**BEFORE THE UNITED STATES JUDICIAL PANEL**
**ON MULTIDISTRICT LITIGATION**

| In re Aflibercept Patent Litigation | MDL No. 3103 |
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**AMGEN'S OPPOSITION TO PLAINTIFF'S MOTION FOR TRANSFER TO THE NORTHERN DISTRICT OF WEST VIRGINIA PURSUANT TO 28 U.S.C. § 1407**

# TABLE OF CONTENTS

# TABLE OF AUTHORITIES

**Cases**

**Statutes**



**Rules**

Pursuant to Panel Rule 6.1(c), Defendant Amgen Inc. ("Amgen") respectfully submits this opposition to Regeneron's Motion for Transfer of Action to the Northern District of West Virginia Pursuant to 28 U.S.C. § 1407 for Coordinated Pretrial Proceedings (the "Motion").

## I. INTRODUCTION

Regeneron's request that this Panel centralize an action against Amgen in the Central District of California with five other actions in the Northern District of West Virginia should be rejected because the common issues are few and the differences are many. When examined carefully, the specific circumstances of the actions show that Regeneron cannot demonstrate that there are enough efficiencies to be gained through centralization, which is fatal when compared to the risk of prejudice to Amgen and the other defendants.

Glossing over the facts, Regeneron overreaches in arguing that this Panel's Hatch-Waxman Act precedent controls whether this action, which arises under the Biologics Price and Competition Act ("BPCIA"), should be centralized. There are key differences between the two statutory schemes, including the subject matter they govern. These differences produce important legal and factual distinctions relevant to whether centralization is appropriate. The BPCIA governs "biosimilars," which are biologic medicines—large, complex molecules produced using living organisms permitting only similarity, not identity, with the reference product—and include medicines such as antibodies and vaccines. The Hatch-Waxman Act governs "generics," which are less complex chemically synthesized drugs (small molecules) that are, as a result, structurally identical to a reference product. Although biosimilars are highly similar to an approved reference product, biosimilars, unlike generics, generally exhibit high molecular complexity and sensitivity to changes in manufacturing processes.

In recognition of these differences and the importance of processes used to manufacture biologics, the BPCIA requires a biosimilar applicant to provide manufacturing information to the

reference product sponsor and provides a framework for litigating patent infringement claims relating to manufacturing processes. In contrast, the Hatch-Waxman Act limits the type of patents that reference sponsors can list in an FDA database known as the "Orange Book"—a listing that forms the basis for the subsequent patent litigation. Manufacturing process patents are expressly prohibited from being listed in the Orange Book. This means Hatch-Waxman cases usually involve a much smaller set of overlapping, statutorily limited patents, and infringement is often conceded by generic manufacturers. BPCIA litigation, on the other hand, generally involves litigation of a much larger individualized and fact-specific list of patents for each biosimilar applicant.

That is the case here, as Regeneron has asserted 32 patents against Amgen but only 13 that are common among all defendants. Importantly, Regeneron fails to mention that the common patents are primarily directed either to pharmaceutical formulations of aflibercept or protein manufacturing processes. Each defendant, including Amgen, independently developed its own aflibercept formulation, and its own processes for producing aflibercept. Thus, they will differ from each other in material respects. Regeneron ignores these differences and proclaims that the actions involve "nearly identical" products. But these differences will be at the heart of the disputes and produce unique infringement, validity, and claim construction issues for each defendant. Moreover, the number of common patents pales when compared to the large number of non-overlapping patents that Regeneron has asserted. Thus, "the potential for [this litigation, if centralized,] to become mired in the unique factual and legal issues raised in each action . . . is significant." *In re Constellation Techs. LLC Pat. Litig.*, 38 F. Supp. 3d 1392, 1393 (J.P.M.L. 2014).

Centralization is also directly at odds with the "just and efficient" conduct of these actions. Despite claiming that Amgen will "not be prejudiced in any way" from having its case transferred to West Virginia, Regeneron's opening submission declines to mention that three of the other

defendants have sought to dismiss or transfer their actions from West Virginia for improper personal jurisdiction. If these motions are granted, the net effect of centralization would be unjust: Amgen would be forced to defend suit in a jurisdiction where it could not have been properly sued, with only one other party (Mylan) that has already had a trial decision on the merits.

Furthermore, Amgen has not waived its *Lexecon* right to have its case transferred back to California after pretrial proceedings. This further diminishes the likelihood that any meaningful efficiencies would be achieved through centralization.

Regeneron's motion is largely predicated on an argument that centralization is necessary to achieve efficiencies associated with preliminary injunction proceedings. In fact, far from promoting efficiency, the procedural status of the actions shows that centralization will unnecessarily complicate case management of the West Virginia actions. The West Virginia Court has already set a schedule for preliminary injunction proceedings against three other defendants. That schedule is expedited, because each of those defendants has already provided its 180-day notice of commercial marketing. The schedule is tailored to allow the parties sufficient time for discovery and briefing in advance of a hearing set for May 2, 2024, and presumably a decision by the court before expiration of Regeneron's regulatory exclusivity on May 18, 2024. Dkt. 1-7 at 3. In sharp contrast to this compressed schedule, the parties in the Amgen action are not even set to discuss a preliminary injunction briefing schedule with the court until April 5, 2024. Ex. 1 at 3. Centralizing and forcing Amgen to litigate on the same schedule as the other litigants in West Virginia, as Regeneron demands, is unrealistic, unnecessary, disruptive, and unfair to Amgen.

Finally, centralization in West Virginia will not serve the convenience of the parties or witnesses. There is nothing convenient about West Virginia for Amgen or Regeneron. Most of Amgen's documents and witnesses are in California, not West Virginia. Most of Regeneron's

documents and witnesses are likely in New York, not West Virginia. Amgen will not be on the same schedule for injunction proceedings. Informal coordination amongst the parties would be a more efficient and preferable alternative. Should the need arise, given the limited number of cases and overlapping counsel, the parties and courts can rely on informal coordination to avoid unnecessarily burdening witnesses or counsel with appearing in duplicative pre-trial proceedings.

There will be significant differences between the Amgen action and the other actions. Centralization is not only unnecessary, as Regeneron has failed to meet its burden of showing sufficient efficiencies, but also threatens to disrupt and unnecessarily complicate the ongoing actions in West Virginia and prejudice Amgen. This Panel should deny Regeneron's motion.

## II. ARGUMENT

Transfer may be ordered only when (1) the actions sought to be centralized and transferred share common issues of fact, (2) transfer would promote the just and efficient conduct of the actions, and (3) transfer would serve the convenience of the parties and witnesses. 28 U.S.C. § 1407; *In re Eli Lilly & Co. Oraflex Prods. Liab. Litig.*, 578 F. Supp. 422, 423 (J.P.M.L. 1984) (denying centralization because the Panel was "not persuaded that these common questions of fact will, in the future course of this litigation, predominate over individual questions of fact present in each action"). Because "only a minimal number of actions are involved," Regeneron bears "a heavier burden to demonstrate that centralization is appropriate." *In re JumpSport, Inc., ('845 & '207) Pat. Litig.*, 338 F. Supp. 3d 1356, 1357 (J.P.M.L. 2018).

Amgen's case is about a unique biosimilar product, with its own formulation, made using confidential processes developed independently by Amgen scientists and engineers. Any "efficiencies" to be gained are unlikely to be achieved in view of the technology and procedural differences between the cases, and because Amgen has not waived its *Lexecon* rights. By contrast, the risk and prejudice to Amgen and the other defendants is significant. The relatively small

number of asserted patents that are common to all defendants means that a centralized proceeding would be a complicated conglomerate of issues and disputes. And because all the other defendants in the pre-trial stage have moved to dismiss or transfer their actions from West Virginia, there is a distinct possibility that Amgen would be required to conduct pre-trial proceedings in a court where it could not have been sued and where there are no other defendants in the pre-trial stage.

**A. Differences predominate the primary issues to be tried among the cases.**

Regeneron begins by arguing this Panel's prior decisions in Hatch-Waxman cases should control whether centralization is appropriate for these BPCIA matters. Dkt. 1-1 at 1-2, 5-6. The Panel, however, has never addressed centralization of BPCIA cases. As discussed above, BCPIA cases arise under a materially different statutory scheme than the Hatch-Waxman cases cited by Regeneron.[1] Contrary to the central theme of Regeneron's brief, "[c]entralization of any litigation—including patent cases—is not automatic, and will necessarily depend on the facts, parties, procedural history and other circumstances in a given litigation." *In re Select Retrieval, LLC, ('617) Pat. Litig.*, 883 F. Supp. 2d 1353, 1354 (J.P.M.L. 2012) (citation omitted); *In re Uponor, Inc., F1960 Plumbing Fittings Prod. Liab. Litig.*, 895 F. Supp. 2d 1346, 1348 (J.P.M.L. 2012) ("Centralization is not a cure-all for every group of complicated cases.").

When viewed in their totality, the specific facts and circumstances here demonstrate that any efficiencies to be gained through centralization are speculative, and there is significant risk of both unnecessary complication and disruption of the matters against the other defendants, and prejudice to Amgen. Material differences predominate the underlying liability issues among the cases. Regeneron seeks to brush aside these differences by drawing attention to the number of commonly asserted patents in all actions (allegedly thirteen). But the mere presence of common

[1] For example, the BPCIA, unlike the Hatch Waxman Act, contemplates litigation of process patents, (*infra* Section II.B.4), and early preliminary injunction proceedings, (*infra* Section II.C).

patents alone is not sufficient to warrant consolidation under § 1407. *See In re JumpSport*, 338 F. Supp. 3d at 1357 (declining to centralize cases although each involved infringement allegations on the same two patents). And when compared with the large number of patents that do not overlap among all defendants (at least 45), it becomes clear that centralization risks overcomplicating these matters while achieving little in the way of efficiency. Indeed, all the other defendants in the pre-trial stage potentially impacted by Regeneron's motion oppose centralization and recognize the disruptive impact of Regeneron's request, unlike the vast majority of Hatch Waxman cases cited by Regeneron where most parties did not even oppose centralization.

**1. There are factual differences because Amgen's biosimilar product is unique and made using proprietary processes.**

In attempting to paint Amgen and other defendants with the same broad brush, Regeneron does not even try to address the specific nature of the common patents. Here is why. Of the thirteen common patents, four come from a single patent family with claims that have already been held invalid by either the U.S. Patent & Trademark Office's ("USPTO") Patent Trial and Appeal Board ("PTAB") or the West Virginia court.[2] Regeneron also disclaimed a fifth patent that had been challenged before the PTAB, stating that "the patent is no longer needed." *See* Ex. 6. These five patents are thus irrelevant to the centralization question.

The eight remaining patents concern either specific formulations of aflibercept, or processes related to protein manufacturing. Regeneron fails to allege, let alone establish, how common factual issues will predominate a case involving these patents. Indeed, Amgen independently developed its own aflibercept formulation and process for making aflibercept. In

[2] Ex. 2 (USPTO holding all challenged claims of U.S. Patent No. 9,254,338 unpatentable); Ex. 3 (USPTO holding claims of U.S. Patent No. 10,130,681 unpatentable); Ex. 4 (USPTO holding claims of U.S. Patent No. 10,888,601 unpatentable); Ex. 5 (N.D.W. Va. Court holding claims of U.S. Patent Nos. 10,888,601 and 11,253,572 invalid as obvious).

doing so, Amgen applied its decades of experience and innovation in formulating and manufacturing of biologic medicines to the development of its biosimilar.

The action against Amgen will thus involve unique issues relating to non-infringement, such as: (a) whether Amgen's unique biosimilar product has certain components required by Regeneron's formulation patents; (b) whether Amgen's confidential manufacturing processes use certain steps required by Regeneron's process patents; and (c) whether the delivery device containing Amgen's biosimilar product has certain features. Although Regeneron has failed to present information regarding the specific issues to be litigated in the other actions, each of the other defendants also has likely developed its own formulations and processes that raise different infringement questions. That Regeneron has asserted over two dozen patents against other defendants, that are not asserted against Amgen, strongly suggests as much.[3] This is yet another difference from the Hatch-Waxman cases cited by Regeneron, where typically only a small number of patents are at issue and infringement is often conceded, leaving a common issue of validity to be litigated by the parties. This counsels against centralization. *E.g.*, *In re Uniloc USA, Inc., & Uniloc Luxembourg, S.A., HPE Portfolio Pat. Litig.*, 304 F. Supp. 3d 1356, 1357 (J.P.M.L. 2018) (denying centralization where "the products at issue also vary significantly"); *In re Blue Spike, LLC, Pat. Litig.*, 278 F. Supp. 3d 1379, 1380 (J.P.M.L. 2017) (denying centralization where "Defendants' accused products vary considerably").

[3] Patents asserted against other biosimilars but not Amgen include: two formulation patents, including U.S. Patent Nos. 11,732,024 and 11,103,552; fourteen process patents, including: U.S. Patent Nos. 7,771,997; 9,562,238; 9,932,605; 10,927,342; 11,312,936; 11,549,154; 11,332,771; 11,268,109; 11,053,280; 11,174,283; 11,299,532; 11,186,625; 11,485,770; and 11,525,833; and ten device-related patents, including: U.S. Patent Nos. 10,182,969; 11,577,025; 11,478,588; 11,439,758; 11,433,186; D906,102; D934,069; D961,376; D961,377; and D858,754.

Furthermore, Amgen's action will involve additional defenses unique to Amgen's confidential manufacturing processes. Pursuant to 35 U.S.C. § 273, Amgen has advanced a defense against 12 Regeneron patents, including two of the common patents, based on Amgen's prior use of its manufacturing processes more than one year before Regeneron's patent applications were filed. *See, e.g.*, Ex. 7, Answer at ¶ 421; Ex. 7, Counterclaims at ¶¶ 112, 287, 332, 368, 405, 417, 453, 465, 501, 513, 546, and 579.[4] This defense involves discovery and evidence relating to Amgen's manufacturing process and is a personal defense specific to Amgen. *E.g.*, *In re Genetic Techs. Ltd. ('179) Pat. Litig.*, 883 F. Supp. 2d 1337, 1338 (J.P.M.L. 2012) (no centralization where "certain defendants have idiosyncratic potentially dispositive defenses that will implicate significant unique facts").

Finally, any potential efficiencies with respect to issues of patent invalidity are speculative. Because Regeneron has asserted so many patents against each defendant (no fewer than 24 against each defendant; 32 against Amgen), Regeneron will be required to narrow its case, including for trial, to a more limited number of patents. There are no assurances that Regeneron will seek only to adjudicate common patents or issues at trial; indeed, this would be unlikely given the varying infringement questions among defendants. There is thus no basis to conclude that centralization will meaningfully alleviate discovery burdens for the parties nor guarantee a streamlined resolution of the issues relating to claim construction, infringement and invalidity. *E.g., In re Alexsam, Inc. ('608 & '787) Pat. & Contract Litig.*, 437 F. Supp. 3d 1374, 1375 (J.P.M.L. 2020) (denying centralization where "the same patent claims are not at issue in all actions"); *In re Droplets, Inc.,*

[4] Regeneron fails to acknowledge this unique and fact-dependent defense in its opening submission, even though Amgen informed Regeneron about this defense in November 2023.

*Pat. Litig.*, 908 F. Supp. 2d 1377, 1378 (J.P.M.L. 2012) (fact that "the claim terms in dispute are not identical from action to action" weighs against centralization).

**2. There are unlikely to be common claim construction issues because Amgen has a different product and process.**

Regeneron also exaggerates the risk of inconsistent claim construction rulings if the actions are not centralized. *First,* in the action against Mylan that has already proceeded through trial, the District Court Judge issued an order construing claim terms of only four patents—two of which he later found invalid, and thus, should not be at issue against Amgen. *See* Ex. 8 at 1; Ex. 5. As to the other two patents, Judge Kleeh addressed claim construction issues that are related to non-infringement defenses that Mylan sought to advance concerning its formulation and manufacturing process, and which are not applicable to Amgen. *See In re Droplets, Inc., Pat. Litig.*, 908 F. Supp. 2d at 1378 (fact that "the claim terms in dispute are not identical from action to action" weighs against centralization).

*Second*, the case against Amgen is likely to involve different claim construction issues from the other defendants for the reasons described above. These differences will "hinder [Amgen's and the other defendants'] ability to adopt common positions regarding the interpretation of common claims of the various patents, which thereby diminishes potential efficiencies created by centralization." *In re ArrivalStar S.A. Fleet Mgmt. Sys. Pat. Litig.*, 802 F. Supp. 2d 1378, 1379 (J.P.M.L. 2011) (denying centralization despite the actions involving "similar allegations of infringement or invalidity of one or more of sixteen patents in a common family of [] patents"). That different claim construction issues will likely arise weighs against centralization.

**3. Centralization unnecessarily complicates the actions because there are many non-overlapping issues for each defendant.**

In seeking to centralize these different actions, Regeneron asks this Panel to construct a truly massive litigation. By Amgen's calculations, the end result of centralization would be a single

case for pre-trial proceedings involving four different defendants, and 57 different patents with a total of 70 named inventors as potential fact witnesses.[5]

Because only a small portion of these patents overlap, the overwhelming majority of any centralized proceeding would involve issues unique to one or more of the defendants. Furthermore, the non-overlapping patents involve a wide variety of technologies, including those directed to methods of treatment, processes for making aflibercept, methods of making host cells for recombinant proteins, cell culture media, sterilization processes, drug delivery devices, packaging components, and packaging design. Regeneron fails to address how such a complicated proceeding could be managed in a streamlined and effective matter. Rather, reasoned decision-making dictates that it cannot. *E.g.*, *In re Uniloc USA, Inc.*, 304 F. Supp. 3d at 1357 (denying centralization of actions involving seven patents because "only two of the seven patents are related, which makes it unlikely that the cases will involve a significant number of common claim terms," "[t]he patents were invented by eighteen separate inventors," "the products at issue also vary significantly" and "all patents are not asserted against all defendants"); *In re Blue Spike, LLC, Pat. Litig.*, 278 F. Supp. 3d at 1380 (denying centralization where "the degree of overlap among the 34 asserted patents varies widely among the cases."); *In re Constellation Techs. LLC Pat. Litig.*, 38 F. Supp. 3d at 1393 (denying centralization where "only one patent . . . is at issue in all actions" and all twenty-nine patents raised in the actions "involve a wide range of technologies and do not descend from a common patent 'family' (*i.e.*, the patents have many different inventors)").

**B. Centralization is at odds with the "just and efficient" conduct of the actions.**

The "basic purpose underlying the enactment of 28 U.S.C. § 1407 was to secure, in multidistrict civil litigation as in all other civil litigation, the 'just, speedy and inexpensive

[5] Amgen assumes Mylan would not be involved in these pre-trial proceedings, because Mylan's case may be on a different schedule. Ex. 9.

determination of every action.'" *In re Nat'l Student Mktg. Litig.*, 368 F. Supp. 1311, 1316 (J.P.M.L. 1972) (quoting Fed. R. Civ. P. 1). Centralization would serve neither purpose here.

**1. The defendants in four cases have moved to dismiss or transfer their actions from West Virginia.**

Regeneron's opening submission fails to mention, let alone address, the fact that defendants Celltrion, Formycon, and Samsung have each moved to dismiss Regeneron's complaints based on lack of personal jurisdiction. Celltrion and Formycon further alternatively seek transfer to another jurisdiction under 28 U.S.C. § 1404. Briefing on those motions to dismiss will not be completed until February 26, 2024. *See* Dkt. 1-10 at 3-4.

There is thus a substantial possibility that nearly all the purported efficiencies argued by Regeneron would be eliminated. There is likewise a significant risk to Amgen that it would be transferred to a jurisdiction with only one other party (Mylan), which has already had a trial decision on the merits that the parties are preparing to appeal. Although there are still outstanding patents asserted against Mylan that remain to be litigated, that case will be on a different schedule relative to Amgen's case. *See* Ex. 9. Mylan has argued that any attempt to consolidate Mylan's actions with the other actions would be prejudicial and disruptive to Mylan. *See id.* at 6-8 ("[T]he Court should place the Biocon Defendants on track to reach a final trial with minimal and expedited discovery, without subjecting them to the ongoing procedural entanglements confronting the other aflibercept applicants.").[6] This would leave Amgen to litigate alone in a jurisdiction where it could not have been properly sued, an outcome that would be unjust.[7] The uncertain future of these West

[6] Biocon Biologics Ltd. ("Biocon") is a co-defendant in the Mylan litigation. Biocon and Mylan are collectively referred to in this brief as "Mylan."

