylea if FYB203 is allowed to launch.

[redacted]

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 156 of 203

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

Indeed, Formycon's own evidence suggests that Eylea will likely experience price erosion in response to FYB203's launch strategy. Formycon's documents [redacted]

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 157 of 203

[redacted] Sheridan Ex. F-2 at -654. Further, Formycon's [redacted]. Sheridan Ex. F-4.

Despite this evidence, Formycon asserts that Regeneron will not suffer price erosion because Regeneron's estimates are speculative, "many reference biologics have suffered little to no price erosion upon biosimilar launch," and because Medicare payors "are currently not seeking to proactively manage costs in this space." Opp. 19. These arguments are unpersuasive.

Formycon argues that Mr. Clark's testimony and Dr. Sheridan's analysis regarding price erosion is "plainly speculation." Opp. 19. However, as discussed above, Mr. Clark's testimony is based on more than "speculation" — it is based on significant experience in the field. Clark Decl. ¶ 1. Further, price erosion is a known phenomenon with the launch of competing biosimilars. Indeed, [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]. Sharma Decl. ¶ 54. Because [redacted] the Court finds that Regeneron, too, will likely experience price erosion as it competes with a new biosimilar entrant.

Further, if Regeneron is forced to lower prices on Eylea and Eylea HD because of biosimilar entry, such price erosion will likely be permanent. [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

Mr. Sharma suggests in his declaration that Regeneron could later reverse rebates and discounts. Sharma Decl. ¶¶ 61-66. In support, he advances two main arguments: first, he suggests that Regeneron could structure its discounts to be "conditional" upon FYB203 remaining in the market or reverse disadvantageous contracting practices at a later date. Sharma Decl. ¶¶ 63-64. Second, Mr. Sharma argues that Regeneron can return to the pre-launch status quo because "Payers' choice set after the launch and withdrawal of FYB203 would be the same as it would have been in a world without FYB203 at all" and any losses would be reversible. Id. ¶¶ 65-66. Mr. Sharma, though, does not have experience working in the ophthalmology or pharmaceutical industries, and neither argument is consistent with industry practice. [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted] Should Regeneron nonetheless attempt to revert prices on Eylea to their original values despite the foregoing, it would suffer further harm in the form of reputational damage and loss of goodwill.

Given ample evidence in the record showing declines in reference product pricing following a biosimilar's launch, and the [redacted] the Court finds that Regeneron is likely to suffer price erosion if FYB203 is allowed to launch. And based on this same body of evidence, the Court finds that the price of Regeneron's Eylea is unlikely to return to pre-launch levels even if FYB203 is later taken off the market following trial and a decision on the merits.

[redacted] "[p]rice erosion is most likely to occur in cases . . . in which no generic competitors have yet entered the marketplace, placing the patentee in an exclusive position." Hoffmann-La Roche, 2010 WL 4687839, at *12. Currently, Regeneron is the only company with an aflibercept product on the market, [redacted]

[redacted]

Moreover, Regeneron's irreparable harm from price erosion would be irreversible even if Formycon eventually loses at trial and FYB203 exits the market. Contrary to Mr. Sharma's assertions, Sharma Decl. ¶¶ 63-64, contractual price concessions would be locked in for at least the terms of the contracts. And, because Medicare reimbursement rates lag market pricing, future price increases would leave physicians paying a higher rate to purchase Eylea than they were being reimbursed. [redacted] In short, Regeneron could only raise its prices by risking the "loss of consumer good will by customers who will have grown accustomed to lower prices." Sanofi-Synthelabo, 488 F. Supp. 2d at 343.

3. Disruption of Patentee-Payor Relationships

When "third-party payors control a substantial portion of . . . sales," the entry of a competing drug product has the "potential to irreversibly alter the reimbursement relationship" and create irreparable harm to patentees. Hoffmann-La Roche, 2010

WL 4687839, at *12. These harms are distinct from price erosion and arise from irreversible formulary position losses. And courts have recognized this economic reality in the pharmaceutical market when an infringing drug launches. See King Pharm. Inc. v. Corepharma, LLC, 2010 WL 1850200, at *3 (D.N.J. May 7, 2010) (crediting economist's testimony that "payors . . . will move [the patentee]'s patented product off of their formularies in the presence of generic competitors").

Harm to payor relationships and status are well-recognized as irreparable. See Indivior Inc., 2018 WL 3496643, at *12 ("Courts have found that a reduction of market share due to the loss of formulary status and a change in tier pricing, constitutes irreparable harm."); Abbott Lab'ys, 544 F.3d at 1361-62 (similar).

The Court finds that the entry of FYB203 will "irreversibly alter the reimbursement relationship" and impose long term damage to Regeneron. Hoffmann-La Roche, 2010 WL 4687839, at *12. FYB203's launch is also likely to disrupt Regeneron's relationships with payors permanently. Sheridan Decl. ¶¶ 85-87. When a lower-cost treatment (e.g., a biosimilar) comes on the market, [redacted] This requirement is known as a "step

edit," referring to patients having to "step through" the cheaper alternative before trying the more expensive drug. Clark Decl. ¶ 14. Once insurers and other payors implement a step edit, the more expensive medication becomes a second-line treatment, [redacted] Sheridan Decl. ¶¶ 64, 76, 84; Clark Decl. ¶ 11. Harms from step edits are incalculable because there "is no effective way to . . . ascertain the people who do not knock on the door . . . because of the existence of the infringer." Celsis In Vitro, 664 F.3d at 930 (citation omitted).

Regeneron's evidence showed that Eylea is now a first-line treatment for [redacted] patients with angiogenic eye disorders. Clark Decl. ¶ 14; Sheridan Decl. ¶ 64. In other words, those patients receive insurance coverage for Eylea without first trying another treatment option or experiencing a "single step edit." And only [redacted] are currently subject to a "double step edit" under which they must try two other medications before receiving coverage for Eylea. Sheridan Decl. ¶ 64; Clark Decl. ¶ 14.

[redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted] It is thus reasonable to expect that an aflibercept biosimilar launching likely will encourage more payers to implement an Eylea step edit. This effect will be more pronounced if the biosimilar launches at a substantial discount relative to Eylea. [redacted] As discussed above, [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

Harm to Regeneron from step edits is likely irreversible.

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

This Court concludes that the likely harm to Regeneron from a "loss of formulary status and a change in tier pricing, constitutes irreparable harm." Indivior Inc., 2018 WL 3496643, at *12.

4. Reputational Harm

As this Court has already noted in related cases, reputational injury is a well-recognized form of irreparable harm. Douglas Dynamics, 717 F.3d at 1344-45. This can occur when a doctors or patients know that a patentee is responsible for removing an available drug. See AstraZeneca LP v. Apotex, Inc., 623 F. Supp. 2d 579, 613 (D.N.J. 2009) ("AstraZeneca claims that an unauthorized launch by Apotex (followed by a subsequent exit) would result in intangible and unquantifiable damage to AstraZeneca's reputation and goodwill. For example, they assert that doctors who would have prescribed Apotex's BIS may blame AstraZeneca for the sudden unavailability of Apotex's generic BIS once Apotex is forced to leave the market. . . . The Court agrees that an unauthorized

launch by Apotex would have some intangible effects on AstraZeneca's goodwill."), supplemented, 623 F. Supp. 2d 615 (D.N.J. 2009), aff'd, 633 F.3d 1042 (Fed. Cir. 2010); Baxalta Incorp. v. Genentech, Inc., 2018 WL 3742610, at *11 (D. Del. Aug. 7, 2018) (where defendant already launched its product prior to the preliminary injunction hearing, patentee would suffer reputational harm when doctors would know that patentee was responsible for removing an available drug).

Regeneron has established that it will suffer reputational harms in the pharmaceutical community and among healthcare professionals if FYB203 is permitted to launch but later is removed from the market. If FYB203 launches and then is taken off the market as a result of litigation, providers and, most importantly, patients will blame Regeneron for the loss of their chosen treatment. Sheridan Decl. ¶¶ 85-87. Unlike a course of antibiotics or a temporary pain-relief medication, patients must take aflibercept regularly for a long time. Sharma Decl. ¶ 21 ("The recommended treatment regime with Eylea® is an injection every 4 weeks . . . for the first 12 weeks (3 months), followed by an injection once every 8 weeks (2 months); Mylan Trial Tr. 137:3-14 (Yancopoulos). FYB203's removal from the market after a trial, once it has been administered to perhaps thousands of patients,

will disrupt these patients' course of treatment. Not only may patients feel uncomfortable switching medication mid-course; they will also have to seek approval from private insurers and Medicare and Medicaid for a different product, a process likely to interrupt their treatment. Sheridan Decl. ¶ 87.

Mr. Sharma testified that Dr. Sheridan's testimony regarding loss of goodwill and reputation were "unsupported and flawed." Sharma Decl. ¶¶ 67-71. However, Mr. Sharma testified that he has previously provided analytical support for an expert declaration advancing similar theories of reputational harm. Sharma Tr. 142:6-13; 213:12-214:19. Dr. Sheridan's opinion is consistent with the other evidence presented and consistent with opinions previously advanced by Mr. Sharma's colleague. The Court finds that this harm to Regeneron's relationships with its customers and their treatment regimens would be a likely result were FYB203 permitted to launch.

Formycon argues that Baxalta, the case cited by Regeneron to establish that such reputational harms are legally cognizable, "proves too much." Opp. 23. This is incorrect. In Baxalta, the accused drug was already on the market and would remain available for a subset of patients irrespective of any injunction, and doctors would blame the patentee for removing that drug as a

treatment choice for the remainder of patients. See 2018 WL 3742610, at *11. Formycon also ignores altogether the case of Douglas Dynamics. Because Regeneron has established that it likely would be blamed for the removal of FYB203 should FYB203 launch and then be removed from the market post-judgment for Regeneron, Regeneron has demonstrated irreparable reputational harm.

5. Marketing and Training Costs

Courts often consider the effect of infringing activity on the patented product's salesforce and marketing activity. See Sanofi-Synthelabo, 488 F. Supp. 2d at 343 ("Sanofi has shown for the purposes of this motion that it will be irreparably harmed . . . by layoffs of employees involved in marketing Plavix," a patented product, upon the launch of a lower cost generic); Bio-Rad Lab'ys, Inc v. 10X Genomics, Inc., 967 F.3d 1353, 1378 (Fed. Cir. 2020) (crediting the trial court's finding that the patentee would have to "increase its marketing costs" in considering irreparable harm).

Regeneron presented evidence that it would have to invest in new marketing and training efforts upon the launch of one or more infringing biosimilars, [redacted]

[redacted] Clark Decl. ¶ 18. Neither Mr. Sharma's declaration nor Formycon's briefing addresses Mr. Clark's testimony. As such, the Court credits Regeneron's representations that it will have to develop new training programs in response to FYB203 launching. Forcing a patentee to "increase its marketing costs" can contribute to the irreparable harm analysis. See Bio-Rad Lab'ys, 967 F.3d at 1378. The likely increased costs—to market both Eylea and Eylea HD—would irreversibly divert resources from other projects that Regeneron might undertake in the absence of infringement, and contribute to the irreparable harm suffered by Regeneron.

6. Research and Development

Regeneron also suggests, as a separate form of irreparable harm, that its research and development (R&D) funding and spending will be negatively affected if FYB203 launches. The Court rejects this as a basis of irreparable harm here.

As it did in Mylan and the Samsung cases, the Court again finds Regeneron did not meet its burden with this element of claimed irreparable harm. See In re: Aflibercept Patent Litigation, ECF No. 162, at 42-46 and ECF No. 171, at 150-152. The Federal Circuit cautioned against allowing generalized assertions that loss of revenue would lead to a loss of research and development opportunities because

> that claim of injury is not materially different from any claim of injury by a business that is deprived of funds that it could usefully reinvest. If a claim of lost opportunity to conduct research were sufficient to compel a finding of irreparable harm, it is hard to imagine any manufacturer with a research and development program that could not make the same claim and thus be equally entitled to preliminary injunctive relief. Such a rule would convert the "extraordinary" relief of a preliminary injunction into a standard remedy, available whenever the plaintiff has shown a likelihood of success on the merits.