[7] The reason there are other cases in West Virginia to begin with, is that the first defendant to be sued (Mylan) resides and had to be sued there according to venue and jurisdictional requirements.

Virginia actions and potential prejudice to Amgen further confirms that centralization is neither necessary nor appropriate.

**2. Amgen has not waived its *Lexecon* rights.**

Section 1407 "obligates the Panel to remand any pending case to its originating court when, at the latest, those pretrial proceedings end." *Lexecon Inc. v. Milberg Weiss Bershad Hynes & Lerach*, 523 U.S. 26, 27 (1998). Amgen has not waived its *Lexecon* rights, so its case will be transferred back to the Central District of California for trial. The Honorable Judge Holcomb presently presides over the Amgen case. Judge Holcomb is a member of the Patent Program in the Central District of California, and has significant experience handling patent matters, including complex matters such as this one. Judge Holcomb will need to become familiar with the parties, patents, claim construction rulings, and facts at issue in advance of trial, whether or not the Amgen case is transferred for pre-trial purposes. *E.g.*, *In re Gerber Probiotic Prods. Mktg. & Sales Practices Litig.*, 899 F. Supp. 2d 1378, 1380 (J.P.M.L. 2012) (recognizing disadvantages of "multiple trials after the Panel remands actions to the [] transferor court[]" and need for "transferor courts to spend time to re-familiarize themselves with [] actions" upon remand).

**3. There are limited efficiencies to be gained from the prior Mylan action.**

Contrary to Regeneron's assertions, any efficiencies to be gained by centralization in West Virginia are limited. Although the court in West Virginia held a trial on three Regeneron patents, the court declared the claims at issue for two of those patents invalid. *See* Ex. 5. Because those and related patents have already been held invalid, they should not be counted to serve as a basis for efficiencies relating to any preliminary injunction or pre-trial proceedings against Amgen.

The Amgen action thus will involve at most one patent that was tried in the Mylan action: U.S. Patent No. 11,084,865 ("the '865 Patent"), which is directed to pharmaceutical formulations of aflibercept. Amgen's independently developed biosimilar product will involve non-

infringement issues that were not at issue in the Mylan case. *See supra* Section II.A.1. There is no basis to conclude that proceeding before the West Virginia court would be more efficient.

As to any other patents that Regeneron asserts against Amgen, Regeneron has not demonstrated that the West Virginia Court is in any better position to handle the underlying issues pertaining to those patents than the court in the Central District of California. Indeed, Judge Holcomb is particularly well equipped to handle the Amgen matter, given his technical background and participation in the Central District of California's Patent Program.

**4. Management of a centralized case is complicated because the defendants are also competitors.**

The defendants, including Amgen, are all direct competitors and each considers the details of its product and manufacturing processes and the research and development that created them to be highly confidential, and potentially trade secrets. If centralized, the defendants would require additional discovery protections, which would "complicate case management due to the need to protect trade secret and confidential information." *In re Proton–Pump Inhibitor Prods. Liab. Litig.*, 273 F. Supp. 3d 1360, 1362 (J.P.M.L. 2017); *In re Spray Polyurethane Foam Insulation Prods. Liab. Litig.*, 949 F. Supp. 2d 1364, 1364 (J.P.M.L. 2013) (denying centralization as "placing direct competitor manufacturer defendants into the same litigation would require protecting trade secret and confidential information from disclosure to all parties and complicate case management"). Mylan has raised this exact concern before the West Virginia court. Ex. 9 at 9 ("[N]on-infringement defenses across multiple patent families are likely to be disparate and unique to each defendant, not to mention highly confidential, which will further complicate any possible consolidation of the Biocon Defendants with those of the other, later-filed biosimilar applicants.").

Twenty of the 32 patents asserted against Amgen are related to confidential manufacturing processes. The inclusion of so many process patents implicating highly confidential information

is one of many distinctions between this BPCIA case and the Hatch-Waxman cases cited by Regeneron. Unlike the Hatch-Waxman Act, which precludes the listing of process patents in the Orange Book, the BPCIA requires a biosimilar applicant to provide to the reference product sponsor "such other information that describes the process or processes used to manufacture the biological product," which information is then used to prepare a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted against that specific biosimilar applicant. *Compare* 21 C.F.R. § 314.53(b)(1) *with* 42 U.S.C. §§ 262(l)(2)(A), (3)(A). Thus, this confidentiality issue is heightened in this BPCIA case as compared to the Hatch-Waxman cases cited by Regeneron.

The prior history of these cases illustrates the dangers and difficulties associated with confidentiality issues. In the action against Amgen, Regeneron improperly disclosed Amgen's confidential information on the public record. *See* Ex. 10 at 2. In the Mylan action, the defendant has alleged that Regeneron breached the protective order and has filed a motion seeking sanctions. Ex. 11. And despite being entered on December 27, a redacted post-trial decision in the Mylan action was not made publicly available until January 31 because the parties were unable to agree on what information is confidential. Centralization in West Virginia would greatly complicate efforts by the Court and the parties to manage the confidentiality of each defendant's information.

### C. There are no efficiencies to be gained by transferring Amgen to West Virginia for preliminary injunction proceedings.

Regeneron is wrong again in arguing that centralization is necessary so that it can pursue preliminary injunctive relief against each defendant in a single consolidated proceeding, under the "identical schedule" set forth by the West Virginia court. Dkt. 1-1 at 5; *see id*. at 8-9. The West Virginia preliminary injunction proceedings are on a compressed and expedited schedule to permit a hearing on the merits on May 2, 2024. Dkt. 1-7 at 2. That schedule requires document production

to be completed today (February 2), with Regeneron to file its motion-in-chief on February 22, followed by defendants' oppositions on March 21, and Regeneron's reply on April 18. *Id.* at 3.

Regeneron's unrealistic efforts to force Amgen onto the expedited West Virginia preliminary injunction schedule have already been rejected twice. First, by this Panel in denying Regeneron's request for expedited relief on its motion. Second, by the District Court in the Central District of California in rejecting Regeneron's request for *ex parte* relief to enter its requested preliminary injunction schedule. Instead, the District Court ordered that the Amgen action proceed on a different schedule "[i]n view of the fact that this case was filed after the West[] Virginia cases[.]" Ex. 1 at 2. The Amgen action will necessarily trail the West Virginia cases by some time, as the Court set a hearing date of April 5, 2024 to discuss a briefing schedule for injunctive relief. *Id.* at 3.

Given the advanced stage of the preliminary injunction proceedings against the other defendants, it would be disruptive to the other defendants and unfair to Amgen to shoehorn Amgen into those proceedings, as Regeneron proposes. *See e.g.*, *In re JumpSport, Inc.*, 338 F. Supp. 3d at 1357 (denying centralization where procedural differences "would complicate any centralized proceeding and likely would result in delays to the completion of discovery and the anticipated trial date"). This would also severely prejudice Amgen and its ability to develop its defenses and arguments in response to any preliminary injunctive relief sought by Regeneron.

The only reasonable conclusion is that two sets of separate preliminary injunction proceedings are required whether the Amgen action is transferred to West Virginia or not. The presence of two different time-sensitive preliminary injunction proceedings also distinguishes this case from the Hatch-Waxman cases cited by Regeneron. The Hatch-Waxman Act provides a 30-month stay of generic approval upon the timely filing of a patent infringement lawsuit, thus

avoiding early preliminary injunction proceedings. *See* 21 U.S.C. § 355(j)(5)(B)(iii). In contrast, the BPCIA contemplates preliminary injunctions during a 180-day period following a biosimilar applicant's notice of commercial marketing. *See* 42 U.S.C. § 262(l)(8)(A). Regeneron rushed to transfer the Amgen case during preliminary injunction proceedings in West Virginia, but transfer would disrupt and delay those proceedings rather than create any efficiency.

Moreover, Regeneron overlooks the substantial differences that may be at issue in Amgen's preliminary injunction proceeding relative to the other defendants' proceedings. "A party can obtain a preliminary injunction by showing that (1) it is 'likely to succeed on the merits,' (2) it is 'likely to suffer irreparable harm in the absence of preliminary relief,' (3) 'the balance of equities tips in its favor,' and (4) 'an injunction is in the public interest.'" *Disney Enters., Inc. v. VidAngel, Inc.*, 869 F.3d 848, 856 (9th Cir. 2017) (internal brackets omitted) (quoting *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008)). *First*, as of today, Regeneron has not identified which patents (or claims) it intends to assert in seeking a preliminary injunction against Amgen, and thus has necessarily failed to show that there is any overlap of issues with the preliminary injunction proceedings in West Virginia. *Second*, as discussed above in Section II.A.1, there are substantial differences between Amgen's biosimilar product and manufacturing processes and the other biosimilar defendants. As a result, an analysis of Regeneron's likelihood to succeed on the merits will be substantially different for each defendant and may implicate different claim construction issues and different defenses. *Third*, Amgen also is differently situated from the other defendants with respect to the remaining preliminary injunction factors. For example, discovery on the issue of balance of hardships and irreparable harm will likely implicate Amgen's confidential and competitively sensitive business information. Thus, any efficiencies to be gained through

centralization are diminished as it relates to preliminary injunctive relief, particularly since it is a factually intensive inquiry.

**D. Centralization in West Virginia will not serve the convenience of the parties and witnesses.**

Regeneron proclaims that centralization would "best serve the convenience of the parties and witnesses." Dkt. 1-1 at 9. But the only party served by centralization is Regeneron. The Court in the Amgen action has already rejected Regeneron's attempt to manufacture a "common schedule" for preliminary injunction proceedings, thereby mooting Regeneron's principal arguments. As for witness convenience, the only specific efficiencies alleged by Regeneron concern the burden that would befall its own witnesses (i.e., the inventors) if required to appear at multiple depositions. But this Panel should be wary of placing undue weight on Regeneron's self-serving interest in restricting the number and manner of its own witness depositions, especially because informal coordination can be used to minimize inconvenience. *See* Section II.D.2 below.

Even if there are potential benefits to Regeneron, left unaddressed in Regeneron's brief is what will happen to Amgen and its witnesses if the case is centralized. There is nothing convenient about West Virginia for Amgen.[8] Amgen does not have any witnesses located in West Virginia (nor does Regeneron). Rather, Amgen's witnesses are primarily located in California, which is where the Amgen action is already pending. Both parties have retained national counsel who reside outside of West Virginia and would therefore be subject to travel for any in-person hearings.

[8] Regeneron argues that "Amgen will not be prejudiced in any way . . . given that it has already intervened in the Mylan Action to obtain access to various records and appeared in that court." Dkt. 1-1 at 10. That is simply not credible. That Amgen hired local counsel in West Virginia to file a limited motion to intervene to obtain access to judicial records in no way diminishes the prejudice and inconvenience that Amgen would suffer if it were forced to litigate a complex 32-patent infringement action in West Virginia along with other direct competitors.

**1. The small number of actions weighs against centralization.**

There are only six actions pending in two districts, and all five West Virginia actions are currently pending before the same judge. The Amgen action is the only proceeding outside of West Virginia. As a small number of cases are at issue, Regeneron "bears a heavier burden to demonstrate that centralization is appropriate." *See In re SLB Enter. Rico Litig.*, 412 F. Supp. 3d 1350, 1352 (J.P.M.L. 2019). This Panel routinely denies centralization in such situations. *See In re Droplets, Inc., Pat. Litig.*, 908 F. Supp. 2d at 1378 (denying centralization of actions "pending in just three districts"); *In re JumpSport*, 338 F. Supp. 3d at 1357; *In re Nelnet Servicing, LLC, Customer Data Sec. Breach Litig.*, 648 F. Supp. 3d 1377, 1377-78 (J.P.M.L. 2022) (denying centralization where "only one of the twenty-two actions . . . is pending outside the District of Nebraska" since "[e]ffectively, then, there are two actions at issue here") (internal quotation marks omitted).

**2. Informal coordination is preferable to transfer under § 1407.**

The overlapping counsel and locations of the witnesses makes informal coordination preferable to centralization. Regeneron, the sole plaintiff in all six actions, is represented by the same counsel for all actions. This facilitates coordination. *See In re Droplets, Inc., Pat. Litig.*, 908 F. Supp. 2d at 1378 (denying centralization because "informal coordination among the three involved courts seems practicable—just as it does among the parties, given that [patent owner] is represented in all actions by the same law firm"); *In re Zeroclick, LLC*, 437 F. Supp. 3d 1362, 1362 (J.P.M.L. 2020) ("These circumstances – the small number of actions, minimal number of districts, and presence of common counsel – suggest that alternatives to centralization are practicable, and that formal centralization under Section 1407 is not necessary.").

Although Regeneron argues that centralization would reduce the burden placed on fact witnesses by having to appear at multiple depositions and court proceedings, informal coordination

amongst the parties can minimize that burden. Indeed, Amgen has tried to engage Regeneron on multiple occasions to discuss a schedule, minimize duplication of discovery, and informally coordinate with the West Virginia actions. *See* Ex. 12. But Regeneron has refused to provide Amgen with basic information required to facilitate coordination with the West Virginia actions. Among other things, Regeneron has rebuffed Amgen's requests for: (i) the list of patents at issue in the preliminary injunction proceedings in West Virginia; (ii) the list of patents that will be at issue in Regeneron's preliminary injunction proceeding against Amgen[9]; (iii) the schedule for further proceedings in the Mylan case; and (iv) information about any potential case schedule for post-injunction proceedings in the other West Virginia actions. *Id*. at 1-3. And although Regeneron has had Amgen's initial document production of over 145,000 pages since September 2023, Regeneron has refused to provide Amgen with any documents, including even those already produced in the other actions. *Id.* at 1.

Amgen is not alone in maintaining that informal coordination is a practicable alternative to formal centralization. Amgen has conferred with all three of the other defendants in pre-trial proceedings, namely Celltrion, Samsung, and Formycon. All four defendants are prepared and willing to informally coordinate wherever it is feasible, including in particular, with respect to discovery following preliminary injunction proceedings.

Rather than engaging in a discussion about informal coordination, Regeneron jumps to the conclusion that Amgen's requests for coordination "across cases pending in multiple jurisdictions with different governing protective orders—appears unworkable." *Id*. at 3; *see also id*. ("To the

[9] In view of the extensive information Regeneron has received about Amgen's product and processes, it surely knows what patents it will assert in a preliminary injunction motion. Should Regeneron disclose the patents it will assert by its reply to this Panel, Amgen may seek an opportunity to respond further by addressing the extent, if any, to which patents Regeneron finally identifies involve common issues of fact and law.

extent that Amgen seeks to enhance efficiency by coordinating pre-trial discovery proceedings with those cases pending in West Virginia, it should accede to Regeneron's request for multi-district litigation transfer."). Yet, Regeneron never explains why coordination among the relatively small number of cases and counsel will be unworkable. The parties have various tools at their disposal to, should the need arise, minimize the potential for duplicative discovery. It cannot be that informal coordination is not feasible because the moving party says so; indeed, this Panel has "often stated that centralization under Section 1407 should be the last solution after considered review of all other options." *In re Gerber Probiotic Prod. Mktg. & Sales Practices Litig.*, 899 F. Supp. 2d at 1379 (internal quotation marks and citations omitted).

## III. CONCLUSION

For the foregoing reasons, Amgen respectfully requests that the Panel deny Regeneron's Motion for Transfer of Action to the Northern District of West Virginia Pursuant to 28 U.S.C. § 1407 for Coordinated Pretrial Proceedings.

Dated: February 2, 2024 */s/ Siegmund Y. Gutman*

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**BEFORE THE UNITED STATES JUDICIAL PANEL**
**ON MULTIDISTRICT LITIGATION**

| In re Aflibercept Patent Litigation | MDL No. 3103 |
|---|---|

## SCHEDULE OF ACTIONS

| *Case Caption* | *Court* | *Civil Action No.* | *Judge* |
|---|---|---|---|
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendants:**<br>Mylan Pharmaceuticals Inc.<br>Biocon Biologics Inc.<br><br>**Counter Claimants:**<br>Mylan Pharmaceuticals Inc.<br>Biocon Biologics Inc.<br><br>**Counterclaim Defendant:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Intervenors:**<br>Amgen USA, Inc.<br>Celltrion, Inc. | N.D. W. Va. | 1:22-cv-00061 | Kleeh, C.J. |
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendant:**<br>Celltrion, Inc. | N.D. W. Va. | 1:23-cv-00089 | Kleeh, C.J. |
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendant:**<br>Samsung Bioepis Co. Ltd. | N.D. W. Va. | 1:23-cv-00094 | Kleeh, C.J. |

| *Case Caption* | *Court* | *Civil Action No.* | *Judge* |
|---|---|---|---|
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendant:**<br>Formycon AG | N.D. W. Va. | 1:23-cv-00097 | Kleeh, C.J. |
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendant:**<br>Samsung Bioepis Co. Ltd. | N.D. W. Va. | 1:23-cv-00106 | Kleeh, C.J. |
| **Plaintiff:**<br>Regeneron Pharmaceuticals, Inc.<br><br>**Defendant:**<br>Amgen Inc.<br><br>**Counter Claimant:**<br>Amgen Inc.<br><br>**Counterclaim Defendant:**<br>Regeneron Pharmaceuticals, Inc. | C.D. Cal. | 2:24-cv-00264 | Holcomb, J. |

Dated: February 2, 2024 */s/ Siegmund Y. Gutman*

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**BEFORE THE UNITED STATES JUDICIAL PANEL ON MULTIDISTRICT LITIGATION**

| In re Aflibercept Patent Litigation | MDL No. 3103 |
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**PROOF OF SERVICE**

In compliance with Rule 4.1(a) of the Rules of Procedure for the United States Judicial Panel on Multidistrict Litigation, I hereby certify that copies of the foregoing Amgen's Opposition to Plaintiff's Motion for Transfer to the Northern District of West Virginia Pursuant to 28 U.S.C. § 1407, and this Proof of Service were served by electronic mail on February 2, 2024 to the following:

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# EXHIBIT 1

*Regeneron Pharms., Inc. v. Amgen Inc.*,
No. 24-264, Dkt. 51 (C.D. Cal. Jan. 23, 2024)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
CIVIL MINUTES—
GENERAL

| Case No. | 2:24-cv-00264-JWH-E | Date | January 23, 2024 |
|---|---|---|---|
| Title | *Regeneron Pharmaceuticals, Inc. v. Amgen, Inc.* | | |

| Present: The Honorable | JOHN W. HOLCOMB, UNITED STATES DISTRICT JUDGE |
|---|---|

| Clarissa Lara | Not Reported |
|---|---|
| Deputy Clerk | Court Reporter |

| Attorney(s) Present for Plaintiff(s): | Attorney(s) Present for Defendant(s): |
|---|---|
| None Present | None Present |

**Proceedings: ORDER GRANTING IN PART AND DENYING IN PART PLAINTIFF'S *EX PARTE* APPLICATION [ECF No. 38]**

Before the Court is the *ex parte* application of Plaintiff Regeneron Pharmaceuticals, Inc. for an order setting a schedule for preliminary injunction proceedings.[1] The Court finds this matter appropriate for resolution without a hearing. *See* Fed. R. Civ. P. 78; L.R. 7-15. After considering the papers filed in support and in opposition,[2] the Court orders that the Application is **GRANTED in part** and **DENIED in part**, for the reasons set forth herein.

As an initial matter, the Court addresses the timing of Regeneron's Application by reminding the parties of the Court's Standing Order:

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[1] Pl.'s *Ex Parte* App. for Scheduling Order Setting Schedule for Preliminary Injunction Proceedings or, in the alternative, an Emergency Status Conference (the "Application") [ECF No. 38].

[2] The Court considered the documents of record in this action, including the following papers: (1) Application (including its attachments); and (2) Def.'s Opp'n to the Application (the "Opposition") [ECF No. 39].