Eli Lilly & Co. v. Am. Cyanamid Co., 82 F.3d 1568, 1578 (Fed. Cir. 1996) (affirming denial of injunction against generic drug competitor). This principle also differentiates a case upon which Regeneron relies, Amgen v. F. Hoffman-LaRoche, 581 F. Supp. 2d 160, 212 (D. Mass. 2008). In Amgen, the district court noted that Amgen's infringed patents were directed to "the source" of "what enables mass production and commercial viability" of the drug at issue. 581 F. Supp.2d at 195. The patents also were "admittedly 'the foundation of Amgen's business,'" and any question into their value or ability to keep other competitors off the market would cause Amgen to lose access to research and development funds. Id. at 212. Regeneron's cited cases also do not support a finding of irreparable harm. In Mylan Institutional, for example, there was evidence of record that the harm to R&D would result from the loss

of "half or more of [patentee's] revenue," [redacted] See Mylan Institutional LLC v. Aurobindo Pharma Ltd, 2016 WL 7587325, at *23 (E.D. Tex. Nov. 21, 2016). The same is true of Regeneron's Janssen case. See Janssen Prods., L.P. v. Lupin Ltd., 109 F. Supp. 3d 650, 697 (D.N.J. 2014) (irreparable harm where evidence indicates "Janssen would lose 70 to 80 percent of its sales upon a generic launch"). Therefore, consistent with this Court's findings in Mylan and the Samsung cases, Regeneron's claimed impact on R&D prospects finds no basis in either fact or law, and the Court does not rely upon it in issuing the permanent injunction.

7. Near-Term Harms to Regeneron

The evidence indicates that FYB203's launch will harm Regeneron's Eylea products on a timeline that requires injunctive relief. [redacted]

Formycon argues that because the uptake of biosimilars in ophthalmology will be slow, any possible irreparable harm is unlikely to materialize on a timeline sufficient to warrant injunctive relief. Opp. 20; Sharma Decl. ¶¶ 40-48. The record does not support that argument.

a. Regeneron is likely to experience immediate share loss

As an initial matter, anti-VEGF drugs with biosimilars have seen significant market share erosion over a short time period. For example, despite launching in mid-2019, as of 2020, bevacizumab biosimilars achieved a higher share of the market than branded Avastin. Sheridan Ex. 33 at 14. By Q3 2023, biosimilars made up 87% of all bevacizumab sales. Id.

This experience is consistent with industry expectations for biosimilars generally. The Samsung Bioepis Biosimilar Market Report for Q1 2024 states: "On average, biosimilars gain 53% market share within three years (12 quarters) post initial launch." Sheridan Ex. 33 at 11. Those averages, however, reflect data for biosimilars with variable uptake speeds, which can be categorized as fast or slow. Id. Ophthalmology biosimilars are classified as exhibiting a "fast uptake speed." Id.

Formycon's argument that ophthalmologists will be slow to adopt an aflibercept biosimilar is thus outdated. For example,

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 174 of 203

Formycon points out a quote from a 2022 Cardinal Health report for the proposition that "biosimilar uptake in ophthalmology will be slow." Opp. 20; Sharma Ex. 8 at -253 (ECF No. 175-4); Clark Ex. 3 at -253 (same report). However, as the page itself makes clear this study predates the launch of Byooviz, a ranibizumab biosimilar, which Cardinal Health "expected to launch in June 2022. Sharma Ex. 8 at -253; Clark Ex. 3 at -253 (same report). Since then, ophthalmology biosimilars have experienced additional uptake since then, and ophthalmologists are likely aware that others are in the pipeline. Sheridan Ex. 33 at 11 (Samsung Bioepis Biosimilar Market Report showing rapid uptake of Ranibizumab (Lucentis) biosimilars in the first four quarters post-launch). While ophthalmologists may have hesitated to embrace an ophthalmology biosimilar before any were available, these attitudes have likely changed now that doctors have been using such products for years.

[redacted]

In fact, the most recent survey data from the same group that conducted the earlier study shows that ophthalmologists are more comfortable prescribing biosimilars today. Samsung Bioepis's

recent study on biosimilars noted "Fast Uptake Speed" as a feature of "[o]ncology, pegfilgrastim and ophthalmology biosimilars." Sheridan Ex. 33 at 11. There is no reason to credit the idea that physicians will be hesitant to prescribe biosimilars when the data shows the opposite and continues to trend in that direction.

b. Regeneron is likely to experience immediate price erosion

Regeneron is also likely to experience immediate price erosion, as demonstrated by the example of ranibizumab biosimilars. [redacted] Lucentis's experience thus presents applicable evidence that ophthalmology biosimilar entry will cause price erosion of the reference product, and it also suggests that Eylea's price erosion may be particularly steep. [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

The Court finds that price erosion is likely to occur as soon as aflibercept biosimilars launch, [redacted]

c. Regeneron will likely experience immediate harm to payor relationships

Regeneron also faces substantial risk that its Eylea vial product – the subject of the Asserted Product Patent – will become subject to step edits shortly after a biosimilar's launch. [redacted]

** SEALED **

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]

d. FYB203's launch will immediately cause Regeneron's other harms

Regeneron's marketing and training efforts would occur immediately following any FYB203 launch, and its most significant reputational harms would likely be incurred whenever FYB203 is removed from the market, such as after a final judgment of infringement is issued.

Accordingly, the Court finds it likely that Regeneron would suffer immediate harm from FYB203 launching.

8. Complexities in the Competitive Landscape

Accepted methods of calculating lost profits would likely not account for the harm to Regeneron from FYB203 launch.

First, a damages expert quantifies lost profits in a patent infringement matter based on the but-for competitive landscape; that is, an analysis of what the competitive market would have been at a particular moment in time absent an infringing product's entry. Sheridan Decl. ¶ 88. Where the marketplace at issue is dynamic or in flux, limiting the analysis to a particular moment

in time requires simplifying assumptions and tends to understate damages. Id.

The market for anti-VEGF ophthalmic treatments is in flux, given the entry and exit of several competing products, approvals of new indications for existing products, and changing patient populations. Id. ¶¶ 89, 99-100. Eylea currently faces competition from non-infringing products — other anti-VEGF biologics like Avastin and Lucentis — which in turn have their own biosimilars and may generate yet more biosimilar entrants. Id. ¶ 90. In addition, up to [redacted] other aflibercept biosimilars could seek to launch in 2024 unless enjoined, with more to follow. Id. Isolating and fully capturing the impact of one biosimilar would be difficult, if not impossible. Id. ¶ 93. And the market position of Eylea HD is particularly dynamic, given the product's recent launch. Regeneron will have to adjust its marketing strategies in response to each entry and exit, which will affect the market in turn. Id. ¶¶ 91, 95.

Second, the harms to Regeneron from price erosion are also not readily calculable or compensable. The evidence showed that it will be nearly impossible to calculate and fully compensate for price erosion. Id. ¶¶ 92-93. This is because, in part, the price erosion will extend beyond any damages period and may impact future

price negotiations in unquantifiable ways. Id.; [redacted]

Third, the impact of payor policies will be difficult to calculate over the life of the product and are likely to be undervalued in any such calculation. If payors implement step edits, moving patients away from Eylea, many of these customers will never purchase Eylea. There is no way to know how many patients Regeneron will lose because of these step edits, and those losses are likely to be permanent. Sheridan Decl. ¶¶ 75-76. The parties thus could not quantify adequately the patients who would have been treated with an Eylea product had they not first been forced to step through an infringing biosimilar.

Fourth, Regeneron has shown that it would be difficult to account for the harm it will suffer to its reputation and the efforts it will undertake to develop new training programs in response to FYB203 launching. Although it is likely that these harms would result from FYB203 launching, the scope of harm is yet unknown and would be difficult to address in a damages model.

These factors pile uncertainty upon uncertainty in any damages model. Thus, the market positions of Eylea and Eylea HD but-for one specific infringing biosimilar's launch would be particularly difficult to estimate. And were a damages expert to

attempt estimating Regeneron's damages due to FYB203 launch, he or she would have to employ a slew of simplifying assumptions, resulting in a lower damages amount that would not fully reflect the harm Regeneron would have suffered.

9. Causal Nexus

To obtain injunctive relief, a patentee must show "some causal nexus between [a defendant's infringement] and [the] . . . alleged harm" — i.e., "show that the patentee is irreparably harmed by the infringement." Apple Inc. v. Samsung Elecs. Co., 735 F.3d 1352, 1363-64 (Fed. Cir. 2013) ("Apple III").

In cases involving "complex, multi-featured" products, such as "smartphones and tablets," where consumer demand is driven by some features of the finished good and not others, this nexus analysis can be complicated. Id. at 1362; see also Genband US LLC v. Metaswitch Networks, Corp., 861 F.3d 1378, 1384 (Fed. Cir. 2017) (discussing "the causation approach suitable for a multi-feature, multi-purchaser context"). In such cases, a patentee must show "some connection between the patented feature and demand" for the accused product, though it need not "show that a patented feature is the exclusive reason for consumer demand." Apple III, 735 F.3d at 1364.

The nexus inquiry can be much simpler for products that

"ha[ve] a small number of features," like medications. Id. at 1361-62. That is because the nexus inquiry has "little work to do . . . when the infringing product contains no feature relevant to consumers' purchasing decisions other than what the patent claims." Genband, 861 F.3d at 1384 n.2. Accordingly, the multi-feature nexus analysis is straightforward for patents that cover the product itself instead of a "feature" or "attribute[] of the finished consumer good" because "it is not possible to separate" the patent "from the product itself in evaluating consumer demand and nexus." Janssen Prods., 109 F. Supp. 3d at 700. In such cases, nexus is "apparent." Genband, 861 F.3d at 1384 n.2. If the "Patent encompasses nearly the entire Device[, then] . . . Demand for the Device can fairly be described as demand for the Patent." Apnea Scis. Corp. v. Koncept Innovators, Inc., 2016 WL 9086937, at *6 (C.D. Cal. Nov. 7, 2016); see also Power Probe Grp., Inc. v. Innova Elecs., Corp., 2023 WL 7043388, at *13 (D. Nev. Oct. 25, 2023) (distinguishing multi-featured nexus inquiry because "Plaintiff's patent encompasses the entire product at issue, not merely a feature, and Plaintiff's evidence that it will likely suffer irreparable harm absent an injunction demonstrates the requisite causal nexus").

Applying the above principles to the pharmaceutical context,

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 182 of 203

the nexus requirement is satisfied if a manufacturer "would not be able to make the products proposed in its" regulatory filing without infringing the asserted patents. Janssen Prods., 109 F. Supp. 3d at 699; see also Mylan Institutional LLC v. Aurobindo Pharma Ltd., 857 F.3d 858, 873 (Fed. Cir. 2017) (upholding nexus finding because "[w]ithout infringing the . . . patents" defendants "would not be able to make the . . . product described in its ANDA") (internal quotation marks omitted).

If the connection between the infringed patent and the harm is undeniable, courts often find irreparable harm without discussing the nexus factor. See Metalcraft of Mayville, Inc. v. The Toro Co., 848 F.3d 1358, 1368-69 (Fed. Cir. 2017) (affirming the grant of a preliminary injunction after reciting, but not discussing, the nexus requirement of the irreparable harm factor); see also In re Depomed Patent Litig., 2016 WL 7163647, at *78 (D.N.J. Sept. 30, 2016), aff'd sub nom. Grunenthal GMBH v. Alkem Lab'ys Ltd., 919 F.3d 1333 (Fed. Cir. 2019) (finding irreparable harm after reciting, but not discussing, the nexus requirement).