> The other parties' opposition . . . to an *ex parte* application is due 24 hours—***not*** the next ***court day***—after the other parties' receipt of the *ex parte* application. ***In view of that 24-hour deadline for opposition papers, in the absence of a true emergency, the Court takes a dim view of applicants who file their* ex parte *applications on Fridays or on the day before a court holiday.***[3]

"The opportunities for legitimate *ex parte* applications are extremely limited." *Lum v. Mercedes-Benz USA, LLC*, 2012 WL 13012454, at *4 (C.D. Cal. Jan. 5, 2012) (citation omitted). To justify *ex parte* relief, the moving party must make two showings: (1) "the evidence must show that the moving party's cause will be irreparably prejudiced if the underlying motion is heard according to regular noticed motion procedures"; and (2) "it must be established that the moving party is without fault in creating the crisis that requires *ex parte* relief, or that the crisis occurred as a result of excusable neglect." *Mission Power Engineering Co. v. Continental Cas. Co.*, 883 F. Supp. 488, 492 (C.D. Cal. 1995).

Regeneron argues that *ex parte* relief is warranted because the Court should "urgently" enter a scheduling order to keep this action on track with four other cases pending in the United States District Court for the Northern District of West Virginia against drug manufacturers seeking to commercialize biosimilar versions of Eyelea.[4]

A preliminary injunction schedule will indeed promote judicial economy. But Regeneron has not made a sufficient showing regarding why this Court should adopt the same schedule set in the West Virginia cases. In view of the fact that this case was filed after the Western Virginia cases, the Court concludes that it is appropriate for this case to trail the Western Virginia cases.

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[3] Standing Order [ECF No. 48] 13:7-12 (emphasis in original). The Court hastens to note that its Standing Order was entered after Regeneron filed its Application. Nevertheless, Defendant Amgen, Inc. complied with the Court's requirement. *See* Opposition 1:7-10 ("Amgen apologizes for burdening the Court with this filing on a Saturday evening. Amgen understands that a response to an *ex parte* application is typically due within 24 hours, so it responds today to ensure compliance with the Court's procedures.").

[4] *See generally* Application.

The Court appreciates Amgen's willingness "to discuss a reasonable schedule,"[5] and, therefore, the Court **SETS** a Scheduling Conference on April 5, 2024, in this case to discuss preliminary injunction proceeding briefing.

The parties agree that the Application discusses information that Amgen has designated as confidential under 42 U.S.C. § 262(*l*)(1).[6] Accordingly, the Court **ORDERS** that the Application for Leave to File Under Seal [ECF No. 37] and the Application (including its attachments) are **SEALED**.

Therefore, for the foregoing reasons, the Court **ORDERS** as follows:

1. The Application is **GRANTED in part**, to the extent it requests setting a preliminary injunction proceeding schedule, and the Application is **DENIED in part**, to the extent it requests the specific schedule proposed by Regeneron.

2. The Court **SETS** a Scheduling Conference on April 5, 2024, at 11:00 a.m. in Courtroom 9D of the Ronald Reagan Federal Building and U.S. Courthouse, 411 W. 4th Street, Santa Ana, California, to discuss the preliminary injunction proceedings.

3. The Application for Leave to File Under Seal and the Application (including its attachments) are **SEALED**.

**IT IS SO ORDERED.**

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[5] Opposition 2:25.

[6] App. for Leave to File Under Seal Unredacted *Ex Parte* App (the "Application for Leave to File Under Seal") [ECF No. 37] 2:9-12; Opposition 2:10-12.

# EXHIBIT 2

*Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*,
IPR2021-00881, Paper 94 (PTAB Nov. 9, 2022)

Trials@uspto.gov
571-272-7822

Paper 94
Date: November 9, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN PHARMACEUTICALS INC., CELLTRION, INC., and APOTEX, INC.
Petitioners,

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

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IPR2021-00881[1]
Patent 9,254,338 B2

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Before ERICA A. FRANKLIN, JOHN G. NEW, and SUSAN L. C. MITCHELL, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

# JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
Denying in part and Dismissing in part Petitioners' Motion to Exclude
Denying in part and Dismissing in part Denying Patent Owner's Motion to Exclude
*35 U.S.C. § 318(a)*

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[1] IPR2022-00258 and IPR2022-00298 have been joined with this proceeding. *See* Papers 35 and 36.

# I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review of claims 1, 3–11, 13, 14, 16–24 and 26 ("the challenged claims") of U.S. Patent No. 9,254,338 B2 (Ex. 1001, "the '338 patent"). We have jurisdiction under 35 U.S.C. § 6, and enter this Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioners have shown by a preponderance of the evidence that the challenged claims are unpatentable. *See* 35 U.S.C. § 316(e).

Additionally, we deny in part and dismiss in part the Motions to Exclude Evidence.

## *A. Procedural History*

The original petitioner in this case was Mylan Pharmaceuticals, Inc. ("Petitioner Mylan"). Petitioner Mylan filed a Petition requesting an *inter partes* review of the challenged claims under 35 U.S.C. § 311. Paper 1 ("Petition" or "Pet."). Petitioner Mylan supported the Petition with the Declarations of Thomas Albini M.D. (Ex. 1002), and Mary Gerritsen Ph.D. (Ex. 1003). Regeneron Pharmaceuticals, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 10 ("Prelim. Resp."). Patent Owner supported the Preliminary Response with the Declarations of Diana V. Do, M.D. (Ex. 2001). With our authorization, Paper 13, Petitioner Mylan filed a Reply to the Preliminary Response, and Patent Owner filed a Sur-reply to address further issues involving 35 U.S.C. § 325(d). Paper 16 ("Reply"); Paper 19 ("Sur-reply").

On November 10, 2021, pursuant to 35 U.S.C. § 314, we instituted trial to determine whether any challenged claim of the '338 patent is unpatentable based on the six grounds raised in the Petition:

| Claims Challenged | 32 U.S.C. § | Reference(s) |
|---|---|---|
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Dixon[2] |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Adis[3] |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Regeneron 2008[4] |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | NCT-795[5] |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | NCT-377[6] |
| 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon, Papadopoulos,[7] Dix[8] |

Paper 21 ("Institution Decision" or "Inst. Dec.").

On February 9, 2022, we instituted an *inter partes* review in IPR2022-00258 and granted the motion for joinder with IPR2021-00881, adding Celltrion, Inc. as a petitioner in the instant proceeding. Paper 35. On the

[2] James A. Dixon et al., "VEGF Trap-Eye for the treatment of neovascular age-related macular degeneration," 18(10) *Expert Opin. Investig. Drugs* 1573–1580 (2009) (Ex. 1006, "Dixon")).
[3] Adis Data Information BV, "Aflibercept," 9(4) *Drugs R&D* 261–269 (2008) (Ex. 1007, "Adis").
[4] Press Release, Regeneron, "Bayer and Regeneron Dose First Patient in Second Phase 3 Study for VEGF Trap-Eye in Wet Age-Related Macular Degeneration" (May 8, 2008) (Ex. 1013, "Regeneron 2008").
[5] Vascular Endothelial Growth Factor (VEGF) Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD) (VIEW1), NCT00509795, ClinicalTrials.gov (Apr. 28, 2009), https://clinicaltrials.gov/ct2/show/NCT00509795 (Ex. 1014, "NCT-795").
[6] VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD (VIEW2), NCT00637377, ClinicalTrials.gov (Mar. 17, 2008), https://clinicaltrials.gov/ct2/show/NCT00637377 (Ex. 1015, "NCT-377").
[7] Papadopoulos et al., US 7,374,758 B2, issued May 20, 2008, (Ex. 1010, "Papadopoulos").
[8] Patent Application Publication No. 2006/0217311 A1 by Dix et al., published Sep. 28, 2006 (Ex. 1033, "Dix").

same date, we also instituted an *inter partes* in IPR2022-00298 and likewise granted the motion for joinder with IPR2021-00881, adding Apotex, Inc. as a petitioner in the instant proceeding. Paper 36. Accordingly, we refer to Mylan Pharmaceuticals, Inc., Celltrion, Inc. and Apotex, Inc., collectively, as "Petitioners."

Patent Owner filed a Corrected Patent Owner Response to the Petition. Paper 41 (redacted, public version), Paper 40 (sealed version), (collectively, "PO Resp.").[9] Patent Owner supported the Patent Owner Response with the declarations of Diana V. Do, M.D. (Ex. 2001; Ex. 2051); Lucian V. Del Priore, M.D., Ph.D. (Ex. 2048 (sealed version); Ex. 2048 (redacted, public version)); Alexander M. Klibanov, Ph.D. (Ex. 2049); David M. Brown, M.D. (Ex. 2050); Richard Manning, Ph.D. (Ex. 2052 (sealed version); Ex. 2052 (public, redacted version)).

Petitioners filed a Reply to the Patent Owner Response. Papers 61 (sealed version), 62 (redacted, public version) (collectively, "Pet. Reply"). Petitioners supported the Reply with Supplemental Declarations from Dr. Albini (Ex. 1114) and Dr. Gerritsen (Ex. 1115), along with a Declaration from Dr. Hofmann (Ex. 1137) (sealed version), (Ex. 1137) (redacted, public version). Patent Owner filed a Sur-reply to Petitioners' Reply. Paper 73 ("PO Sur-reply").

Patent Owner and Petitioners each filed a Motion to Exclude Evidence. Papers 83 ("PO Mot."), 81 ("Pet. Mot."). Each party filed an Opposition to the corresponding motion. Papers 85 ("PO Opp."), 84 ("Pet.

[9] In this Decision, we refer only to the public versions of papers and exhibits and not to confidential material.

Opp.”). Each party also filed a Reply to the corresponding Opposition. Papers 86 (“PO Mot. Reply”), 87 (“Pet. Mot. Reply”).

On August 10, 2022, the parties presented arguments at an oral hearing. Paper 78 (Order Granting Requests for Oral Hearing). The hearing transcript has been entered in the record. Paper 93 (“Tr.”).

### *B. Real Parties-in-Interest*

Petitioner Mylan identifies itself, Viatris Inc., Mylan Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, and Johnson & Johnson as real parties-in-interest. Pet. 3, Paper 18 (Petitioner Mylan’s Amended Mandatory Notices). Petitioner Celltrion, Inc. identifies itself, Celltrion Healthcare Co. Ltd., and Celltrion Healthcare U.S.A., Inc. as real parties-in-interest. *See* IPR2022-00258, Paper 2, 3. Petitioner Apotex, Inc. identifies itself, Apotex Corp., Apotex Pharmaceutical Holdings Inc., and Aposherm Delaware Holdings Corp. as real parties-in-interest. *See* IPR2022-00298, Paper 1, 3. Patent Owner identifies itself as the real party-in-interest. Paper 5, 2.

### *C. Related Proceedings*

Petitioners and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880 (PTAB May 5, 2021) (“the -880 IPR”) as a related matter. Pet. 3; Paper 5, 2. The -880 IPR challenges claims 1 and 8–12 of U.S. Patent No. 9,669,069 B2 (“the ’069 patent”). The parties further identify *Chengdu Kanghong Biotechnol. Co. v. Regeneron Pharms., Inc*., PGR2021-00035 (petition dismissed and proceeding terminated, Paper 8 (PTAB June 25, 2021)) challenging the claims of U.S. Patent No. 10,828,345 B2 (“the ’345 patent”), which is related to the ’338 patent and the ’069 patent. Pet. 4; Paper 5, 2.

Petitioners identify additional patents and patent applications that claim priority to the '338 patent, namely: U.S. Patent Nos. 10,130,681 B2, 10,857,205 B2, 10,828,345 B2, and 10,888,601 B2; and U.S. Application Serial Nos. 17/072,417, 17/112,063, and 17/112,404. Pet. 4.

### *D. The '338 Patent*

The '338 patent relates to methods for treating angiogenic eye disorders. Ex. 1001, 1:63–64. Angiogenic eye disorders include age-related macular degeneration ("AMD") and diabetic macular edema ("DME"). *Id.* at 1:24–34. According to the Specification, "[r]elease of vascular endothelial growth factor (VEGF) contributes to increased vascular permeability in the eye and inappropriate new vessel growth. Thus, inhibiting the angiogenic-promoting properties of VEGF appears to be an effective strategy for treating angiogenic eye disorders." *Id.* at 1:44–48.

The Specification describes inhibiting the angiogenic-promoting properties of VEGF by administering a VEGF antagonist. *Id.* at 4:37–42. VEGF antagonists may include "VEGF receptor-based chimeric molecule(s), (also referred to herein as a 'VEGF-Trap' or 'VEGFT'). An exemplary VEGF antagonist . . . is a multimeric VEGF-binding protein comprising two or more VEGF receptor-based chimeric molecules referred to herein as 'VEGFR1R2-Fc[Δ]C1(a)' or 'aflibercept.'" *Id.* at 2:30–37. "VEGFR1R2-FcΔC1(a) comprises three components: (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130 to 231 of SEQ ID NO:2; and (3) a multimerization component [] comprising amino acids 232 to 457 of SEQ ID NO:2." *Id.* at 4:58–5:3 (citing U.S. Patent No. 7,396,664 B2).

The Specification discloses that, despite the known methods for treating eye disorders using VEGF antagonists, "there remains a need in the

art for new administration regimens for angiogenic eye disorders, especially those which allow for less frequent dosing while maintaining a high level of efficacy." *Id.* at 1:53–61. The Specification discloses that

> [t]he present inventors have surprisingly discovered that beneficial therapeutic effects can be achieved in patients suffering from angiogenic eye disorders by administering a VEGF antagonist to a patient at a frequency of once every 8 or more weeks, especially when such doses are preceded by about three doses administered to the patient at a frequency of about 2 to 4 weeks.

*Id.* at 2:3–10. The Specification describes this dosing regimen as sequentially administering initial, secondary, and tertiary doses. *See id.* at 1:62–2:3. The Specification refers to "sequentially administering" as "each dose of VEGF antagonist is administered to the patient at a different point in time, e.g., on different days separated by a predetermined interval (e.g., hours, days, weeks or months)." *Id.* at 3:22–26. The Specification refers to the "initial dose" as "the dose which is administered at the beginning of the treatment regimen;" the "secondary doses" as "the doses which are administered after the initial dose;" and the "tertiary doses" as "the doses which are administered after the secondary doses." *Id.* at 3:31–38.

### *E. Illustrative Claims*

Petitioners challenge claims 1, 3–11, 13, 14, 16–24 and 26 of the '338 patent. Claims 1 and 14, the only independent claims, are set forth below as illustrative of the claimed subject matter.

> 1. A method for treating an angiogenic eye disorder in a patient, said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;

> wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.

Ex. 1001, 23:2–18.

> 14. A method for treating an angiogenic eye disorder in a patient, said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
>
> wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising VEGFR1R2-FcΔC1(a) encoded by the nucleic acid sequence of SEQ ID NO:1.

*Id.* at 24:2–15.

## II. PATENTABILITY ANALYSIS

### *A. Principles of Law*

To prevail in its challenges to the patentability of all claims of the '338 patent, Petitioners must demonstrate by a preponderance of the evidence that the claims are unpatentable. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d) (2019). "In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable." *Harmonic Inc. v. Avid. Tech., Inc.*, 815 F.3d 1356, 1363

(Fed. Cir. 2016); *see also* 35 U.S.C. § 312(a)(3) (2012) (requiring *inter partes* review petitions to identify "with particularity . . . the evidence that supports the grounds for the challenge to each claim"). That burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015); *see also In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1375–78 (Fed. Cir. 2016) (discussing the burden of proof in *inter partes* review).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Schering Corp. v. Geneva Pharms*, 339 F.3d 1373 (Fed. Cir. 2003) (quoting *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987)). It is well settled that "a reference can anticipate a claim even if it 'd[oes] not expressly spell out' all the limitations arranged or combined as in the claim, if a person of skill in the art, reading the reference, would 'at once envisage' the claimed arrangement or combination." *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015) (quoting *In re Petering*, 301 F.2d 676, 681 (1962)).

### *B. Level of Ordinary Skill in the Art*

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1323 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioners assert that a person of ordinary skill in the art at the time of the invention would have had

> (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of

> therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field, including the publications discussed herein. Typically, such a person would have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders (such as AMD), including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists.

Pet. 22 (citing Ex. 1002 ¶¶ 26–28; Ex. 1003 ¶¶ 20–24).

In the Patent Owner Response, Patent Owner asserts in a footnote that it disagrees with Petitioners' definition of the person having ordinary skill in the art ("POSA"). PO Resp. 15 n.7. According to Patent Owner, "the POSA is an ophthalmologist with experience in treating angiogenic eye disorders, including through the use of VEGF antagonists." *Id.* (citing Ex. 2051 ¶ 28). According to Dr. Do, "only an ophthalmologist would have the firsthand experience of diagnosing and treating angiogenic eye disorders to which the patent is plainly directed." Ex. 2051 ¶ 28. Patent Owner, however, asserts that it "does not believe that parties[']differing definitions of 'the POSA' matter for any argument in [the] Patent Owner Response." PO Resp. 15 n.7.

Having considered the arguments and evidence, we maintain that Petitioners' definition of one of ordinary skill in the art is reasonable and consistent with the '338 patent and the prior art of record. On the other hand, we find Patent Owner's definition to be inappropriately limited to those having "firsthand experience" regarding the diagnosis and treatment of angiogenic eye disorders, as explained by Dr. Do. *See* Ex. 2051 ¶ 28. While it may be that the claimed methods would be performed an ophthalmologist, a person having ordinary skill in the art need not be limited to those

performing the claimed method. Rather, we find that Petitioners' definition more appropriately considers that knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders, may be possessed by other professionals that are not ophthalmologists. Accordingly, we adopt Petitioners' definition for purposes of this Decision.

We have reviewed the credentials of Petitioners' declarants, Drs. Albini and Gerritsen, and Patent Owner's declarants, Drs. Do, Del Priore, Klibanov, Brown, and Manning, and consider each of them to be qualified to provide the opinions for which their testimony has been submitted.

### *C. Claim Construction*

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 100(b) (2019). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17).

Petitioners and Patent Owner propose constructions for certain claim terms. *See* Pet. 11–22; PO Resp. 7–24. In the following discussion, we address those proposed constructions.

*1. "A method for treating an angiogenic eye disorder in a patient"*

At the institution stage, we made a preliminary finding that the preambles of claims 1 and 14, i.e., "[a] method for treating an angiogenic eye disorder in a patient," are limiting. Inst. Dec. 18. We also determined preliminarily that the claimed methods do not require any "specific degree of efficacy." *Id.* at 20–21. In the following discussion, we address the parties' arguments and our final claim construction for this phrase.

*a) Petitioners' Position*

According to Petitioners, "[t]he 'method for treating' preamble of independent claims 1 and 14 is 'merely a statement of purpose or intended' use for the claimed dosing regimen(s) and is non-limiting." Pet. 17 (citing *Bristol-Myers Squibb Co. v. Ben Venue Lab'ys, Inc.*, 246 F.3d 1368, 1375 (Fed. Cir. 2001)). Petitioners further assert that the preamble provides no antecedent basis for any other claim element, nor results in a manipulative difference in the steps of the claims. *Id.* at 20 (citing *In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018)).

Petitioners assert that even if the preamble is limiting, the plain and ordinary meaning of the "method of treating an angiogenic eye disorder" does not require a therapeutically effective treatment. *Id.* at 20. Rather, Petitioners assert that the plain and ordinary meaning merely requires "administering a therapeutic to a patient, without a specific degree of efficacy required." *Id.* at 20–21 (citing, Ex. 1002 ¶ 43).

*b) Patent Owner's Response*

Patent Owner asserts that "the claimed 'method for treating' must actually treat, not merely intend to treat" because the preamble reciting a method for treating "is a positive limitation of the claim that must be practiced to satisfy the claim." PO Resp. 9. Further, Patent Owner asserts

that "the claimed method for treating requires treatment of a patient with a high level of efficacy, on par with the prevailing standard-of-care at the time of filing." *Id.* at 13 (citing Ex. 2051 ¶¶ 54–84). In support of that position, Patent Owner relies on the results of Regeneron's Phase III studies, which Patent Owner asserts "shows that a similar proportion of subjects in each of the VEGF Trap-Eye dosing arms, including the Q8 dosing arm, met the primary endpoint of loss of ≤15 letters on ETDRS[10] (95.1% or 95.6%) as compared to monthly ranibizumab (94.4%)" and "reports similar mean improvement in vision as compared to monthly ranibizumab, with an average gain of 7 or more letters for the Q8 dosing regimen." *Id.* at 14–15 (citing Ex. 1001, 14:3–23 (Table 1)). According to Patent Owner, a POSA would have concluded from the study data that "VEGF Trap-Eye, including on a Q8 dosing schedule, achieved and maintained a high level of efficacy that was non-inferior to standard-of-care Lucentis." *Id.* at 15.

Patent Owner also contends that the prosecution history confirms that the claimed treatment methods must achieve a high level of efficacy because "Regeneron relied on Heier 2012 (Ex. 1018) to overcome a double patenting rejection by arguing that the 'treatment protocol' encompassed by the claimed invention resulted in surprising efficacy, *i.e., noninferiority to ranibizumab*, despite less frequent dosing than the standard of care) *i.e.*, monthly dosing of ranibizumab)." *Id.* at 16 (citing Ex. 1017, 288–91, 315).

Further, Patent Owner argues that "the POSA would have understood that a less frequent dosing regimen that was inferior to the standard-of-care, or worse yet—ineffective—would not have been viewed as treatment by 2011." *Id.* at 17. In support of that position, Patent Owner asserts that

[10] Early Treatment Diabetic Retinopathy Study ("ETDRS").

although another medication, Macugen, "demonstrated some level of efficacy" by slowing vision loss with a recommended dosing schedule of once every 6 weeks, "once Lucentis was approved and showed that it could restore vision, no one considered Macugen to be effective treatment and practitioners stopped using it." *Id.* at 17. According to Patent Owner, that example demonstrates that "the POSA would have understood what the '338 Patent makes explicit—that the claimed 'method for treating' must provide highly effective treatment (non-inferior to the standard-of-care at the time of patent filing) to the patient." *Id.* at 17–18 (citing Ex. 2051 ¶¶ 46–84). Additionally, Patent Owner asserts that the claims do not encompass "ineffective treatment methods, such as the administration of non-therapeutically effective dose amounts," because methods that are not "therapeutically effective" "would not be 'treatment' as the term is understood by the POSA." *Id.* at 19–20 (citing Ex. 2051 ¶¶ 47–53).

Patent Owner also challenges Petitioners' contention that the '338 patent only requires a patient to exhibit a loss of fifteen or fewer letters on the ETDRS visual acuity chart within 104 weeks of treatment initiation. *Id.* at 20–21 (citing Pet. 21). Patent Owner argues that "the POSA *would not have considered* such loss of ≤15 letters on ETDRS to reflect an effective method for treating an angiogenic eye disorder by 2011." *Id.* at 21. According to Patent Owner, the POSA would have understood that a loss of fifteen or fewer letters or a gain of letters on ETDRS are "common clinical trial endpoints [that] are used to measure results of angiogenic eye disorder treatments in the art, and in the '338 Patent specification." *Id.* at 21. Patent Owner contends that those clinical trial endpoints were "not to define an outcome that reflects an effective treatment method." *Id.*

*c) Petitioners' Reply*

In the Reply, Petitioners maintain that the preamble is not limiting, but rest on their arguments in the Petition regarding that issue. Pet. Reply 7. Petitioners explain that for the remainder of the Reply arguments, Petitioners apply the Board's preliminary holding that the preamble is limiting. *Id.*

Petitioners maintain also that, if limiting, the preamble should be afforded its plain and ordinary meaning, i.e., "administering a therapeutic agent to a patient, without a specific degree of efficacy required." *Id.* (citing Ex. 1002 ¶ 43). Petitioners assert that Patent Owner's proposed construction "necessitates reading-in the 'high level of efficacy' concept [into the claims]—'one of the cardinal sins of patent law.'" *Id.* at 8 (quoting *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001)). Petitioners contend that "[t]he Claims as-written inherently encompass *all* levels of efficacy not just a 'high' one." *Id.* at 9. According to Petitioners, the Specification does not include any clear disavowal in that regard. *Id.* at 10.

Petitioners note that although the claims do not recite the term "efficacy," the Specification defines the term by stating:

> "efficacy" means that, from the initiation of treatment, the patient exhibits a loss of 15 or fewer letters on the [ETDRS] visual acuity chart. In certain embodiments, "efficacy" means a gain of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or more) letters on the ETDRS chart from the time of initiation of treatment.

*Id.* at 10–11 (quoting Ex. 1001, 7:24–32). Petitioners assert that if the term "efficacy" is incorporated within the claims, it would require, "at most, a patient exhibit a loss of fifteen or fewer letters on the ETDRS visual acuity chart within 104 weeks of treatment initiation." *Id.* at 11 (citing Ex. 1002

¶ 43). Petitioners contend that "[t]he specification nowhere defines or guides how a POSA should ascertain, measure, or differentiate a '*high* level of efficacy.'" *Id.* (citing Ex. 1114 ¶¶ 30–40). Petitioners assert further that Patent Owner has not demonstrated what actually constitutes "'non-inferiority' for each 'standard of care' (*e.g.*, a BCVA score), and how a POSA could assess that with reasonable certainty." *Id.* at 13–14 (citing Ex. 1114 ¶¶ 30–40).

*d) Patent Owner's Sur-reply*

In the Sur-reply, Patent Owner continues to urge that the intrinsic record supports construing the preambles of claims 1 and 14 such that "treat" means "achieving a high level of efficacy." PO Sur-reply 4. In particular, Patent Owner alleges that the Specification and the prosecution history refer to: (a) the changed state-of-art; (b) an expectation of efficacy comparable to the "high level of efficacy" achieved with existing ranizumab treatment; and (c) a distinction between the claimed regimens from extended dosing regimens in the art that result in visual acuity losses. *Id.* at 5. According to Patent Owner, "[i]n view of the high level of efficacy that was expected of anti-VEGF therapies in the art, nothing more is needed" to support construing the claims to require the same high level of efficacy. *Id.*

In response to Petitioners' assertion that the Specification defines "efficacy" as "a loss of 15 or fewer letters" on the ETDRS visual acuity chart, Patent Owner asserts that "lexicography is inapplicable." *Id.* at 7–8. In support of that position, Patent Owner states that "it is undisputed that (1) 'efficacy' is not a claim limitation for construction; and (2) the specification provides no express definition for 'treating' or 'treatment.'" *Id.* Further, Patent Owner asserts that "it is undisputed that 'the POSA *would not have considered* a loss of ≤15 letters on ETDRS' to reflect the level of efficacy

expected for a method for treating angiogenic eye disorders by 2011." *Id.* at 9. According to Patent Owner, "the POSA would know with reasonable certainty that, by 2011, a highly effective treatment for angiogenic eye disorders is one that is on par to Lucentis or off-label Avastin and can produce visual acuity gains, not just slow vision losses." *Id.* at 11 (citing Ex. 2050 ¶¶ 84, 99).

*e) Discussion*

Having considered the record as a whole, we determine that the preamble of method claims 1 and 14, i.e., "[a] method for treating an angiogenic eye disorder in a patient" is limiting. Although we agree with Petitioners that the preamble sets forth "'a statement of purpose or intended' use for the claimed dosing regimen," *see* Pet. 17, that does not the end our inquiry. As noted in the Institution Decision, the Federal Circuit has explained that its case law does not support a "binary distinction between statements of mere intended purpose on the one hand and limiting preambles on the other." *Eli Lilly and Company v. Teva Pharms. Int'l GmbH,* 8 F.4th 1331, 1340 (Fed. Cir. 2021). Rather, as the Federal Circuit reiterated, "there is no 'litmus test' for determining whether a preamble is limiting." *Id.* (citing *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 952 (Fed. Cir. 2006) and *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002)). As the Court instructed, we consider whether to treat a preamble as a claim limitation based upon "the facts [in this] case in light of the claim as a whole and the invention described in the patent." *Id.* (quoting *Storage Tech. Corp. v. Cisco Sys., Inc.*, 329 F.3d 823, 831 (Fed. Cir. 2003)).

Here, the claims are directed to methods of administering, i.e., using, a VEGF antagonist for an intended purpose of "treating an angiogenic eye disorder in a patient." *See* Claims 1 and 14, Ex. 1001, 23:2–3; 24:3–4. The

Specification repeatedly characterizes the method as one for treating angiogenic eye disorders in patients. *See, e.g.*, *id.* at 1:18–20, 63–66, 2:23–27; 3:19–20; 5:11–13. Apart from the preamble, the independent claims do not elsewhere recite or indicate any other use for the method steps comprising the administration of a VEGF antagonist. Thus, we determine that the preamble sets forth the essence of the invention—treating an angiogenic eye disorder in a patient. As the Federal Circuit explained in *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339 (Fed. Cir. 2003), "preamble language will limit the claim if it recites not merely a context in which the invention may be used, but the essence of the invention without which performance of the recited steps is nothing but an academic exercise," and that this principle frequently holds true for method claims. *Id.* at 1345 (citing *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002)). We find that such is the case here.

Additionally, we find that the preamble provides antecedent basis for claim terms "the patient" recited in the body of each independent claim, and "angiogenic eye disorders" recited in dependent claims 6, 7, 18, and 20. Indeed, without the preamble, it would be unclear to whom the doses of VEGF are administered.

Thus, in view of Federal Circuit case law regarding statements of intended purpose in claims directed to method of using compositions, and in view of the evidence of record, namely, the claim language and the written description of the '338 patent, we find that the preambles of method claims 1 and 14 are limiting insofar as they require "treating an angiogenic eye disorder in a patient."

Having determined that the preambles of claims 1 and 14 are limiting, we next consider the parties' proposed constructions for the preamble claim

term "treating" in the context of the recited "method for treating an angiogenic eye disorder in a patient." As noted above, Petitioners argue that, if the preamble is limiting, a POSA would have applied the plain and ordinary meaning of "treating," which Petitioners assert is "administering a therapeutic to a patient, without a specific degree of efficacy required." Pet. 20–21 (citing, Ex. 1002 ¶ 43). According to Petitioners, it is enough that a therapeutic is administered with the "intentional purpose" of treating an angiogenic eye disorder, without showing actual therapeutic effectiveness. *Id.* at 20. Patent Owner, on the other hand, argues that "treating" an angiogenic eye disorder requires achieving "a high level of efficacy, on par with the prevailing standard-of-care at the time of filing." PO Resp. 13 (citing Ex. 2051 ¶¶ 54–84). Based on our consideration of the record as a whole, we determine that Petitioners have the better position.

We begin by noting that the claims do not recite any dosage amounts or that the administered doses are "therapeutically effective" separately or cumulatively. Instead, the claimed method focuses on treating an angiogenic eye disorder with a specific compound, i.e., a VEGF antagonist, based on a specific temporal regimen, i.e., sequentially administering an initial dose, followed by a prescribed time frame for secondary and tertiary dose(s). As discussed above, we determined that the preamble limits the claims in terms of requiring the doses of VEGF antagonist administered to be for the purpose of treating an angiogenic eye disorder in a patient. We find that the intrinsic evidence supports finding that it is the administration of the VEGF antagonist to such patient for the purpose of providing an improvement of or beneficial effect on their angiogenic eye disorder that satisfies the "treating" portion of the preamble.

In particular, we find instructive the Specification's discussion regarding the "Amount of VEGF Antagonist Administered." *See* Ex. 1001, 6:29–7:14. In that discussion, the Specification explains,

> The amount of VEGF antagonist administered to the patient in each dose is, *in most cases*, a therapeutically effective amount. As used herein, the phrase "therapeutically effective amount" means a dose of VEGF antagonist that results in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or a dose of VEGF antagonist that inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder.

*Id.* at 6:48–55 (emphasis added). That description, along with the absence of the phrase "therapeutically effective" in the claims,[11] signals for us the inventors' intention to not limit the claims to the administration of doses that ultimately prove to be therapeutically effective in a given patient. Instead, the Specification describes administration of VEGF antagonist doses for treating angiogenic eye disorder in a manner that encompasses doses that result in disclosed improvements and benefits, referred to as "therapeutically effective amounts," and doses that do not. Indeed, as guidance, the Specification discloses that "a therapeutically effective amount *can* be from about 0.05 mg to about 5 mg," without any guarantee that any particular dosage regimen administered within that range of dosage amounts will necessarily be "therapeutically effective," and without limiting the treatment methods based upon such results. Ex. 1001, 6:55–58 (emphasis added).

[11] We emphasize that it is the above-referenced Specification description *and* the lack of the phrase "therapeutically effective" in the claims that is instructive for our construction here. We do not suggest here, or in general, any categorical rule regarding a requirement for therapeutic effectiveness based upon the inclusion or omission of that claim phrase alone.

Patent Owner's arguments and evidence fail to persuasively support a different finding. For example, according to Patent Owner's expert, Dr. Do,

> *the [Specification] passages . . . from column 6 merely observe that an amount which is therapeutically effective is effective "in most cases" even if some patients do not respond*. That is consistent with the data reported in the specification that show that while around 96% of the treated subjects achieved the "primary endpoint (prevention of moderate or severe vision loss as defined above)," the remaining 4% did not achieve this endpoint.

Ex. 2051 ¶ 50 (quoting Ex. 1001, 12:66–13:23) (emphasis added). That, however, is not what the Specification states. Rather, the Specification expressly describes a "therapeutically effective amount" as "a dose of VEGF antagonist that *results* in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or . . . inhibits, prevents, lessens, or delays the progression of an angiogenic eye disorder." Ex. 1001, 6:50–55. In other words, the Specification refers to the dose that ultimately *results* in one of those beneficial effects in a given patient as a "therapeutically effective dose" for that patient. If the same dosage amount is administered to another patient, but does not provide a beneficial result, the Specification does not recognize that same dosage amount as therapeutically effective in the non-responsive patient. Thus, when the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, *in most cases*, a therapeutically effective amount," and discloses that "a therapeutically effective amount *can* be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays

the progression of an angiogenic eye disorder," or it may not. *Id.* at 6:48–50. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

We reject Patent Owner's proposed construction because it requires importing limitations into the claims. Patent Owner's proposes that the claims require not only achieving a therapeutically effective result, but more specifically, achieving a "high level of efficacy that was noninferior to the standard of care by the time the patent was filed in 2011." In the Sur-reply, Patent Owner describes a "highly effective treatment for angiogenic eye disorders" as "one that is on par to Lucentis or off-label Avastin and can produce visual acuity gains, not just slow vision losses." PO Sur-reply 11 (citing Ex. 2050 ¶¶ 84, 99). The Specification refers to "a high level of efficacy" in one instance, i.e., in the "Background" section. *See* Ex. 1001, 1:55–59. The Specification does not describe there, or elsewhere that "treating," in the context of the claims or in the art, requires achieving a "high level of efficacy" or providing results "on par to Lucentis or off-label Avastin."

Insofar as Patent Owner relies on the extrinsic testimony of Drs. Do and Brown for that description, we do not assign that testimony persuasive weight as it lacks sufficient evidentiary support. As discussed above, we find Dr. Do's testimony at odds with the Specification. In particular, for the reasons discussed above regarding the Specification description of the amount of VEGF antagonist administered to the patient, we find troubling

her assessment that "[i]f administration of the drug is not effective, it would not be a treatment." Ex. 2051 ¶ 46. Additionally, we find much of her testimony regarding the a so-called "high level of efficacy" based on an asserted existing standard of care for angiogenic eye disorder is supported by little more than evidence relating to FDA approvals for Macugen and Lucentis. Dr. Brown's testimony cited by Patent Owner to support the asserted efficacy requirement, simply relies on Dr. Do's testimony without discussing any additional evidentiary support.

Based on the foregoing and our review of the record as a whole, we find no persuasive support for construing the preamble recitation of a "method for treating a patient with an angiogenic eye disorder" as requiring such "treating" to achieve any particular level of effectiveness, much less a "high level of efficacy." Rather, as discussed above, we find that the evidence of record and the Specification support construing the phrase as meaning administering a compound, i.e., the recited VEGF antagonist, to such patient for the purpose of improving or providing a beneficial effect in their angiogenic eye disorder.

*2. "Initial dose," "Secondary Dose," and "Tertiary Dose"*

Petitioners assert that the Specification provides express definitions for these terms, specifically that "'initial dose' means 'the dose which is administered at the beginning of the treatment regimen'; 'secondary dose(s)' means 'the dose(s) which are administered after the initial dose'; and 'tertiary dose(s)' means 'the dose(s) which are administered after the secondary dose(s).'" Pet. 12–13 (quoting Ex. 1001, 3:31–45; Ex. 1002 ¶ 41).

Patent Owner disagrees with Petitioners and asserts that each recited dose should be construed by more than just the administration timing. *See* PO Resp. 22–24. In particular, Patent Owner contends that the claim term "tertiary dose(s)" should be construed to mean "dose(s), administered after the initial and secondary doses, that *maintain(s) the efficacy gain* achieved after the initial and secondary doses." PO Resp. 22. Thus, Patent Owner's proposed construction of "tertiary dose(s)" also includes a requirement for the "initial dose" and "secondary dose(s)," i.e., that they achieve an "efficacy gain." Patent Owner contends that the Specification description of a "tertiary dose" as "the dose(s) which are administered after the secondary dose(s)," is not a formal definition because it does not follow the same linguistic format used to define other terms in the Specification. *Id.* at 23. According to Patent Owner, a proper construction for the term "includes both the order and purpose of the 'tertiary dose.'" *Id.* at 23. According to Patent Owner, "if 'tertiary dose' were defined based only on its temporal sequence, the Challenged Claims would encompass administering ineffective doses of the recited antagonist—*e.g.*, infinitesimal quantities that are not capable of achieving any efficacy." *Id.* at 24. Patent Owner asserts that such a definition of the term "would be an incongruous interpretation of claims directed to a 'method for treating' angiogenic eye disorders." *Id.*

Based on our review of the Specification and consideration of the arguments and the evidence, we find that the Specification expressly defines the terms "initial dose," "secondary doses," and "tertiary doses." The Specification states,

> The terms "initial dose," "secondary doses," and "tertiary doses," refer to *the temporal sequence of administration of* the VEGF antagonist. Thus, the "initial dose" is the dose which is administered at the beginning of the treatment regimen (also referred to as the "baseline dose"); the "secondary doses" are the doses which are administered after the initial dose; and the "tertiary doses" are the doses which are administered after the secondary doses.

Ex. 1001, 3:31–38 (emphasis added). Based on those express definitions in the Specification, we do not find cause to construe the terms differently. In particular, we do not find that the Specification requires the "tertiary doses" to maintain any efficacy gain achieved after the initial and secondary doses, or that the term suggests any specific level of efficacy. The Specification unequivocally states that "[t]he terms 'initial dose,' 'secondary doses,' and 'tertiary doses,' refer to the *temporal sequence of administration* of the VEGF antagonist," and that "the 'tertiary doses' are the doses which are administered after the secondary doses." Ex. 1001, 3:31–38 (emphasis added). Patent Owner has not directed us to any portion of the Specification or other persuasive evidence that supports adding an efficacy requirement to that definition.

*3. "4 weeks" and "8 weeks"*

Petitioners contend that "[a] skilled artisan would understand the phrase "'4 weeks'—as it appears in the Challenged Claims—to be synonymous with monthly administration" and "'8 weeks' . . . to be synonymous with bi-monthly (or every-other-month administration)." Pet. 16 (citing Ex. 1001, 7:54–56, 14:41–52; Ex. 1002 ¶ 42). Patent Owner does not challenge this construction. Based record as a whole, we determine that express construction of these claim terms is unnecessary for purposes of rendering this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d

1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc*., 200 F.3d 795, 803 (Fed. Cir. 1999)).

*4. "VEGFR1 Component," "VEGFR2 Component," and "Multimerization Component"*

Petitioners contend that "VEGFR1 Component," "VEGFR2 Component," and "Multimerization Component" all refer to separate amino acid domains of SEQ ID NO:2. Pet. 16–17. Petitioner contends that "[a] skilled artisan would understand these terms to collectively refer to aflibercept (a/k/a VEGF Trap or VEGF Trap-Eye or VEGFR1R2-FcΔC1(a))." *Id.* at 17 (citing Ex. 1001, 2:32–37; Ex. 1002 ¶ 44). Patent Owner does not address Petitioners' contention or these terms in its claim construction analysis. As Petitioners' contention does not appear to be a proposed claim construction, we find it more appropriate to address such contention and these terms below, in the context of our anticipation and obviousness analysis.