This Court finds that Regeneron has shown "some causal nexus between [FYB203's infringement] and [the] . . . alleged harm," which is sufficient to demonstrate that it "is irreparably harmed by the infringement." Apple III, 735 F.3d at 1363-64.

Formycon's FYB203 product is not a "complex, multi-featured" product like "smartphones and tablets," where consumer demand is driven by some features of the finished product and not others. Id. at 1362. In Apple III, for example, the patentee sought to enjoin the sale of various smartphones and tablets, and the patents at issue were directed to specific features of those devices, like pinch-to-zoom and double-tap-to-zoom functionalities that allow users to navigate the display screens. Id. at 1358. FYB203 does not have analogous segregable features that one can mentally divide and then ask: "Is this a feature that drives demand?" There is no "feature" that parallels, for example, a double-tap to zoom gesture on a smart phone. Thus, Regeneron need not show the specific "connection between the patented feature and demand" that is required in cases involving multi-featured products. Id. at 1364.

In other words, the nexus inquiry has "little work to do" because FYB203 "contains no feature relevant to consumers' purchasing decisions other than what the patent claims," which is the drug product. Genband, 861 F.3d at 1384 n.2. The multi-feature nexus analysis does not apply to the Product Patent because its claims cover FYB203 itself — a 40 mg/mL ophthalmic formulation containing aflibercept [redacted] — not a "feature" or "attribute[] of the finished consumer

good." Janssen Prods., 109 F. Supp. 3d at 700. Indeed, in assessing another nexus question, the Court previously noted that there was a connection between the Product Patent's claims and certain unexpected properties because Eylea exhibited those properties and Eylea "is the invention disclosed and claimed in the ['865] patent." Mylan, 2024 WL 382495, at *60. So too here. The claims require a vial comprising aflibercept, an organic co-solvent, a buffer, and a stabilizing agent and 98% native conformation as measured by size exclusion chromotography. Formycon's FYB203 product—not a component or feature thereof—is the subject of the infringed claims. As a result, "it is not possible to separate" the Product Patent "from the product itself in evaluating consumer demand and nexus." Janssen Prods, 109 F. Supp. 3d at 700. Thus, nexus is "apparent." Genband, 861 F.3d at 1384 n.2.

In yet another framing of this concept that applies in the pharmaceutical context, the nexus requirement is satisfied here because Defendants "would not be able to make the products proposed in its" BLA without infringing the Product Patent. Janssen Prods., 109 F. Supp. 3d at 700. This Court already has held that Formycon's FYB203, likely infringes the asserted claims of the Product Patent.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 185 of 203

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

[redacted]. Because "without infringing the . . . patents" Formycon "would not be able to make the . . . product described in" their BLA, Formycon's infringement causes FYB203's sales and Regeneron's harm. Mylan Inst'l, 857 F.3d at 873.

Even were the Court to ignore that Formycon has sought and received FDA approval only for FYB203 and ask instead whether Formycon could have made and obtained approval for some non-infringing alternative biosimilar product, the result of the Court's analysis would be the same. Dr. Trout explained that Formycon could not "simply alter the FYB203 formulation to attempt to avoid infringement" and that "any necessary changes would require additional testing and other product changes, with no guarantee that a non-infringing product would work as intended." Trout Decl. App'x C. ¶ 5.

The Court also holds that Regeneron has demonstrated nexus even under the multi-feature standard. In another case, the Court previously recognized that Eylea had three unexpected properties — "(1) safety and (2) efficacy" and "(3) the durability to be dosed half as frequently" — and held that these properties have a nexus to and stem from the claimed inventions of the Product

Patent. ECF No. 664 at 196-98. With respect to efficacy and extended dosing intervals, the Court found: "The record at trial demonstrated that the unexpected properties stemmed from the claimed compositions as a whole, including the 40 mg/ml aflibercept concentration. . . . [T]he aflibercept protein does contribute to the longer half-life of Eylea, . . . but aflibercept's concentration is also critical to its half-life." Id. at 196. With respect to safety, the Court found: "[T]he stability of the claimed compositions, including the required 98% native conformation, indicated to the POSA that the there's a relatively lower risk of inflammation." Id. (quotation marks omitted). These features help drive Eylea's success; Formycon's infringement of the Product patent will thus likewise drive the success of its product, and cause Regeneron's harm.

Formycon's reliance (Opp. 24) on Biogen, thus is misplaced. There, it was not disputed that the preliminary injunction "patents do not cover the actual product." 2023 WL 7130655, at *4 (footnote omitted). Here, that is precisely what the Product Patent covers — the FYB203 drug product. In fact, the Court previously has held that Eylea is the invention claimed in the Product Patent and now has held that FYB203 likely infringes those claims. ECF No. 664 at 113, 197. The Biogen court also

emphasized that until after the patentee filed its preliminary injunction motion it had "never identified any of the PI patents as protecting the Tysabri drug in its Form 10-K." 2023 WL 7130655, at *5. Regeneron, on the other hand, has long identified the Product Patent in its securities filings as one of its patents "of particular relevance" to Eylea. Sheridan Ex. 1 at 90 (ECF No. 101-24).

The nexus requirement is thus satisfied.

D. The Balance of Equities Favors an Injunction.

This third injunctive relief factor requires the Court to balance the harm an injunction would cause to the party opposing an injunction with the harm the movant would suffer should the requested injunction be denied. Robert Bosch LLC v. Pylon Mfg. Corp., 659 F.3d 1142, 1156 (Fed. Cir. 2011). In performing this balancing of hardships, the Court considers only the harm to the parties, not to the interests of third parties such as customers or patients. Acumed LLC v. Stryker Corp., 551 F.3d 1323, 1330 (Fed. Cir. 2008).