*D. Anticipation*

Petitioners assert that claims 1, 3–11, 13, 14, 16–24 and 26 are anticipated by each of Dixon, Adis, Regeneron, NCT-795, and NCT-377. Pet. 37–61; Pet. Reply 18–32. Patent Owner disagrees. PO Resp. 24–52; PO Sur-reply 14–30. Because we have determined that Petitioners' anticipation ground based on Dixon is representative of the remaining anticipation grounds and is sufficient to resolve the anticipation challenge, we focus here on Petitioners' anticipation challenge based on Dixon.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Schering Corp. v. Geneva Pharms*, 339 F.3d 1373, 1379

(Fed. Cir. 2003) (quoting *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

*1. Dixon*

Dixon describes a review of clinical trial data regarding administering VEGF Trap-Eye to treat neovascular AMD. Ex. 1006, 1573. Dixon discloses that "VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD." *Id.* Dixon describes VEGF Trap-Eye as "a fusion protein of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment." *Id.* at 1575. Dixon discloses that "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure, but there are substantial differences between the preparation of the purified drug product and their formulations." *Id.*

Dixon discloses that current therapy requires "frequent intraocular injections, as often, as monthly, without a defined stopping point," and that "[t]he time and financial burden of monthly injections has led to the initiation of studies to examine the efficacy of alternative dosing schedules." *Id.* at 1574, 1577. Dixon discloses that:

> [d]ue to its high binding affinity and the ability to safely inject high doses into the eye, VEGF Trap-Eye may have longer duration of effect in the eye. Two Phase III studies in wet AMD, VIEW 1 and VIEW 2, are currently under way and seek to compare monthly ranibizumab to monthly or bimonthly VEGF Trap-Eye.

*Id.* at 1577. Specifically, Dixon discloses that the Phase III trial initiated in August of 2007 "will evaluate the safety and efficacy of intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses),

compared with 0.5 mg of ranibizumab administered every 4 weeks." *Id.* at 1576. Dixon discloses that in a Phase II trial, patients treated with monthly doses of 2.0 or 0.5 mg VEGF Trap-Eye achieved improvements according to the Early Treatment of Diabetic Retinopathy Study ("ETDRS") scale. *Id.*

*2. Discussion*

Petitioners assert that Dixon inherently anticipates the challenged claims. *See* Pet. 37. Specifically, Petitioners assert that "the Challenged Claims require only a dosing regimen without any particular efficacy or result . . . and therefore, 'proof of efficacy is not required in order for a [prior art] reference to be enabled for purposes of anticipation.'" *Id.* at 38 (quoting *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1326 (Fed. Cir. 2005)) (emphasis omitted).

Petitioners identify the disclosures in Dixon that Petitioners assert disclose each element of claim 1. *See* Pet. 39–41. Specifically, Petitioners assert that Dixon discloses a method of treating an angiogenic eye disorder (neovascular AMD) in a patient, by administering a VEGF antagonist (VEGF Trap-Eye). *Id.* at 39–40 (citing Ex. 1006, 1573, 1577). Petitioners assert that Dixon discloses a dosing regimen of sequentially administering an initial dose (day 0), two secondary doses (4 and 8 weeks), and at least one tertiary dose (every 8 weeks beginning at week 16). *Id.* at 40 (citing Ex. 1006, 1576; Ex. 1002 ¶¶ 119–128).

Petitioners assert also that Dixon discloses the specific VEGF receptor-based chimeric molecule recited by claim 1 because Dixon discloses that VEGF Trap-Eye is "a fusion protein of binding domains of VEGF receptors-1 and -2 attached to the Fc fragment of human IgG" and has "the same molecular structure" as aflibercept. *Id.* (citing Ex. 1006, 1575–1576; Ex. 1002 ¶ 127). Petitioners further assert that "[t]he amino

acid sequence and structural information for VEGF Trap-Eye recited in the third 'wherein' clause was well-known and widely-published to skilled artisans." *Id.* at 40–41 (citing Ex. 1010, Fig. 24A–C, 10:15–17; Ex. 1033, ¶¶ 13–14, 30; Ex. 1002 ¶¶ 147–50).

Petitioners also address the limitations in independent claim 14 and the challenged claims that depend from claims 1 and 14, i.e., dependent claims 3–11, 13, 16–24 and 26. *See* Pet. 41–44.

Patent Owner contends that Petitioners have failed to demonstrate that the challenged claims are anticipated by Dixon for two primary reasons. First, Patent Owner argues that Dixon does not expressly or inherently disclose the amino acid or nucleic acid sequence of VEGF Trap-Eye. PO Resp. 25–35. Second, Patent Owner argues that Dixon does not expressly or inherently disclose a "method for treating." *Id.* at 37–52. Because it is undisputed that Dixon discloses the remaining claim elements for each of the challenged claims, we focus the remainder of our discussion on the two elements of claims 1 and 14 challenged by Patent Owner.

*a) VEGF Trap-Eye Sequence*

Independent claim 1 recites that the VEGF antagonist is:

> a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.

Ex. 1001, 23:12–18.

For independent claim 14, the VEGF antagonist is recited as:

> a VEGF receptor-based chimeric molecule comprising VEGFR1R2-FcΔC1(a) encoded by the nucleic acid sequence of SEQ ID NO:1.

*Id.* at 24:13–15.

Patent Owner asserts that Dixon does not expressly disclose the amino acid sequence or the nucleic acid sequence of VEGF Trap-Eye. PO Resp. 25. Additionally, Patent Owner contends that Dixon does not inherently disclose those sequences. *Id.* at 26. According to Patent Owner, "Petitioner has failed to establish inherent anticipation because the POSA would not have necessarily known or determined that 'VEGF Trap-Eye' had the claimed amino acid or nucleic acid sequence based on public information available as of the priority filing date of the '338 Patent." *Id.* at 25–26. In particular, Patent Owner asserts that Dixon does not disclose that its VEGF antagonist, i.e., "VEGF Trap-Eye," shares the same amino acid sequence of aflibercept. *Id.* at 28.

Moreover, Patent Owner asserts that "[i]t is undisputed that VEGF Trap-Eye was not publicly available before EYLEA's FDA approval on November 18, 2011." PO Resp. 24. (citing Ex. 2130, 319:16–320:9). According to Patent Owner, its clinical trials involving VEGF Trap-Eye were conducted under strict confidentiality, as was its submission of information to FDA regarding VEGF Trap-Eye pre-approval. *Id.* Based on those assertions, Patent Owner contends that a POSA would not have had access to the amino acid or nucleic acid sequence of VEGF Trap-Eye before the priority filing date of the '338 Patent. *Id.*

Although Patent Owner recognizes that Dixon discloses that VEGF Trap-Eye and aflibercept share a "molecular structure," Patent Owner asserts that "a shared 'molecular structure' does not necessarily evidence an identical amino acid sequence. *Id.* at 28. According to Patent Owner, "[t]he term 'molecular structure' was repeatedly used in the literature to refer to the three-dimensional structure of the protein, rather than a protein's amino acid sequence." *Id.* Patent Owner contends that Dixon "suggests that the

'molecular structure' of VEGF Trap-Eye refers to a more general selection and arrangement of receptor binding domains and an Fc region, not a precise amino acid or nucleic acid sequence." *Id.* at 29. Thus, according to Patent Owner, "the POSA would have understood that Dixon's statements concerning the 'molecular structure' of VEGF Trap-Eye could have referred to the protein's three dimensional (3D) structure, or overall configuration of VEGF binding domains, rather than its primary structure (*i.e.*, amino acid sequence)." *Id.*

Patent Owner asserts also that the POSA would have understood Dixon's description of VEGF Trap-Eye as "a fusion protein of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment" to correspond to a genus of protein sequences reported in the art. *Id.* at 29. In particular, Patent Owner refers to its own engineered VEGF fusion proteins, i.e., "VEGF Trap" molecules which, in only some cases include both VEGFR1 and VEGRF2 binding domains. *Id.* Patent Owner asserts that the term "VEGF TrapR1R2" refers to a subset of VEGF Trap proteins known to encompass a genus of protein sequences, "any one of which could satisfy Dixon's structural definition, but would not necessarily possess the amino acid sequence of the Challenged Claims." *Id.* at 30–31.

Additionally, Patent Owner asserts that the POSA would have been aware of different reported molecular weights for VEGF Trap-Eye. *Id.* at 31. Specifically, Patent Owner asserts that the molecular weight of VEGF Trap-Eye was separately reported as 110 kDa and 115 kDa, whereas the molecular weight of aflibercept was routinely reported as 115 kDa. *Id.* (citing Ex. 1075, 403; Ex. 2048 ¶¶ 87–91; Ex. 2079 ¶¶ 76–783). According to Patent Owner, "[t]he POSA would have recognized that reported differences in molecular weights among VEGF Trap-Eye proteins, as well as

those between the reported molecular weights of VEGF Trap-Eye and aflibercept, could reflect differences in the amino acid sequence." *Id.* at 31.

Having considered the arguments and the evidence, we determine that based on the record as a whole, Petitioners have shown by a preponderance of the evidence that Dixon inherently discloses a VEGF antagonist comprising the amino acid sequence recited in claim 1 and the nucleic acid sequence recited in claim 14 by disclosing VEGF Trap-Eye.

Dixon describes the VEGF Trap-Eye as follows:

> *VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure*, but there are substantial differences between the preparation of the purified drug product and their formulations. Both aflibercept and VEGF Trap-Eye are manufactured in bioreactors from industry standard Chinese hamster ovary cells that overexpress the fusion protein. However, VEGF Trap-Eye undergoes further purification steps during manufacturing to minimize risk of irritation to the eye. VEGF Trap-Eye is also formulated with different buffers and at different concentrations (for buffers in common) suitable for the comfortable, non-irritating, direct injection into the eye.

Ex. 1006, 1575 (emphasis added). Patent Owner's argument that Dixon's description of VEGF Trap-Eye and aflibercept as having the "same molecular structure" refers only to the three-dimensional secondary and tertiary structures of the fusion protein, rather than the protein's amino acid sequence is unpersuasive. *See* PO Resp. 28 (citing Ex. 2049 ¶¶ 57–63). We decline to accept such a limited and unduly arbitrary definition of "molecular structure."

We take judicial notice that it is an axiom of protein chemistry that proteins have primary, secondary, tertiary, and quaternary structure. *See* Fed. R. Evid. 201; W.H. Brown et al., *Polypeptides and Proteins*, Chapter 27.3, 1075–96, in ORGANIC CHEMISTRY (Fourth Ed.) (2005) (Ex. 3002).

Indeed, Patent Owner's expert, Dr. Del Priore recognizes that "[i]t is well established that protein molecules, like VEGF Trap-Eye, have multiple levels of 'structure,' including primary, secondary, tertiary, and quaternary structures." Ex. 2048 ¶¶ 50, 67. Primary structure is the sequence of the amino acids constituting a polypeptide chain. Ex. 3002, 1075. Secondary structure refers to spontaneously-arising ordered arrangements (conformations) of amino acids in localized regions of a polypeptide chain, such as an α-helix or β-pleated sheet. *Id.* at 1089–90. Secondary structure is caused by the patterns of the amino acid distribution within the polypeptide chain. *Id.* The tertiary structure of a protein refers to the overall folding pattern and arrangement in space of all of the atoms in a single polypeptide chain. Such three-dimensional structure is caused by the interactions of amino acids in the chain, including that caused by disulfide bonds, hydrophobic interactions, hydrogen bonding, and salt linkages. *Id.* at 1091. Quaternary structure is formed by the interactions of multiple polypeptide monomers into aggregate arrangements. *Id.* at 1095.

All of these structures are intensely interrelated in defining the final three-dimensional shape of the protein, which, in turn, is critical to the role played by the protein, whether as a structural protein, enzyme, etc. The location of amino specific acids in the polypeptide chain (the primary structure) determines the ability of those amino acids to interact with each other, and these interactions form the final complex, three-dimensional shape of the chain (secondary and tertiary structures). Ex. 3002, 1093–1094; *see, e.g.*, Ex. 1108, 32–35, 184–189. Consequently, primary, secondary, and tertiary structures are all interrelated, and primary structure necessarily drives secondary and tertiary structures. A completed protein molecule may

consist of an aggregation of folded polypeptide chains, and that provides the final, quaternary structure of the protein molecule. *Id.* at 1095.

Dixon expressly teaches that aflibercept and VEGF Trap-Eye have the "same molecular structure." Ex. 1006, 1575. Patent Owner argues that this disclosure should exclude the primary structure, i.e., the amino acid sequence, from this definition of molecular structure, and offers examples of how proteins having different amino acid sequences can have similar shapes. *See, e.g.*, PO Resp. 28–29. We agree with Patent Owner to the extent that protein molecules, or more often, the active sites of protein molecules can have similar shapes. Indeed, that feature enables the binding function of receptor agonists and antagonists. *See* Ex. 1001, 1:44–49, 2:29–39, 4:35–45. But to argue, as Patent Owner does, that proteins, or parts of proteins, *can* have similar or the same three-dimensional shapes is not the same as saying that aflibercept and VEGF Trap-Eye have the *same* molecular structure, i.e., are the same molecule, as disclosed by Dixon.

We find that Patent Owner offers no plausible reason why the primary structure of protein should be omitted from the definition of "molecular structure" and, given the interrelatedness of primary, secondary, and tertiary structure in determining the shape of a polypeptide chain, we can see no reason to omit it. Rather, we conclude that a person of ordinary skill in the art would understand that Dixon's disclosure that "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure" means that VEGF Trap-Eye and aflibercept have the same primary, secondary, and tertiary structure. Therefore, a person skilled in the art would understand that VEGF Trap-Eye and aflibercept have the same amino acid sequence and nucleic acid sequence, and that those sequences are the same as what is recited for the VEGF antagonist in the challenged claims. *See, e.g.*,

Ex. 1024, 2, 5–7, 8; Ex. 1127, 1; Ex. 1128, 1–2; Ex. 1017, 136–138. Thus, Dixon inherently discloses the sequences recited in the challenged claims of the '338 patent.

There is even further reason to conclude that Dixon inherently discloses the amino acid sequence and the nucleic acid sequence of VEGF Trap-Eye. Petitioners point to Patent Owner's statements to the Patent Office during the prosecution of two prior art patents "that the sequence of 'the active ingredient of EYLEA™' [aflibercept ophthalmic solution]—namely, 'aflibercept, also known as VEGF trap, VEGF-trap, VEGF Trap-Eye and VEGF-Trap$_{R1R2}$' is set forth in [Patent Owner's prior art] patents." Pet. Reply 22 (quoting Ex. 1024, 2, 5–7, 8 ("aflibercept meets all of the limitations of claims 1 and 2" of the prior art patent); Ex. 1115 ¶¶ 10–32; Ex. 1010, Figs. 24A–C, SEQ ID NOS: 15 and 16; Ex. 1102, 2, 5–7; Ex. 1023, Figs. 24A–C, SEQ ID NOS: 15 and 16)). Petitioners also point to Patent Owner's statement to the Patent Office during prosecution of the '338 patent, that the Example 4 data correspond to VIEW 1/VIEW 2—in other words, "the same trials, and thus *the same molecule*," as disclosed by Dixon. *Id.* (citing Ex. 1017, 288–91).

It is therefore Petitioners' position that the sequence recited in the challenged claims, and in Patent Owner's prior art patents "is unquestionably VEGF Trap-Eye/aflibercept," which was used in the VIEW 1/VIEW 2 studies, and is disclosed in Dixon. Thus, according to Petitioners, Dixon inherently discloses the claimed amino acid and nucleic acid sequences. *Id.* at 22–23.

Patent Owner urges that Dixon does not inherently discloses the claimed amino acid sequence because a person of ordinary skill in the art would have had reason to doubt that the VEGF Trap-Eye disclosed by Dixon

could only have been aflibercept. According to Patent Owner, the skilled artisan would have understood that the VEGF Trap-Eye could have instead been one of a possible genus of VEGF compounds, and not necessarily aflibercept. PO Resp. 30. Patent Owner advances four arguments in support of this contention: (1) the skilled artisan could have concluded that VEGF Trap-Eye was a genus of proteins with different amino acid sequences; (2) the prior art reported VEGF Trap-Eye to have different molecular weights than aflibercept; (3) Dixon does not discloses that "VEGF Trap Eye" corresponds to only the recited sequence; and (4) Patent Owner consistently characterized "VEGF Trap-Eye" as an ophthalmology product and "aflibercept'" as an oncology drug. *Id.* at 30–34. Patent Owner's position, therefore, is that because a person of ordinary skill could not be certain that the VEGF Trap-Eye disclosed by Dixon had the claimed amino acid sequence recited in claim 1 of the '338 patent, Dixon does not anticipate the challenged claims.

We find Patent Owner's arguments unavailing. In an anticipation analysis, we consider whether a claim limitation that is not expressly disclosed "is *necessarily* present, or inherent, in the single anticipating reference." *Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1337 (Fed. Cir. 2010) (emphasis added). Patent Owner has made multiple acknowledgements that the VEGF Eye-Trap used in the VIEW 1/VIEW 2 test (and disclosed by Dixon) possessed the same sequence recited by the challenged claims of the '338 patent.

For example, during prosecution of the '338 patent, Patent Owner admitted to the Patent Office that:

> The [Heier 2012][12] paper shows results of a treatment protocol of the type claimed on over 2,400 patients. The studies summarized in the Heier [2012] paper correspond to the clinical trials disclosed in Example 4 of the present application which involve the use of the VEGF receptor-based chimeric molecule known as aflibercept or "VEGF Trap."

Ex. 1017, 136, 289. Heier 2012 describes results of the VIEW 1 and VIEW 2 phase III clinical studies, which are also disclosed in Dixon. *Compare* Ex. 1018, 2539–2540, *with* Ex. 1006, 1579 ref. 46–47. Patent Owner thus acknowledged, during prosecution, that VEGF Trap-Eye with the claimed amino acid sequence used in Example 4 of the '338 patent is the same drug used in the VIEW 1 and VIEW 2 studies disclosed by both Dixon and Heier 2012.

Similarly, Patent Owner stated in its September 30, 2009 Quarterly Report (Form 10-Q) submission to the United States Securities and Exchange Commission ("SEC," Ex. 1021):

> We also have six product candidates currently in clinical development, including three in late-stage clinical development. Our late stage programs are aflibercept (VEGF Trap), which is being developed in oncology in collaboration with the sanofi-aventis Group, VEGF Trap-Eye, which is being developed in eye diseases using intraocular delivery in collaboration with Bayer HealthCare LLC, and ARCALYST which is being developed for the treatment of gout.

Ex. 1021, 17. Specifically, Patent Owner stated that:

> Aflibercept is a protein-based product candidate designed to bind all forms of Vascular Endothelial Growth Factor-A (called VEGF-A, also known as Vascular Permeability Factor or VPF), VEGF-B and the related Placental Growth Factor (called PlGF),

[12] J.S. Heier et al., *Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-related Macular Degeneration*, 119(112) OPHTHALMOLOGY 2537-48 (2012) ("Heier 2012") (Ex. 1018).

> and prevent their interaction with cell surface receptors. VEGF-A (and to a less validated degree, VEGF-B and PlGF) is required for the growth of new blood vessels (a process known as angiogenesis) that are needed for tumors to grow and is a potent regulator of vascular permeability and leakage.

*Id.* at 18. Furthermore:

> *VEGF Trap-Eye is a specially purified and formulated form of VEGF Trap for use in intraocular applications*. We and Bayer HealthCare are testing VEGF Trap-Eye in a Phase 3 program in patients with the neovascular form of age-related macular degeneration (wet AMD). We and Bayer HealthCare also are conducting a Phase 2 study of VEGF Trap-Eye in patients with diabetic macular edema (DME).

*Id.* at 19 (emphasis added). Patent Owner further states that:

> The Phase 3 trials in wet AMD, known as VIEW 1 and VIEW 2 (VEGF Trap: Investigation of Efficacy and Safety in Wet age-related macular degeneration), are comparing VEGF Trap-Eye and Lucentis® (ranibizumab injection), marketed by Genentech, Inc., an antiangiogenic agent approved for use in wet AMD. VIEW 1 is being conducted in North America and VIEW 2 is being conducted in Europe, Asia Pacific, Japan, and Latin America. The VIEW 1 and VIEW 2 trials are both evaluating VEGF Trap-Eye doses of 0.5 milligrams (mg) and 2.0 mg at dosing intervals of four weeks and 2.0 mg at a dosing interval of eight weeks (after three monthly doses) compared with Lucentis dosed according to its U.S. label, which specifies doses of 0.5 mg administered every four weeks over the first year. As-needed dosing (PRN) with both agents will be evaluated in the second year of the studies. VIEW 1 and VIEW 2 are now fully enrolled, and initial data are expected in late 2010.

*Id.*

Patent Owner thus admits in the passages quoted above that VEGF Trap-Eye is its drug used in the VIEW1 and VIEW 2 studies disclosed by Dixon. Patent Owner makes it clear in the above-quoted passages that

VEGF Trap-Eye is a single drug (of three in late-stage clinical testing), and not, as Patent contends, a genus of drugs.

Counsel for Patent Owner also admitted at oral argument that the VEGF Trap-Eye used in the VIEW 1 and VIEW 2 phase III clinical studies had the same amino acid sequence as recited in claim 1:

> JUDGE NEW: So in other words, if I say, here's VEGF Trap-Eye. Go use it in your VIEW 1 test. And you use it in your VIEW 1 test, it's going to have that sequence, is it not?
>
> MS. FISHMAN: I guess I'm a little confused by your question. Yes, we know today that VEGF Trap-Eye has the same sequence as the claims. And yes, when that was given to the clinical investigators in the studies that were performed, it had that sequence.
>
> JUDGE NEW: So in other words, it was inherent. It was necessarily part of that drug.
>
> MS. FISHMAN: It was the drug that was tested.

Tr. 37:6–15.

Based on the foregoing discussion and our consideration of the record as a whole, we find that the VEGF Trap-Eye disclosed in Dixon necessarily comprised the same amino acid sequence and nucleic acid sequence recited in claims 1 and 14 of the '338 patent.

Whether a person of ordinary skill in the art at the time of filing would have known the exact amino acid sequence of VEGF Trap-Eye, even when using it in a clinical test, is irrelevant to its determining whether it is inherently disclosed. *See* Tr. 37:15–18 (Patent Owner arguing that use of VEGF Trap-Eye in VIEW 1 study not anticipatory because "it was an experimental use under confidentiality restrictions"). The test for inherency,

rather, is whether the limitation of the claim is *necessarily* present in the anticipating reference. *Verizon*, 602 F.3d at 1337. Patent Owner has acknowledged, repeatedly, that the VEGF Trap-Eye used in the VIEW 1 and VIEW 2 clinical studies disclosed by Dixon is the same drug disclosed by the '338 patent, with the same amino acid sequence recited by claim 1. Therefore, the claimed amino acid sequence was necessarily present in the VEGF Trap-Eye used in the studies, whether a person of skill in the art at that time knew it or not. That is sufficient to meet the requirements of an inherent disclosure. *See Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 471 F.3d 1363, 1367 (Fed. Cir. 2006) (holding that "[o]ur cases have consistently held that a reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time").

Accordingly, we find that, based on a preponderance of the evidence, Dixon inherently discloses the VEGF antagonist recited in claims 1 and 14.

*b) Treating an Angiogenic Eye Disorder*

Patent Owner contends that the POSA would not have understood that Dixon expressly or inherently discloses a "method for treating." PO Resp. 38. According to Patent Owner, Dixon does not expressly disclose the limitation because it merely discusses a study "designed to evaluate the efficacy and safety of VEGF Trap-Eye" without providing any data showing that the claimed dosing regimen would "effectively treat." *Id.* at 38–39.

Patent Owner asserts also that Dixon does not inherently disclose a "method for treating" because Dixon represents an "invitation to investigate," which "is not an inherent disclosure." *Id.* at 39 (quoting *Metabolite Lab'ys Inc. v. Lab'y Corp. of Am. Holdings*, 370 F.3d 1354, 1367 (Fed. Cir. 2004)). According to Patent Owner, "[b]ecause the recited 'method for treating' is not the necessary result of carrying out the

disclosures set forth [in Dixon], Petitioner cannot show this limitation is inherently present." *Id.* at 39. Patent Owner asserts that "due to the inherent variability in protein production, the POSA would not necessarily produce a VEGF Trap-Eye protein that could treat an angiogenic eye disorder according to the claimed dosing regimen." *Id.* at 39–40. Additionally, Patent Owner asserts that "[a]nother challenge to obtaining VEGF Trap-Eye protein is that 'post-translational modifications of a protein can affect the biologic activity of a protein *in vivo*.'" *Id.* at 40 (quoting Ex. 2130, 110:4–8).

According to Patent Owner, the facts here are akin to those considered by the Federal Circuit in *Rapoport v. Dement*, 254 F.3d 1053 (Fed. Cir. 2001). PO Resp. 42–43. Patent Owner asserts,

> [h]ere, as in *Rapoport*, Petitioner's references do not disclose a VEGF Trap-Eye protein that, when administered on the recited dosing schedule, necessarily results in treatment of an angiogenic eye disorder." *See* Ex.2049, ¶105 (unpredictability in the production of VEGF Trap-Eye can result in a protein that would not provide treatment of an angiogenic eye disorder according to the claimed dosing regimen of the '338 Patent); Ex. 2048, ¶¶103-104.

*Id.* at 43.

Further, according to Patent Owner, "[e]ven if 'VEGF Trap-Eye' is made correctly, properly purified, and formulated, administration according to the disclosed regimen will not necessarily result in an effective treatment for all patients with angiogenic eye disorders," for example, "some sub-populations of [wet]AMD patients" or patients with pre-existing conditions wherein increased clearance of intravitreally administered drugs has been observed. *Id.* at 43–44 (citing Ex. 2048 ¶¶ 112–121). Patent Owner asserts that even using the ETDRS as the metric for efficacy, the administration of

Dixon's dosing regimen in some patients will still not necessarily result in treatment. *Id.* at 45–46.

We begin by noting that Patent Owner has mischaracterized *Rapoport* as being akin to this case. In *Rapoport*, the claims at issue were directed to "[a] method for treatment of sleep apneas comprising administration of a therapeutically effective regimen of" a particular drug compound. *Id.* at 1056. The Court began by noting that "the disputed phrase 'treatment of sleep apneas' is technically part of the preamble," and that there was "no dispute in this case that the phrase should be treated as a claim limitation." *Id.* at 1059. The Court determined that the ordinary meaning of the phrase "narrowly refers to treatment of the underlying disorder itself" and found no cause to broaden the phrase to include "treatment of symptoms associated with sleep apnea," such as anxiety, depression, fatigue, malaise, irritability, anger and hostility. *Id.* at 1059–1060. The cited art suggested administering the recited compound to sleep apnea patients with an intent to treat anxiety and not the underlying condition of sleep apnea. *Id.* at 1061. The Court upheld the Board's conclusion that the cited art did not anticipate the claims because that art "does not disclose administration of [the recited compound] to patients suffering from sleep apnea to treat sleep apnea." *Id.* at 1063. Unlike in *Rapoport*, Petitioners here have shown persuasively that Dixon discloses administering VEGF Trap-Eye for the purpose of treating angiogenic eye disorder, as recited by the challenged claims.

As discussed above, in Section II.C.1., we have determined that the preamble reciting "[a] method for treating an angiogenic eye disorder in a patient" does not require achieving a particular level of efficacy. Thus, Patent Owner's arguments that Dixon does not inherently disclose the claimed methods because Dixon's disclosed dosing regimen will not

necessarily be effective for some patients lacks merit as those arguments rely upon a claim construction for "method for treating" that we have not adopted.

Patent Owner also contends that Dixon cannot anticipate the claimed methods for treating angiogenic eye disorder because the reference lacks utility. PO Resp. 47. Specifically, Patent Owner asserts that Petitioners cannot demonstrate utility because Dixon "do[es] not include any results that correspond to a dosing regimen encompassed by the Challenged Claims." *Id.* at 49. Additionally, Patent Owner asserts that Dixon is not anticipatory prior art because it describes "experimental uses." *Id.* at 47.

Based on our consideration of the record as a whole, Patent Owner's argument that Dixon cannot be anticipatory because it lacks utility is not well-taken as it is insufficiently supported. Dixon describes the use of VEGF Trap-Eye in a method for treating an angiogenic eye disorder in a patient. Ex. 1006, 1573. For such therapy, Dixon reports "Phase I and II trial data indicating safety, tolerability and efficacy." *Id.* Whether those results "correspond to a dosing regimen encompassed by the Challenged Claims," is immaterial, as we have determined that the challenged claims do not recite or otherwise require any particular level of efficacy. Moreover, as the Federal Circuit has explained, "a prior art reference need not demonstrate utility in order to serve as an anticipating reference under section 102." *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1326 (Fed. Cir. 2005). "As long as the reference discloses all of the claim limitations and enables the 'subject matter that falls within the scope of the claims as issue,' the reference anticipates—no 'actual creation or reduction to practice' is required." *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009)

(quoting *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1380–81 (Fed. Cir. 2003)).

Patent Owner alleges further that Dixon is not anticipatory because it describes "experimental uses which the Supreme Court has held do not constitute prior art." PO Resp. 47. Patent Owner asserts that "the experimental use doctrine should apply to printed publications" that disclose such experimental uses. *Id.* at 51. From there, Patent Owner contends that "because [Dixon] only disclose[s] the initiation and design of studies for which Regeneron retained control and were being performed to perfect the invention encompassed by the Challenged Claims, they describe a use that is merely experimental, and cannot anticipate." *Id.* According to Patent Owner, "the claimed treatment method was not 'ready for patenting' and the trials were for experimental purposes to perfect the invention." *Id.* at 52.

Petitioners, on the other hand, allege that Dixon is not subject to the experimental use exception. Pet. Reply 18. In particular, Petitioners assert that Dixon, a published paper, is available as anticipatory prior art because "[p]ublished papers and press releases indisputably place subject matter beyond an inventor's control and into the public domain." Pet. Reply 20. In response, Patent Owner asserts that Petitioners' allegation "ignores the fact that nothing has been placed into the public domain about whether the claimed method works for its intended purpose." PO Sur-reply 29.

Based on our consideration of the record as a whole, we do not find Patent Owner's argument that Dixon is subject to the experimental use exception persuasive for the reasons discussed by Petitioners. We emphasize here that Dixon is a printed publication that discloses each element of the claimed invention. In particular, the reference discloses treating an angiogenic eye disorder by administering VEGF-Trap Eye

according to the dosing regimen recited by the challenged claims to the patient. Dixon concludes that "[a]nti-VEGF therapy has vastly improved the treatment of neovascular AMD in terms of both safety and efficacy." Ex. 1006, 1576. Based on those disclosures, Patent Owner's position that Dixon did not place the claimed invention into the public domain because Dixon did not disclose "whether the claimed method works for its intended purpose" fails. As discussed above, we have found that the intended purpose of the claimed methods is to treat an angiogenic eye disorder and that such treatment only requires administering the recited dosing regimen to a patient for that purpose, without any requirement that such treatment achieves any particular level of efficacy. Thus, Patent Owner has not established that Dixon is unavailable as anticipatory prior art because Dixon did not disclose an unclaimed feature for the method of treating, i.e., a particular level of effectiveness.

Accordingly, we find that, based on a preponderance of the evidence, Dixon discloses treating an angiogenic eye disorder in a patient, as required by the challenged claims.

As noted above, Patent Owner does not dispute that Dixon discloses the remaining elements of independent claims 1 and 14, or the additional limitations of the challenged dependent claims. Based on the foregoing discussion and our consideration of record as a whole, we determine that Petitioners shown persuasively that Dixon discloses each element of independent claims 1 and 14, as well as the additional limitations of the challenged dependent claims. Accordingly, we determine that Petitioners have shown by a preponderance of the evidence that claims 1, 3–11, 13, 14, 16–24 and 26 are anticipated by Dixon.

### *E. Remaining Grounds*

As noted above, Petitioners assert that claims 1, 3–11, 13, 14, 16–24 and 26 are also anticipated by each of Adis, Regeneron 2008, NCT-795, and NCT-377. Pet. 44–62. Petitioners additionally assert that claims 1, 3–11, 13, 14, 16–24 and 26 would have been obvious over Dixon, alone or in combination with Papadopoulos or Dix. Pet. 62–69.

We do not reach Petitioners' remaining anticipation and obviousness grounds as we have already determined that Petitioners have shown by a preponderance of the evidence that each of the challenged claims are unpatentable because they are anticipated by Dixon. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1359 (2018) (holding that a petitioner "is entitled to a final written decision addressing all of the claims it has challenged"); *see also Bos. Sci. Scimed, Inc. v. Cook Grp. Inc.*, 809 F. App'x 984, 990 (Fed. Cir. 2020) (non-precedential) (recognizing that the "Board need not address issues that are not necessary to the resolution of the proceeding" and, thus, agreeing that the Board has "discretion to decline to decide additional instituted grounds once the petitioner has prevailed on all its challenged claims").

## III. MOTIONS TO EXCLUDE

Petitioners and Patent Owner have each filed a motion to exclude evidence. For each motion, the moving party has the burden of proof to establish that it is entitled to the requested relief. 37 C.F.R. § 42.20(c).

### *A. Petitioners' Motion*

Petitioners move to exclude Exhibits 2059, 2060, 2073, 2096, 2128, 2133–2140, 2163, 2169, 2170, 2176, 2190, 2197, 2200, 2205, 2208, 2218, 2229, 2272–2285, 2243, 2244, 2250, 2259, in their entirety, and portions of

Exhibits 2048–2050 and 2052. Pet. Mot. 1. Patent Owner opposes the motion. PO Opp.

*1. Authentication of Weber Exhibits*

Petitioners contend that the Exhibits 2059, 2060, 2073, 2096, 2128, 2133–2140, 2163, 2169, 2170, 2176, 2190, 2197, 2200, 2205, 2208, 2218, 2229, 2272–2285, 2243, 2244, 2250, 2259 should be excluded as unauthenticated under Federal Rule of Evidence ("FRE") 901. Pet. Mot. 2–3. For this challenge, Petitioners refer to those exhibits as the "Weber Exhibits." *Id.* at 2. As background, Petitioners timely objected to those exhibits as lacking authentication. Paper 43. Patent Owner responded to the objections by submitting the declaration of Doris Weber (Ex. 2286), Patent Owner's senior litigation support specialist who testifies that the Weber Exhibits are "true and correct" copies of what each exhibit purports to be.

In its motion, Petitioners challenge Ms. Weber's declaration by asserting it does not satisfy FRE 901(1) because Ms. Weber's deposition testimony confirms that she is not a custodian of the Weber Exhibits and has no personal knowledge of the creation, authorship, maintenance, or modification of those exhibits or the underlying documents from which they were prepared. Pet. Mot. 2 (citing Ex. 1150, 128:8–131:23).

Petitioners argue further that none of the Weber Exhibits are self-authenticating under FRE 902, and that Exhibits 2060, 2128, 2169, 2170, 2229, 2273, and 2285 are "incomplete and/or excerpted versions of *un-produced*, supposedly confidential originals," which, Petitioners contend, casts further doubt on their authenticity and reliability. *Id.* at 3.

Patent Owner argues that, in her sworn declaration, Ms. Weber explains that she has personal knowledge of the facts recited therein, and

that each of the Weber Exhibits is a true and correct copy of what it purports to be. PO Opp. 2 (citing Ex. 2286 ¶ 1). Patent Owner explains that, at Petitioners' request, Ms. Weber appeared for deposition and "testified as to the processes whereby she confirmed the authenticity" of the Weber Exhibits. *Id.* For example, Ms. Weber explained that she "personally collected the documents addressed in her declaration from Regeneron storage, reviewed them, and confirmed that they are true and correct copies kept in accordance with Regeneron's procedures." *Id.* (citing, e.g., Ex. 1150 at 25:16–26:18, 29:23–30:23, 34:10–14, 41:7–13, 42:13–43:24). Patent Owner notes that, "[w]here possible, Ms. Weber also personally confirmed these details with individual custodians." *Id.* (citing, e.g., Ex. 1150, 35:23–37:2, 40:6–24, 44:3–45:6). Patent Owner contends that Ms. Weber's declaration and deposition testimony satisfies the threshold for authentication and that she "need not have personally authored or maintained the documents to serve as an authenticating witness." P.O. Opp. 2–3. Further, Patent Owner argues that Petitioners' assertion that certain of the authenticated Weber Exhibits are "incomplete and/or excerpted versions of unproduced" originals is unsupported—and in some cases directly contradicted by the record. *Id.* at 3 (citing, e.g., IPR2021-00881, Ex. 1150, 32).

Based on our consideration of the arguments and the evidence, we are not persuaded that the Weber Exhibits are not authenticated. To authenticate an item of evidence, FRE 901(a) requires only that "the proponent must produce evidence sufficient to support a finding that the item is what the proponent claims it is." By way of example, FRE 901(b)(1) explains that testimony of a witness with knowledge "that an item is what it is claimed to be" may satisfy the authentication requirement. Fed. R. Evid. 901(b)(1).

We find that Patent Owner has demonstrated sufficiently that Ms. Weber, in her capacity as a Senior Litigation Support Specialist with Patent Owner, was in a position to declare that the Weber Exhibits are true and correct copies of the original documents. In particular, we find no reason to question the veracity of Ms. Weber's testimony that the Weber exhibits were stored on the server at Regeneron, that access to the servers was restricted, and that she collected them for the purpose of this proceeding. *See, e.g.*, Ex. 1150, 25–43. We also credit Ms. Weber testimony that, in preparing her Declaration, she consulted individual document custodians to confirm the location of the documents on Regeneron's regulatory archive. *See, e.g., id.* at 35–45.[13]

Therefore, we find that that Patent Owner has provided testimonial evidence that sufficiently authenticates the Weber Exhibits. Accordingly, we deny Petitioners' Motion to Exclude the Weber Exhibits based upon this FRE 901 ground.

*2. Relevance of Exhibits 2059, 2060, 2073 and 2128*

Petitioners also move to exclude Exhibits 2059, 2060, 2073, and 2128 under FRE 402 as being irrelevant. Pet. Mot. 3–8. Petitioners additionally move to exclude Exhibits 2060 and 2128 under FRE 403 as being unduly prejudicial. *Id.* at 4–5 and 7–8.

Petitioners assert that Exhibits 2059, 2060, 2073, and 2128 are non-publicly available, internal, documents, and do not demonstrate the knowledge of a person of ordinary skill in the art or are irrelevant prior art

[13] We also find that Patent Owner's expert, Dr. Brown, credibly testified as an individual with knowledge that Exhibits 2128 and 2096 are what they purport to be. *See* PO Opp. 7 (citing Ex. 1110, 62:18–63:20).

teachings, and should therefore be excluded as irrelevant non-prior art under FRE 402. Pet. Mot. 4–8. Additionally, Petitioners note that Patent Owner fails to cite Exhibits 2059, 2060, and 2073 in either the Patent Owner Response or Sur-Reply (Papers 40, 73), demonstrating that they do not tend to make any fact of consequence more or less probable and are therefore irrelevant to this proceeding. *Id.* (citing *SK Innovation Co. v. Celgard, LLC*, IPR2014-00679, Paper 58, 49 (PTAB Sept. 25, 2015).

Referring to FRE 403, Petitioners contend that any probative value of Exhibits 2060 and 2128, which are excerpted from larger documents, is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder, because they could allegedly deny the factfinder a complete set of materials to judge the accuracy of its claim. Pet. Mot. 4–5 and 7–8.

Patent Owner argues that it relies on the Exhibits 2059 and 2073 not for their prior art teaching, but, rather, as illustrating the inherent variability in producing VEGF Trap-Eye. PO Opp. 4, 6 (citing Exhibit 2049 at ¶¶ 95–105). Patent Owner also disputes Petitioners' assertion that non-prior art evidence is necessarily irrelevant. *Id.* (citing, e.g., *Organik Kimya AS v. Rohm & Haas Co.*, 873 F.3d 887, 893–94 (Fed. Cir. 2017)). Patent Owner argues Petitioners' argument that Exhibit 2060 is irrelevant and lacks merit for the same reasons as asserted for Exhibit 2059. *Id.* at 5. Patent Owner also contends that Petitioners' assertion that Exhibit 2128 is irrelevant because it is a non-public document fails because Patent Owner and its expert rely on Exhibit 2128 "*precisely to show* its confidentiality." *Id.* at 7 (citing, e.g., Ex. 2050 ¶ 71; PO Resp. 24 n.11).