Regeneron contends that, absent injunctive relief, Formycon will launch FYB203 and compete directly with Regeneron, placing a substantial hardship on Regeneron. Regeneron PI Br. at 19-24. Regeneron argues that such sales of FYB203 will cause it to suffer

irreparable harms, including market share erosion, price erosion, disruption of payor relationships, harm to the commercial trajectory of Regeneron's Eylea HD product, reputational harm, and loss of research and development funding. Id. Regeneron submits testimony from Mr. Clark and Dr. Sheridan to substantiate those harms. Clark Decl. ¶¶ 6-19; Sheridan Decl. ¶¶ 60-101.

Formycon argues it too will suffer lost sales of FYB203 if an injunction is entered. [redacted] Opp. at 25; Sharma ¶¶ 81-82. While the precise amount of lost sales of FYB203 is uncertain, Regeneron does not dispute at least some sales will be lost if an injunction is entered. Formycon also argues that an injunction will cause it to "miss out [sic] early mover advantage if it is enjoined while other biosimilars enter the market, jeopardizing its ability to establish long-term market share for FYB203." Opp. at 25.

Regeneron responds that lost sales of FYB203 are not harms that should be given weight in the balance of hardships analysis, as they would be sales of a product that likely will be found to infringe Regeneron's patent rights. Regeneron PI Br. at 24-25. Regeneron further contends that any harms to Formycon from the lost sales of FYB203 will be fully redressed by requiring Regeneron

to post a bond pursuant to Rule 65(c) of the Federal Rules of Civil Procedure. Id. at 25 n.6.

The Court finds the balance of hardships favors the requested injunctive relief here. As described above, the Court finds that the launch and continued sale of FYB203 in the absence of an injunction will result in direct competition between Formycon and Regeneron and cause harms to Regeneron that cannot be fully calculated, quantified, or compensated by remedies available at law. Supra Section II.E; Sheridan Decl. ¶¶ 60-101. Forcing a patentee to compete directly with its patented technology results in substantial hardship on the patentee. Robert Bosch, 659 F.3d at 1156 ("requiring [the patentee] to compete against its own patented invention, with the resultant harms described above, places a substantial hardship on [the patentee]"); Hafco Foundry & Mach. Co. v. GMS Mine Repair & Maint., Inc., 2018 WL 1786588, at *4 (S.D. W. Va. Apr. 12, 2018) (patentee "will be forced to compete against its own patent, in itself, a significant hardship"). Absent an injunction, Formycon will launch and sell FYB203 during the pendency of this litigation, and those sales will cause Regeneron to suffer market share erosion, price erosion, disruption of payor relationships, harm to the commercial trajectory of Eylea HD, and loss of research and development

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 190 of 203

funding. Clark Decl. ¶¶ 6-19; Sheridan Decl. ¶¶ 60-101. In the event FYB203 were later removed from the market, Formycon's at-risk launch also would cause Regeneron to suffer loss of reputation and goodwill should Regeneron attempt to recapture the higher prices eroded by Formycon. Clark Decl. ¶ 11; Sheridan Decl. ¶¶ 84-87. And, in the event FYB203 were later removed from the market by a subsequent injunction, Regeneron also would suffer loss of reputation and goodwill associated with being faulted for the removal of a competing product from the market. Regeneron PI Br. at 23 (citing Baxalta, 2018 WL 3742610, at *11).

While Formycon will lose some prospective revenue from issuance of an injunction, those lost sales of FYB203 do not tip the balance in Formycon's favor. Formycon's lost sales result from its decision to develop and seek to market FYB203, a drug product the Court has determined likely will be found to infringe at least the Asserted Product Patent Claims. Such lost infringing sales typically are not given meaningful weight in a balance of hardships analysis. See Celsis In Vitro, Inc. v. CellzDirect, Inc., 664 F.3d 922, 931 (Fed. Cir. 2012) ("[T]he preliminary record suggests that LTC's losses were the result of its own calculated risk in selling a product with knowledge of Celsis' patent."); Acumed v. Stryker, 551 F.3d 1323, 1330 (Fed. Cir. 2008) (finding

no abuse of discretion where a district court did not to consider [the accused infringer's] expenses in designing and marketing the [accused product], since those expenses related to an infringing product"); Broadcom v. Qualcomm, 543 F.3d 683, 704 (Fed. Cir. 2008) (agreeing that an accused infringer "should not be permitted to prevail on a theory that successful exploitation of infringing technology shields a party from injunctive relief."); Sanofi-Synthelabo v. Apotex, Inc., 470 F.3d 1368 (Fed. Cir. 2006) (noting that the accused infringer's harms were "almost entirely preventable" and "the result of its own calculated risk"); Windsurfing Int'l v. AMF, 782 F.2d 995, 1003 n.12 (Fed. Cir. 1986) ("One who elects to build a business on a product found to infringe cannot be heard to complain if an injunction against continuing infringement destroys the business so elected."). And, even were Formycon's lost sales given full weight here, the Court would find they do not outweigh the above-described irreparable harms that Regeneron would incur in the absence of an injunction.

The Court's conclusion on this factor is further supported by the fact that Formycon has not yet launched FYB203. An injunction therefore will not force Defendant to withdraw its product from the market and face the potential consequences and harms that may flow from such withdrawal. Instead, an injunction simply will

maintain the status quo [pending trial], imposing only a relatively minimal hardship on Formycon. See Impax Labs., Inc. v. Aventis Pharms., Inc., 235 F. Supp. 2d 390, 396 (D. Del. 2002) ("[G]ranting the Motion for Preliminary Injunction will cause Impax only minimal hardship since doing so will leave Impax in the same position as it was in before the injunction was granted, i.e., excluded from the riluzole market."). The harm from a patentee's loss of the value of its patent is more substantial than the harm from an accused infringer's inability to enter the market earlier. See Glaxo Grp. Ltd. v. Apotex, Inc., 64 F. App'x 751, 756 (Fed. Cir. 2003) ("[W]ithout the preliminary injunction, Glaxo would lose the value of its patent while Apotex would only lose the ability to go on to the market and begin earning profits earlier."). Thus, Regeneron's hardship absent an injunction outweighs Formycon's hardship if an injunction delays its early entry into the aflibercept market.

The Court's conclusion is also supported by the bond requirement of Rule 65(c) of the Federal Rules of Civil Procedure. Regeneron must "give[] security in an amount that the court considers proper to pay the costs and damages sustained by any party found to have been wrongfully enjoined or restrained." Fed. R. Civ. P. 65(c). Such a bond will ensure Formycon will be

compensated for any lost revenue in the event the Court's injunction is later reversed. Id.; Glaxo, 64 F. App'x at 756.

With respect to Formycon's contention that an injunction will cause it to "miss out [sic] early mover advantage if it is enjoined while other biosimilars enter the market, jeopardizing its ability to establish long-term market share for FYB203," Opp. at 25, the Court is not persuaded such harm is sufficient to tip the balance of hardships in Formycon's favor. As an initial matter, this argument depends on Formycon's speculation that other biosimilars will enter the market during the time Formycon is enjoined. Additionally, neither of the District of D.C. opinions cited by Formycon in support of its contention that "[c]ourts have properly recognized that such a delay in entry, especially to the advantage of other generic competitors, imposes significant hardship," Opp. at 25, concerned the enforcement of patent rights, and, unlike the present case, both addressed removal of a product after launch, ViroPharma, Inc. v. Hamburg, 898 F. Supp. 2d 1, 28-29 (D.D.C. 2012); Sandoz, Inc. v. Food & Drug Admin., 439 F. Supp. 2d 26, 32 (D.D.C. 2006), which poses a greater risk to an infringer than a pre-launch injunction, see Glaxo, 64 F. App'x at 756; Impax v. Aventis, 235 F. Supp. 2d at 396.

E. The Public Interest Favors an Injunction.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 194 of 203

The final factor in the injunctive relief analysis requires the Court to consider the impact of an injunction on the public interest. Hybritech v. Abbott Labs., 849 F.2d 1446, 1458 (Fed. Cir. 1988). There is a well-recognized "public interest in protecting rights secured by valid patents." Id.; see also, e.g., Sanofi-Synthelabo v. Apotex, Inc., 470 F.3d 1368, 1383-84 (Fed. Cir. 2006); Patlex Corp. v. Mossinghoff, 758 F.2d 594, 599 (Fed. Cir. 1985). This factor "nearly always weighs in favor of protecting property rights in the absence of countervailing factors, especially when the patentee practices his inventions." Apple Inc. v. Samsung Elecs. Co., 809 F.3d 633, 647 (Fed. Cir. 2015).

Regeneron contends the public interest factor favors entry of an injunction because the public benefits from innovation in the pharmaceutical industry and that such innovation is fostered by intellectual property rights. Regeneron PI Br. at 25. Regeneron points out that it has invested billions to discover and develop its own medicines and argues that this work is made possible by Regeneron's intellectual property and the sales of its patent-protected products, including Eylea and Eylea HD. Id.; Clark Decl. ¶ 19.

The Court finds the public interest factor favors entry of an injunction. Intellectual property rights promote innovation across a number of fields, including pharmaceuticals. Opp. at 25. The Court finds there exists a public interest in protecting such rights and encouraging this innovation. Sanofi-Synthelabo, 470 F.3d at 1383-84; Hybritech, 849 F.2d at 1458; Patlex Corp., 758 F.2d at 599. For the reasons discussed above, the Court has found Regeneron is likely to demonstrate Formycon's sales of FYB203 would the Asserted Product Patent Claims and that such claims are likely valid. The public has an interest in safeguarding these patent rights.

Formycon does not identify any interest the public may have in accessing its aflibercept biosimilar beyond a general interest in access to lower-cost drug products. The Court finds such interest is outweighed by the compelling interest in fostering pharmaceutical innovation. In reaching this conclusion, the Court finds itself in company with most of courts that have considered this issue, including the Federal Circuit. See, e.g., Hybritech, 849 F.2d at 1458; Douglas Dynamics v. Buyers Prods.,717 F.3d 1336, 1346 (Fed. Cir. 2013) ("[T]he public has a greater interest in acquiring new technology through the protections provided by the Patent Act than it has in buying 'cheaper knock-offs.'").

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

The Court is not persuaded by the authority relied upon by Formycon to argue the public's interest in access to less expensive medicines outweighs its interest in safeguarding patent rights and promoting innovation. Genentech. Inc. v. Immunex Rhode Island Corp., 395 F.Supp.3d 357, 366 n.6 (D. Del. 2019); Biogen v. Sandoz, 2023 WL 7130655, at *4 (D. Del. June 29, 2023); ViroPharma, Inc. v. Hamburg, 898 F. Supp. 2d 1 (D.D.C. 2012); Sandoz, Inc. v. Food & Drug Admin., 439 F. Supp. 2d 26 (D.D.C. 2006). Formycon's cited cases from the District of Delaware address this factor only in dicta. Further, both Genentech and Biogen ultimately cite to and rely upon the Federal Circuit's decision in Hybritech v. Abbott Labs., 849 F.2d 1446 (Fed. Cir. 1988). Hybritech, however, affirmed the grant of an injunction. 849 F.2d at 1458. Indeed, the district court in Hybritech recognized that the public interest in guarding patent rights "is embodied in the Constitution and our patent laws." Hybritech v. Abbott Labs., 1987 WL 123997, at *21 (C.D. Cal. July 14, 1987). And while the Federal Circuit did note that "the focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief," Hybritech, 849 F.2d at 1458, the district court was able to protect such interests by tailoring its injunction to ensure (1) continuity of

care for patients already being monitored with certain of the accused products and (2) that "the public will [not] have to switch to an alternative technology that is presumably less effective," 1987 WL 123997, at *21. No analogous public interests are at issue here—FYB203 is not yet being sold, so no continuity of care concerns are presented, and there has been no suggestion that Regeneron's own aflibercept products, Eylea and Eylea HD, are not at least equally effective treatments that will be available to patients in the absence of FYB203. Nor is the Court persuaded by Formycon's cited cases from the District of D.C., neither of which concerned the enforcement of patent rights. ViroPharma, 898 F. Supp. 2d at 29-30; Sandoz, 439 F. Supp. 2d at 33.