With respect to FRE 403, Patent Owner argues that Petitioners' assertion that Exhibit 2128 is unreliable or prejudicial as a "hand-picked excerpt" is wrong because Patent Owner's declarant, Dr. Brown, expressly confirmed the authenticity of the Exhibit. PO Opp. 7 (citing Ex. 1110, 63).

Having considered the arguments and the evidence, we are not persuaded by Petitioners' have demonstrated that Exhibits 2059, 2060, 2073, and 2128 should be excluded under FRE 402 as being irrelevant. Although Petitioners assert that Exhibits 2059, 2060, and 2073 are not cited in Patent Owner's Response or Sur-Reply, Patent Owner has demonstrated that those exhibits are referenced in various declaration and deposition testimony of Patent Owner's experts, including Drs. Klibanov, Del Priore, and Brown. Thus, we find that these exhibits are relevant to our consideration of that testimony.

We are also unpersuaded by Petitioners' argument that Exhibits 2060 and 2128 should be excluded under FRE 403 as unduly prejudicial. FRE 403 states that "[t]he court may exclude relevant evidence if its probative value is substantially outweighed by a danger of one or more of the following: unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence." Petitioners' generalized allegation that "[a]llowing [Patent Owner] to cherry-pick a portion of a document denies the factfinder a complete set of materials to judge the accuracy of its claim" (*see* Pet. Mot. 5, 9) lacks particularity as to the potential unfair prejudice posed by admission of these particular exhibits, especially when weighed against the relatively minor, if relevant, role played by the exhibits in Patent Owner's arguments.

Therefore, we deny Petitioners' motion to exclude Exhibits 2059, 2060, 2073, and 2128 under FRE 402 and/or 403.

*3. Alleged Hearsay in Exhibits 2059, 2060, 2128, 2096*

Petitioners move to exclude Exhibits 2059, 2060, 2128 and 2096 as inadmissible hearsay under FRE 802 because they constitute out-of-court statements offered for the truth of the matters asserted. Pet. Mot. 4–9.

Patent Owner contends that Exhibit 2059 falls within the business records exception to the FRE, as demonstrated by Ms. Weber's Declaration. PO Opp. 3. Patent Owner states that Exhibit 2059 is a scientific report that was stored on Regeneron servers, and bears facial indications of trustworthiness (e.g., written on Regeneron letterhead and dated and signed by Dr. Koehler-Stec, a study director and Regeneron employee). *Id.* at 3–4 (citing Ex. 1150, 24:14–26:18).

Patent Owner similarly argues that Exhibit 2060 is a clinical study protocol, stored in Regeneron's regulatory archive, and bears facial indicia of trustworthiness (Regeneron protocol headers and file path information on each page), and was authenticated by Ms. Weber. PO Opp. 5–6 (citing Ex. 2286 ¶ 3; Ex. 1150, 24:14–26:18).

With respect to Exhibits 2128 and 2096, Patent Owner argues that the testimony of Dr. Brown and Ms. Weber support finding that these exhibits fall within the business records exception under FRE 803. PO Opp. 7–9. Patent Owner contends that both Exhibits 2128 and 2096 were generated in the ordinary course of regularly conducted activity (i.e., a clinical investigation), was stored by Regeneron in its regulatory archives and by Dr. Brown's practice at Iron Mountain, and bears facial indications of trustworthiness (i.e., dated signatures by Dr. Brown's partner on every page). *Id.* (citing Ex.1110, 59:23–62:17).

Petitioners reply by asserting that Ms. Weber's testimony does not demonstrate sufficient personal knowledge of Patent Owner's business practices for her to testify regarding these practices. Pet. Reply 3. According to Petitioners, Ms. Weber cannot testify about whether the records were made or kept in the course of a regularly conducted business activity because she was never a custodian of Patent Owner's records or otherwise a qualified witness. *Id.* at 3–4 (citing FRE 803(6) (records of a regularly conducted activity must be "shown by the testimony of the custodian or another qualified witness")). Petitioners assert that Patent Owner's reliance on Exhibits 2059, 2060, 2096, and 2128 as either "scientific report[s]" or clinical trial documents does not support application of FRE 803(6). *Id.* at 4 (citing C*orning Inc. v. DSM IP Assets B.V.*, IPR2013-00043, Paper 97 at 4–7 (PTAB May 1, 2014) (declining to invoke a FRE 803(6) exception to reports of scientific research/tests).

Having considered the arguments and the evidence, we are not persuaded that Petitioners have demonstrated that Exhibits 2059, 2060, 2096, and 2128 should be excluded as inadmissible hearsay. FRE 803 includes a number of exceptions to hearsay, including:

> (6) Records of a Regularly Conducted Activity. A record of an act, event, condition, opinion, or diagnosis if:
>
> (A) the record was made at or near the time by—or from information transmitted by—someone with knowledge;
>
> (B) the record was kept in the course of a *regularly conducted activity of a business*, organization, occupation, or calling, whether or not for profit;
>
> (C) making the record was a regular practice of that activity;

> (D) all these conditions are shown by the testimony of the custodian or another qualified witness, or by a certification that complies with Rule 902(11) or (12) or with a statute permitting certification; and
>
> (E) neither the source of information nor the method or circumstances of preparation indicate a lack of trustworthiness.

Fed. R. Evid. 803(6) (emphasis added).

Despite Petitioners' reliance on *Corning*, we are not persuaded that Exhibits 2059, 2060, 2096, and 2128 constitute inadmissible hearsay evidence. As an initial matter, Exhibits 2096 and 2128 are not "laboratory notebooks" or "laboratory generated data of properties of compositions" of the sort that *Corning* finds to be inadmissible under FRE 803(6). *See Corning*, IPR2013-00043, Paper 97 at 4. Rather Patent Owner explains that those exhibits are agreements between Regeneron and third-party investigators. PO Opp. 8. Such an agreement between a pharmaceutical company and third-party investigators appears to represent a typical business contract rather than a "laboratory notebook." Moreover, the fact that such records were maintained in an access-restricted, searchable electronic archive of Regeneron, as well as in the records of Dr. Brown's practice, also speaks to the routine nature of such records. *See*, *e.g.*, Ex. 2131 ¶¶ 1–5. As such, we conclude that Exhibits 2128 and 2096 fall into the business records exception of 803(6).

We also find that Exhibits 2059 and 2060 are covered by FRE 803(6). These exhibits also are not laboratory notebooks; rather we agree with Patent Owner's characterization of these exhibits as a sample analysis report and a clinical study report. PO Opp. 3, 5. These exhibits were also stored in the Regeneron database of records and appear to be the type of report that would

be routinely made by a pharmaceutical company to summarize and memorialize laboratory tests.

Accordingly, we deny Petitioners' motion to exclude Exhibits 2059, 2060, 2128, and 2096 as inadmissible hearsay under FRE 802.

*4. Petitioners' Remaining Challenges*

Petitioners additionally seek to exclude certain: (a) confidential financial documents (Exhibits 2169, 2170, 2279–2285 and Attachments C1–C12, D1–D4, D7, and X2 of Ex. 2052), Pet. Mot. 9–12; (b) confidential marketing materials (Exhibits 2136–2140, 2163, 2190, 2197, 2208, 2277–2278), along with Dr. Manning's corresponding opinions regarding those exhibits (Ex. 2052 ¶¶ 88–94), Pet. Mot. 12–14; and (c) testimony by Dr. Manning (Ex. 2052 ¶¶ 48–117), Pet. Mot. 14. According to Petitioners these materials should be excluded for a number of reasons, such as unauthenticated, allegedly constituting inadmissible hearsay, and/or being unreliable. *Id.* at 9–14 (citing Fed. R. Evid. 701, 801–03, 901, 1006).

We dismiss the motion to exclude Exhibits 2169, 2170, 2279–2285 and Attachments C1–C12, D1–D4, D7, and X2 of Ex. 2052, Exhibits 2136–2140, 2163, 2190, 2197, 2208, and 2277–2278, along with the portions of the expert testimony that rely on these exhibits, as moot.[14] As Petitioners recognize, these exhibits and challenged portions of Dr. Manning's testimony are relied upon to address Patent Owner's commercial success arguments. Pet. Mot. 9, 12. In the Final Written Decision, however, we do

[14] Some of these exhibits were also included in the "Weber Exhibits" challenged for lack of authentication. As discussed above, in Section III.A.1, we have already determined that Patent Owner has provided sufficient evidence to authenticate those exhibits. Here, we dismiss any remaining challenges to those exhibits as moot.

not reach the commercial success issue as we do not reach the obviousness ground. Thus, we have not considered the financial documents, marketing materials, or testimony that regarding those exhibits challenged by Petitioners in the motion to exclude, nor have we relied on that material in our Final Written Decision. Accordingly, we need not determine whether Petitioners demonstrate that the exhibits are inadmissible.

*B. Patent Owner's Motion*

Patent Owner moves to exclude Exhibits 1118, 1121, 1124, 1154, 1173, in their entirety, and portions of Exhibits 1114, 1137, and Petitioners' Reply (Paper 61). Pet. Mot. 1, 13. Petitioners oppose the motion. Pet. Opp.

*1. Challenged Portions of Petitioners' Reply*

Patent Owner asserts that Petitioners' Reply (Paper 61) improperly contains a new argument that VEGF Trap-Eye was publicly distributed before the critical date. PO Mot. 2 (citing Pet. Reply 22, 29). According to Patent Owner, that argument by Petitioners should be excluded as it attempts to alter the grounds presented in the Petition. *Id.* at 3. Patent Owner requests, as an alternative to excluding the Reply argument that we strike it. *See id.* at 3 n.3 (asserting that "[i]f the Board deems appropriate, this portion of Patent Owner's motion to exclude may be treated as a motion to strike.").

We deny the motion to exclude the referenced argument in Petitioners' Reply, as well as the invitation to consider the motion as one to strike the argument. As Patent Owner notes in the motion, Patent Owner raised this issue previously in this proceeding. Mot. 5. At that time, we denied Patent Owner's request for authorization to file a motion to strike the referenced argument in the Reply. It is improper for Patent Owner to now seek to strike the argument in a motion to exclude. A motion to exclude is not the proper vehicle to address arguments or evidence that a party believes

exceeds the proper scope of a reply. CTPG 79. Moreover, as Petitioners correctly assert, Patent Owner has failed to satisfy the prerequisite for filing a motion to exclude by failing to timely file an objection. *See* 37 C.F.R. § 42.64(b)(1); CTPG 78–79.

Patent Owner has not been left without an opportunity to address the Reply argument. When we denied authorization to file a motion to strike, we authorized Patent Owner to file, with its Sur-reply, a table identifying any portion of the Reply that Patent Owner considers to have exceeded the scope of the Reply. Further, we explained that Patent Owner, alternatively, may address that contention, or the merits of any newly-raised arguments or evidence in its Sur-reply. Indeed, Patent Owner addressed the issue in its Sur-reply for our consideration. Thus, Patent Owner has had an opportunity to identify in its Sur-reply its contentions regarding Petitioners' allegedly inappropriate Reply argument. Moreover, we are in a position to determine whether such argument should be disregarded. *See* CTPG 80.

*2. Exhibits 1118, 1121 and 1124*

Patent Owner asserts that Petitioners' Exhibits 1118, 1121 and 1124 should be excluded because they are not cited in the pleadings and are irrelevant. PO Mot. 6 (citing FRE 402). Additionally, Patent Owner seeks to exclude certain paragraphs in the declarations of Drs. Albini, Gerritsen, and Hofmann that Patent Owner asserts are not cited in the pleadings. *Id.* at 6–7 (citing portions of Ex. 1002, Ex. 1003, Ex. 1114, and Ex. 1137). According to Patent Owner, the referenced declaration paragraphs were not relied upon by Petitioners and should be excluded as irrelevant.

We dismiss as moot the motion to exclude Exhibits 1118, 1121 and 1124 as moot. Because Exhibits 1118, 1121 and 1124 were not cited or relied upon by Petitioners, we have not considered them in rendering our

Final Written Decision. Accordingly, we dismiss the motion as moot with regard to these exhibits.

We deny the motion to exclude the identified paragraphs of the declarations of Dr. Albini (Ex. 1002 and Ex. 1114), Dr. Gerritsen (Ex. 1003) and Dr. Hofmann (Ex. 1137). Each declaration has been cited in pleadings. Although every paragraph in the declarations of these expert may not be cited in pleadings, those portions of the declaration may serve to provide context for the cited paragraphs, or the testimony as a whole. Indeed, as Petitioners note, and Patent Owner does not dispute, some of the challenged portions of the declaration testimony that Patent Owner seeks to exclude are referenced in the declaration testimony of another expert. *See*, e.g., Pet. Opp. 8; PO Reply 4. Further, we do not find that Patent Owner has established that keeping the complete declaration testimony of these experts in the record to be prejudicial. In that regard, Patent Owner asserts only that "allowing uncited evidence to clutter the record and potentially be used by Petitioner[s] in the future is prejudicial." PO Reply 4. It is unclear how Patent Owner allege that Petitioners could use the evidence in the future. It is also unclear and unpersuasive that keeping the referenced paragraphs in the record serves to clutter the record in a prejudicial manner. In any event, we do not find that Patent Owner has met its burden of proof to establish that the identified paragraphs of the declarants' testimony should be excluded as irrelevant.

*3. Exhibits 1154 and 1173*

Patent Owner describes Exhibits 1154 and 1173 as "third-party complaints against Regeneron . . . in purported rebuttal to Patent Owner's arguments on commercial success." PO Mot. 8. Patent Owner asserts that "those complaints and the allegations therein are attorney argument, not

evidence." *Id.* According to Patent Owner, Exhibits 1154 and 1173 should be excluded as irrelevant, unduly prejudicial, and hearsay. *Id.* (citing FRE 401–403 and 802).

We dismiss as the motion to exclude Exhibits 1154 and 1173, along with the arguments and portions of expert testimony that rely on these exhibits, as moot. As Patent Owner notes, Exhibits 1154 and 1173 were submitted by Petitioners to address Patent Owner's commercial success arguments. In the Final Written Decision, however, we do not reach the commercial success issue as we do not reach the obviousness ground. Thus, we have not considered Exhibits 1154 and 1173 and those exhibits are not relied upon for our Final Written Decision. Accordingly, we need not determine whether the exhibits are admissible.

*4. Exhibit 1114, Appendix A*

Patent Owner asserts that Appendix A to Dr. Albini's Reply Declaration (Exhibit 1114) "cherry-picks excerpts from Dr. Albini's deposition testimony from these proceedings." PO Mot. 11. According to Patent Owner, "Appendix A should be excluded on the grounds that it is an improper attempt to circumvent the Board's word count rules through incorporation by reference, and improper summary under F. R. E. 1006." *Id.* Patent Owner asserts that Appendix A is cited once in the Albini Reply Declaration and is "indirectly cited, but never relied on in Petitioner[s'] Reply." *Id.* at 12 (citing Ex. 1114 ¶ 9; Pet. Reply 7). Patent Owner asserts that Appendix A incorporates by reference 35 paragraphs of Dr. Albini's declaration. *Id*. Patent Owner alleges that Appendix A is an improper summary because it contains only excerpts of Dr. Albini's deposition testimony although the entire deposition testimony is of record in this proceeding and can be independently examined by the Board. *Id.* at 13.

We deny the motion to exclude Appendix A of Exhibit 1114. As noted by Petitioners, Dr. Albini explains in his declaration that he "prepared Appendix A . . . which presents a side-by-side comparison of Patent Owner's arguments that they purportedly cite me as support against my *actual* opinions and testimony." Pet. Opp. 11 (quoting Ex. 1114 ¶ 9). In view of that detailed description by Dr. Albini regarding what Appendix A represents and its purpose, along with the fact that the entirety of Dr. Albini's deposition testimony is of record in this proceeding, *see* Ex. 2287, we do not find that Patent Owner has shown persuasively that Dr. Albini's Appendix A improperly provides a summary of his testimony. Further, Patent Owner has not shown that Appendix A violates Rule 42.6(a)(3). That rule states that "*[a]rguments* must not be incorporated by reference from one document into another document." 37 C.F.R. § 42.6(a)(3) (emphasis added). As Petitioners correctly assert, Patent Owner has not shown that Petitioners incorporated by reference any *arguments* into Appendix A or from Appendix A into another document. *See* Pet. Opp. 12.

## IV. CONCLUSIONS

For the foregoing reasons, we conclude that Petitioners have shown by a preponderance of the evidence that claims 1, 3–11, 13, 14, 16–24 and 26 of the '338 patent are unpatentable.[15]

Additionally, we deny in part and dismiss in part Petitioners' and Patent Owner's Motions to Exclude.

[15] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. *See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

In summary:

| Claims | 35 U.S.C. § | References | Claims Shown Unpatentable[16] | Claims Not shown Unpatentable |
|---|---|---|---|---|
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Dixon | 1, 3–11, 13, 14, 16–24, 26 | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Adis | | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Regeneron 2008 | | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | NCT-795 | | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | NCT-377 | | |
| 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon, Papadopoulos, Dix | | |
| **Overall Outcome** | | | 1, 3–11, 13, 14, 16–24, 26 | |

[16] As noted in Section II.E., we do not reach Petitioners' anticipation grounds based on Adis, Regeneron 2008, NCT-795, and NCT-377, or Petitioners' obviousness ground challenging claims 1, 3–11, 13, 14, 16–24 and 26 as we have determined that those claims are unpatentable based on the Dixon anticipation ground, as noted in the table.

## V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that based on a preponderance of the evidence, claims 1, 3–11, 13, 14, 16–24 and 26 of the '338 patent are unpatentable;

FURTHER ORDERED that each of Petitioners' and Patent Owner's Motions to Exclude are *denied in part* and *dismissed in part*; and

FURTHER ORDERED that because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

IPR2021-00881
Patent 9,254,338 B2

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# EXHIBIT 3

*Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*,
IPR2022-01225, Paper 96 (PTAB Jan. 9, 2022)

Trials@uspto.gov
571-272-7822

Paper 96
Date: January 9, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

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IPR2022-01225[1]
Patent 10,130,681 B2

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Before JOHN G. NEW, SUSAN L. C. MITCHELL, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

NEW, Administrative Patent Judge.

# JUDGMENT
## Final Written Decision
## Denying in Part, Granting in Part, and Dismissing in Part Petitioner's Motion to Exclude Evidence, Denying in Part and Dismissing in Part Patent Owner's Motion to Exclude Evidence, Determining Challenged Claims 1, 3–11, 13, 14, 16–24, and 26 Unpatentable
*35 U.S.C. § 318(a)*

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[1] IPR2023-00532, *Celltrion, Inc. v. Regeneron Pharms. Inc.*, has been joined with this proceeding. *See* Paper 38.

# I. INTRODUCTION

We have jurisdiction to hear this *inter partes* review under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioner Mylan Pharmaceuticals Inc. ("Petitioner") has established, by a preponderance of the evidence, that challenged claims 1, 3–11, 13, 14, 16–24, and 26 of Patent Owner Regeneron Pharmaceuticals, Inc.'s ("Patent Owner") U.S. Patent No. 10,130,681 B2 (Ex. 1001, the "'681 patent") are unpatentable. We also grant in part, deny in part, and dismiss in part Petitioner's Motion to Exclude Evidence and deny in part and dismiss in part Patent Owner's Motion to Exclude Evidence.

## *A. Procedural History*

On July 1, 2022, Petitioner filed its Petition (Paper 2, "Petition") seeking *inter partes* review of claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Patent Owner timely filed a Preliminary Response. Paper 14 ("Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-Reply. Paper 16 ("Prelim. Reply"); Paper 18 ("Prelim. Sur-Reply"). On January 1, 2022, and pursuant to 35 U.S.C. § 314, we instituted *inter partes* review of challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Paper 21 ("Institution Decision" or "Dec.").