The Court recognizes the apparent tension between traditional patent law concepts and the BPCIA, particularly as it pertains to the public interest factor. Of course, "the public has a well-recognized interest in protecting patent rights and fostering innovation," Apple, 809 F. 3d at 647, Congress also has enacted significant legislation, the BPCIA, that is designed to foster competition and make alternative and lower-cost therapeutics available to patients, and Courts have expressly found in the BPCIA biosimilar context that "[f]or pharmaceutical drugs that prolong and save lives, there is a critical public interest in affordable

access to those drugs," Genentech, Inc. v. Immunex Rhode Island Corp., 395 F. Supp. 3d 357, 366 n.6 (D. Del. 2019), aff'd, 964 F.3d 1109 (Fed. Cir. 2020); see also Janssen Biotech, Inc. v. Celltrion Healthcare Co., 210 F. Supp. 3d 244, 252 (D. Mass. 2016) (recognizing a strong public interest in "[a] less expensive biosimilar alternative to compete fairly with [the reference product]"). Nonetheless, after considering the applicable authority, even if not squarely within BPCIA's umbrella, the Court ultimately concludes that the public interest factor also weighs in favor of permanent injunctive relief here.

VI. CONCLUSION

Upon consideration of Plaintiff's Motion for Preliminary Injunction, accompanying Memorandum in Support, exhibits attached thereto, and all of the evidence presented before this Court, for the reasons set forth below, it is **ORDERED THAT:**

Pursuant to Federal Rule of Civil Procedure 65, Plaintiff's Motion for a Preliminary Injunction [ECF No. 101] is **GRANTED**. Formycon's Emergency Motion to Strike [ECF No. 210] is **DENIED**.

Pursuant to Federal Rule of Civil Procedure 65(d)(1), and for the reasons provided herein, the Court makes the following findings and conclusions based upon the preliminary record developed in connection with Regeneron's motion.

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

---

1. Defendant Formycon AG ("Formycon") has sought FDA approval via its Biologics License Application No. 761378 to market a biosimilar version of Regeneron's drug EYLEA®. Formycon's product that is the subject of this BLA is also known as "FYB203."

2. Regeneron has demonstrated that it is likely to succeed in proving that the FYB203 formulation described in BLA No. 761378 infringes claims 4, 7, 9, 11, and 14-17 of U.S. Patent No. 11,084,865 (the '865 Patent).

3. Formycon has not demonstrated that there is a substantial question about the validity of the infringed claims of the '865 Patent.

4. Regeneron has demonstrated that any manufacture, importation, or commercialization of FYB203 prior to the expiry of the '865 patent will cause it irreparable harm.

5. Regeneron has demonstrated that the balance of hardships favors Regeneron, not Formycon.

6. Regeneron has demonstrated that the public interest favors granting the preliminary injunction in order to protect intellectual property rights and because the public is already able to receive aflibercept therapy in the form of EYLEA®.

7. Regeneron has demonstrated that there is a reasonable probability of ultimate success upon the question of personal

jurisdiction when the action against Formycon is tried on the merits.

A. Scope of Injunction and Meet-and-Confer Requirement

The Court is mindful that there are complexities associated with the multi-jurisdiction manufacture of Defendant's product for markets outside the United States — markets which are beyond the territorial reach of U.S. patent laws. Microsoft Corp. v. AT&T Corp., 550 U.S. 437, 454-55 (2007) ("The presumption that United States law governs domestically but does not rule the world applies with particular force in patent law."). In order to ensure that the injunction entered by this Court does not ensnare activity that it is not meant to ensnare, and does not disrupt activities directed to non-U.S. markets, **the Court hereby orders the parties to meet and confer regarding the conditions and scope of the injunction and jointly submit to the Court a proposed form of injunction order within five (5) business days of entry of this order.** The Court further finds that because the only harm that Regeneron presented in the record of these injunction proceedings is directed to commercial marketing within the U.S., the proposed form of injunction should likewise be restricted to prohibiting the commercial sale to customers in the U.S. of Formycon products subject to the BLA No. 761378 product.

Regeneron Ex. 2003
Fresenius v. Regeneron
IPR2025-01268
Page 201 of 203

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

B. Meet-and-Confer on Public Order

The Court is filing this Order under seal, as the Court understands that there is information herein that the parties have designated Confidential or Outside Counsel Eyes Only under the Protective Order. The Court expects the parties to confer on preparing and submitting a public version containing appropriate redactions to protect each party's confidential information. The parties shall meet and confer to discuss which portions of this Order can be unsealed. **They shall submit a joint proposed redacted version for the Court's review within seven (7) days of the entry of this Order.**

A. Rule 65(c) Security

Pursuant to Rule 65(c), the Court must require sufficient security from Plaintiff in an amount the Court considers proper to pay the costs and damages sustained by any wrongfully enjoined party. **The parties are hereby ordered to meet and confer regarding an appropriate security amount and form within five (5) days of entry of this Order. They shall thereafter submit a joint proposed order establishing security under Rule 65(c). If no joint proposal is feasible after good faith joint efforts, each party shall submit their own proposal with supporting evidence for the Court's consideration and a proposed order effectuating same within ten**

**** SEALED ****

ORDER GRANTING MOTION FOR PRELIMINARY INJUNCTION

---

(10) days of entry of this order.

It is so **ORDERED.**

The Clerk is **DIRECTED** to transmit copies of this Order **only** to counsel for Regeneron and Formycon in case 1:23-CV-97.

DATED: June 21, 2024

THOMAS S. KLEEH, CHIEF JUDGE
NORTHERN DISTRICT OF WEST VIRGINIA