After institution of trial, Patent Owner filed a Response (Paper 41[2], "PO Resp."), to which Petitioner filed a Reply (Paper 60, "Pet. Reply"), and Patent Owner, in turn, filed a Sur-Reply (Paper 65, "Sur-Reply").

Both Petitioner (Paper 76) and Patent Owner (Paper 77) filed Motions to Exclude Evidence ("Mot. Exclude") and filed Oppositions (Papers 82 and 80, respectively) to the opposing party's Motion to Exclude Evidence (Opp. Mot. Exclude). Both parties also filed a Reply to their opponent's Opposition to their Motions to Exclude ("Reply Mot. Exclude"). Paper 83 (Petitioner), Paper 84 (Patent Owner).

## II. BACKGROUND

### *A. Real Parties-in-Interest*

Petitioner identifies Viatris Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, Johnson & Johnson, Biocon Biologics Inc., Biocon Limited, Biocon Biologics Limited, Biocon Biologics UK Limited, and Biosimilar Collaborations Ireland Limited as real parties-in-interest. Paper 56 at 1. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 72 at 2.

### *B. Related Matters*

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880, IPR2021-00881, IPR2022-01226

[2] Papers 41, 60, and 76 of the record are the unredacted versions of these papers. Papers 42, 59, 75 are the redacted versions.

(PTAB), and *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) as related matters. Paper 5, 1; Paper 6, 1. Patent Owner also identifies *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated before institution). Paper 5, 2–3. Petitioner further identifies the following as judicial or administrative matters that would affect, or be affected by, a decision in this proceeding: *Apotex Inc. v. Regeneron Pharmaceuticals, Inc.*, No. IPR2022-01524 (PTAB), *United States v. Regeneron Pharms., Inc.*, No. 1:20-cv-11217-FDS (D. Mass.), and *Horizon Healthcare Servs., Inc. v. Regeneron Pharms., Inc.*, No. 1:22-cv-10493-FDS (D. Mass.). Paper 6, 1–2.

Petitioner also identifies additional patents and patent applications that claim priority to the '681 patent, namely: US 9,254,338 B2; US 9,669,069 B2; US 10,857,205 B2; US 10,828,345 B2; US 10,888,601 B2; US 11,253,572 B2; and US Appl. Ser. Nos. 17/072,417; 17/112,063; 17/112,404; 17/350,958; and 17/740,744. Paper 6, 2.

On March 22, 2023, this *inter partes* review was joined with IPR2023-00532, *Celltrion, Inc. v. Regeneron Pharms. Inc.* (the "'532 IPR"), which also challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. *See* Paper 38. Petitioner Celltrion Inc. acted as a "silent understudy" in the present proceeding, and a copy of this Final Written Decision will be entered in the '532 IPR.

Of particular relevance to our decision in this proceeding is the Final Written Decision entered in IPR2021-00881 (the "-00881 IPR") on November 9, 2022. *See* IPR 2021-00881, Paper 94 (the "-00881 Decision," Ex. 3001). Both the '681 patent and US 9,254,338 B2 (the "'338 patent") at issue in IPR2021-00881 share a common Specification. *See generally*,

Ex. 1001; IPR2021-00881, Ex. 1001. In the -00881 Decision, the panel found that the challenged claims were unpatentable on at least one of the same grounds asserted against the challenged claims in the present Petition. *See generally* Ex. 3001.

*C. The Asserted Grounds of Unpatentability*

Petitioner contends that claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are unpatentable, based upon the following grounds:

| Ground | Claim(s) Challenged | 35 U.S.C. § | Reference(s)/Basis |
|---|---|---|---|
| 1 | 1, 3–11, 13, 14, 16–24, 26 | 102[3] | Dixon[4] |
| 1 | 1, 3–11, 13, 14, 16–24, 26 | 102 | Adis[5] |

[3] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '681 patent issued has an effective filing date after that date, the AIA versions of §§ 102 and 103 apply.

[4] J.A. Dixon et al., *VEGF Trap-Eye for the Treatment of Neovascular Age-Related Macular Degeneration*, 18(10) EXPERT OPIN. INVESTIG. DRUGS 1573–80(2009) ("Dixon") Ex. 1006.

[5] Adis R&D Profile, Aflibercept: AVE 0005, AVE 005, AVE0005, VEGF Trap – Regeneron, VEGF Trap (R1R2), VEGF Trap-Eye, 9(4) DRUGS R D 261–269 (2008) ("Adis") Ex. 2007.

| Ground | Claim(s) Challenged | 35 U.S.C. § | Reference(s)/Basis |
|---|---|---|---|
| 3 | 1, 3–11, 13, 14, 16–24, 26 | 102 | Regeneron 2008[6] |
| 4 | 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon alone or in view of Papadopoulos[7] and/or Wiegand[8] |
| 5 | 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon in combination with Rosenfeld[9], and if necessary, Papadopoulos patent and/or Wiegand |
| 6 | 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon in combination with Heimann-2007, and if necessary, Papadopoulos and/or Wiegand |

Petitioner also relies upon the Declarations of Dr. Thomas A. Albini (the "Albini Declaration," Ex. 1002) and Dr. Mary Gerritsen (the "Gerritsen Declaration," Ex. 1003). Patent Owner relies upon the Declarations of

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[6] Press Release, Regeneron and Bayer HealthCare Announce Encouraging 32-Week Follow-Up Results from a Phase 2 Study of VEGF Trap-Eye in Age-Related Macular Degeneration (April 28, 2008) ("Regeneron 2008") Ex. 1012.

[7] Papadopoulos et al. (US 7,374,758 B2, May 20, 2008) ("Papadopoulos") Ex. 1010.

[8] Wiegand et al. (US 7,531,173 B2, May 12, 2009) ("Wiegand") Ex. 1007.

[9] P.J. Rosenfeld et al., *Ranibizumab for Neovascular Age-Related Macular Degeneration*, 355 (14) N. ENGL. J. MED. 1419–31; Suppl. App'x 1–17 (2006) ("Rosenfeld") Ex. 1058.

Dr. Diana V. Do (the "Do Declaration," Ex. 2056), Dr. Alexander M. Klibanov (the "Klibanov Declaration," Ex. 2057), David M. Brown (the "Brown Declaration," Ex. 2055), and Dr. Richard Manning (the "Manning Declaration," Ex. 2059). We have reviewed the credentials of Petitioner's and Patent Owner's declarants, and consider each to be qualified to provide the opinions for which their testimony has been submitted.

*D. The '681 Patent*

The '681 patent is directed to methods for treating angiogenic eye disorders by sequentially administering multiple doses of a vascular epithelial growth factor ("VEGF") antagonist to a patient. Ex. 1001, Abstr. These methods include the administration of multiple doses of a VEGF antagonist to a patient at a frequency of once every 8 or more weeks, and are useful for the treatment of angiogenic eye disorders such as, *inter alia*, age related macular degeneration. *Id.*

In an exemplary embodiment, a single "initial dose" of VEGF antagonist ("VEGFT") is administered at the beginning of the treatment regimen (i.e., at "week 0"), two "secondary doses" are administered at weeks 4 and 8, respectively, and at least six "tertiary doses" are administered once every 8 weeks thereafter (i.e., at weeks 16, 24, 32, 40, 48, 56, etc.). Ex. 1001, col. 2, ll. 56–62.

*E. Representative Claim*

Claim 1 is representative of the challenged claims, and recites:

> 1. A method for treating an angiogenic eye disorder in a patient, said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed

> by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
>
> wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2;
>
> wherein exclusion criteria for the patient include all of:
>
> (1) active intraocular inflammation;
>
> (2) active ocular or periocular infection;
>
> (3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 40–63.[10]

*F. Priority History of the '681 Patent*

The '681 patent issued from U.S. Application Ser. No. 15/471,506 (the "'506 application") filed on March 28, 2017, and claims the priority

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[10] For the purposes of this Decision, the terms "aflibercept" and "VEGF Trap-Eye" are used to refer to the same active VEGF antagonist that is recited in challenged claim 1 as "a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2." *See, e.g.*, Ex. 1006, 1575 ("VEGF Trap-Eye and aflibercept … have the same molecular structure."

benefit of, *inter alia*, US Provisional Application Ser. No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

The claims of the '681 patent, including challenged claims 1, 3–11, 13, 14, 16–24, and 26, were allowed on July 26, 2018, and the patent issued on November 20, 2018. Ex. 1017, 509; Ex. 1001, code (45).

## III. MOTIONS TO EXCLUDE EVIDENCE

Both parties have submitted Motions to Exclude Evidence (Papers 76, 77) and have also filed Oppositions (Papers 82, 80) and Replies (Papers 83, 84) to the opposing party's Motion to Exclude. We now consider each party's Motion to Exclude in turn.

### *A. Petitioner's Motion to Exclude*

Petitioner moves to exclude Patent Owner's Exhibits 2037–2039, 2079, 2080, 2084, 2085, 2098, 2101, 2103, 2104, 2122, 2136, 2138–40, 2163, 2169, 2170, 2176, 2190, 2197, 2200, 2208, 2218, 2229, 2243, 2244, 2250, 2259, 2277–79, 2282–85, 2298, 2299, and portions of Exhibits 2055–57 and 2059. Pet. Mot. Exclude, 1. We address each of Petitioner's arguments in turn.

#### 1. Exhibits 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and portions of Exhibit 2059 (¶¶ 11, 28, 29, 43, 47, 50–55, 60, 61, 63–69, 72, 74, 75, 78, 84, 108, 109, 113–16)

Petitioner argues that Patent Owner relies on the testimony of its expert, Dr. Manning, in support of its commercial success contentions. Pet. Mot. Exclude 1 (citing, e.g., PO Resp. 2, 49, 68–69; PO Sur-Reply, 25–28). Petitioner asserts that Dr. Manning in turn relies on various documents

purporting to reflect profit and loss statements for Patent Owner's product. *Id.* at 2 (citing Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and Ex. 2059 at Attachments C1–C12, D1–D4, D7, and X2 (collectively, the "Financial Exhibits")). Petitioner also argues for exclusion of portions of Dr. Manning's Declaration relating to this evidence, i.e., Ex. 2059 ¶¶ 11, 28–29, 43, 47, 50–55, 60–61, 63–69, 72, 74–75, 78, 84, 108–09, 113–16. *Id.* Petitioner states that it timely objected to the challenged Financial Exhibits. *Id.* (citing Papers 23, 48).

Petitioner seeks exclusion of the Financial Exhibits on the bases of: (1) FRE 1006 (compilations of sales data created for this proceeding, without production of the underlying business records); (2) FRE 901 (lack of authentication by a witness with personal knowledge); (3) FRE 801–03 (hearsay of records not within the business record exception); and FRE 702 (alleged unreliability of expert testimony).

As Petitioner states, Patent Owner relies upon these Exhibits as objective secondary evidence of non-obviousness. *See, e.g.*, PO Resp. 65–69. However, and as we explain below, because we find that the challenged claims are anticipated by Dixon, we do not reach Patent Owner's arguments that the claims are non-obvious (Grounds 4–6) or its contentions regarding secondary considerations of non-obviousness. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cir. 2008) (holding that "secondary considerations are not an element of a claim of anticipation"). Consequently, we dismiss Petitioner's motion to dismiss the Financial Documents as moot.

2. Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, 2278, and portions of Exhibit 2059 (¶¶ 61, 73, 85, 88–94, 98, 99, 103)

Petitioner argues that Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278 (collectively, the "Marketing Exhibits") purport to be Patent Owner's supportive internal marketing materials and ATU survey data. Pet. Mot. Exclude 6. Petitioner contends that Patent Owner offers the Marketing Exhibits as evidence of the claimed methods commercial success and as objective indicia of non-obviousness. Petitioner states that it timely objected to the challenged Marketing Exhibits. *Id.* (citing Papers 23, 48).

Petitioner urges us to exclude the Marketing Exhibits under FRE 403 because their probative value is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder.

As in Section III.A.1 above, we do not reach Patent Owner's arguments that the challenged claims are non-obvious (Grounds 4–6), because we conclude that they are anticipated by Dixon (Ground 1). *Cohesive Techs.,* 543 F.3d at 1364. We consequently dismiss Petitioner's motion to exclude the Marketing Exhibits as moot.

3. Exhibits 2079, 2080, 2084, and 2085

Petitioner argues that Exhibits 2079, 2080, 2084, and 2085 (the "Sequence Exhibits") are webpage printouts of the amino acid sequences of human VGFR1 and VGFR2 that should be excluded under FRE 402 and FRE 403. Pet. Mot. Exclude 8. Petitioner contends that Patent Owner's expert, Dr. Klibanov, offers the Sequence Exhibits as evidence of variability in publicly available amino acid sequences of human VGFR1/2. *Id.* (citing,

e.g., Ex. 2057 ¶¶ 76, 78, 79, 82, 86, and 87). Petitioner states that it timely objected to the Sequence Exhibits. *Id.* (citing Paper 48).

Petitioner argues that Exhibits 2079 and 2084 are webpage printouts dated February 28, 2023, that should be excluded as irrelevant non-prior art under FRE 402, and as unfairly prejudicial under FRE 403. Pet. Mot. Exclude 8–9. Petitioner asserts that Exhibits 2079 and 2084 indicate on their faces that they were both printed on February 28, 2023, twelve years after the alleged priority date of the challenged patent, and therefore have no bearing on the patentability of the challenged claims. *Id.* at 9. Petitioner also contends that Patent Owner fails to cite Exhibits 2079, 2080, 2084, and 2085 in its Preliminary Response, Response, or Sur-Reply, demonstrating that they do not have a tendency to make any fact of consequence more or less probable. *Id.* (citing *SK Innovation Co., Ltd. v. Celgard, LLC*, IPR2014-00679, Paper 58, 49 (PTAB September 25, 2015).

Patent Owner responds that the data contained within the Sequence Exhibits antedates the priority date of the '681 patent, i.e., January 13, 2011. PO Opp. Mot. Exclude 8. Patent Owner asserts that Exhibits 2080 and 2085 indicate that they were publicly available as of January 11, 2011. *Id.* (citing Ex. 2080, 1; Ex. 2085, 1). Patent Owner argues that Exhibit 2079 provides the same accession number or identifier, "P17948," and the same title, "VGFR1_HUMAN," and contains the same sequence information as Exhibit 2080, which Patent Owner asserts was publicly available before the priority date. *Id.* (citing Ex. 2079, 9; Ex. 2080, 3). Patent Owner makes corresponding arguments for Exhibits 2084 and 2085. *Id.*

Patent Owner also disputes Petitioner's argument that the Sequence Exhibits are not cited in Patent Owner's Response. PO Opp. Mot. Exclude

10. Patent Owner points to the testimony of Dr. Klibanov, who cites to the Sequence Exhibits, among other exhibits (citing PO Resp. 27 (citing Exs. 2078–2086), also citing *id.* at 26, 27, 29–30, 32).

Petitioner disputes Patent Owner's contention that the information contained in Exhibits 2079 and 2084 was available, in the form of Exhibits 2080 and 2085, before the '681 patent's claimed priority date of January 13, 2011. Pet. Reply Mot. Exclude 3. Petitioner also contends that Exhibits 2079 and 2084 are duplicative of Exhibits 2080 and 2085 and should be excluded under FRE 403 as needlessly cumulative. *Id.* Furthermore, argues Petitioner, to the extent they are not cumulative, they should be excluded because Patent Owner has provided no evidence that the information was available prior to January 13, 2011. *Id.* (citing *In re Lister*, 583 F.3d 1307, 1316 (Fed. Cir. 2009).

Petitioner also asserts that, in arguing the relevance of the Sequence Exhibits, Patent Owner cites to a single sentence in the Response in which the four exhibits in question are among nine that are not themselves directly referenced, but merely cited in Dr. Klibanov's Declaration. Pet. Reply Mot. Exclude 4 (citing PO Resp. 27). Petitioner contends that, because this sentence is the only instance Patent Owner relies on for the Sequence Exhibits, they are not relevant to any issue before the Board and should be excluded under FRE 401 and 402. *Id.*

We are not persuaded by Petitioner's arguments. Exhibits 2079 and 2080 both identify the sequences for VGFR1 (accession no. P17948) presented in each as having the same accession number, P17948, and Exhibit 2080 expressly identifies the entry date of the sequence into the Uniprot protein sequence and functional information database as at least January 11,

2011, which antedates the claimed priority date of the '681 patent. *See* Ex. 2057, 79 (Dr. Klibanov testifies as to the date). Exhibit 2079 provides further identifying information of the sequence identified in the two Exhibits. The two Exhibits thus complement each other, each providing additional information about the other, and indicating an entry date of the sequence as prior to the priority date of the '681 patent. The same is true for Exhibits 2084 and 2085 with respect to VGFR2 (accession no. P35968). Petitioner does not contest that the database was publicly available, and we conclude that the evidence is relevant prior art.

With respect to Petitioner's arguments that the Sequence Exhibits are unduly duplicative, we do not find that a pair of exhibits documenting the amino acid sequence of two proteins relevant to the claimed sequence is unduly cumulative, particularly given the complementary natures of Exhibit 2079 with Exhibit 2080, and Exhibit 2084 with Exhibit 2085. As to the extent of Patent Owner's reliance on the Sequence Exhibits, given the relevance of the Exhibits, we find this argument goes more to the weight of the evidence, rather than its admissibility. We consequently deny Petitioner's motion to exclude the Sequence Exhibits.

4. Exhibits 2098, 2101, 2103, 2104, 2122, 2298, and 2299

a. Exhibit 2098

Petitioner argues that Patent Owner does not cite Exhibit 2098 in its Preliminary Response, Response, or Sur-Reply, and that it is therefore not relevant to any contested issue in this proceeding. Pet. Mot. Exclude 9 (citing FRE 402). Petitioner also asserts that Exhibit 2098 is dated March 14, 2014, and Patent Owner filed it under seal. *Id.* at 10. As such, argues

Petitioner, Exhibit 2098 was not publicly available prior art. *Id.* (citing *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1568–69 (Fed. Cir. 1988).

Patent Owner responds that Exhibit 2098 was cited and relied on by Dr. Klibanov, Patent Owner's expert, and in Patent Owner's Response, through citation to the relevant paragraph of Dr. Klibanov's report. PO Opp. Mot. Exclude 9 (citing PO Resp. 39 (citing Ex. 2057 ¶ 120)). Patent Owner contends that it does not rely upon Exhibit 2098 as prior art, but rather to illustrate the inherent variability in the production of VEGF Trap-Eye, and that this variability was known in the prior art. *Id*. (citing PO Resp. 39–40 (citing Ex. 2057 ¶¶ 117–120); *see also id.* at n.6 (citing Exs. 2096, 2097, 2099, 2100)).

We are not persuaded by Petitioner's argument that Exhibit 2098 should be excluded. Paragraphs 117–119 of the Klibanov Declaration are offered by Patent Owner to demonstrate that it was known in the prior art that synthesis of recombinant human proteins was known to be inherently variable. *See* Ex. 2057 ¶¶ 117–119 (citing e.g., Ex. 2096, 91; Ex. 2097, 4). Exhibit 2098, although not publicly-available prior art, is at least probative of the understanding of one of ordinary skill in the art and, in consequence, admissible. We therefore deny Petitioner's motion to exclude Exhibit 2098.

b. Exhibit 2101

Petitioner next urges us to exclude Exhibit 2101. Petitioner argues that Exhibit 2101, a non-public, internal, technical report, was not cited by Patent Owner in its Preliminary Response, Response, or Sur-Reply, and that it is therefore not relevant to any contested issue in this proceeding under

FRE 402. Pet. Mot. Exclude 10. Petitioner also argues that Exhibit 2101 should be excluded as irrelevant non-prior art. *Id.* (citing FRE 402).

Petitioner contends that Exhibit 2101 should also be excluded under FRE 801–803 as constituting inadmissible hearsay evidence. Pet. Mot. Exclude 10. According to Petitioner, Exhibit 2101 includes out-of-court statements of PO's in-house personnel, offered for the truth of the matters asserted therein. *Id.*

Patent Owner responds that it does not rely on Exhibit 2101 for its prior art teaching; rather, Patent Owner asserts, Exhibit 2101 illustrates the inherent variability in producing VEGF Trap-Eye, which was known in the prior art. PO Opp. Mot. Exclude 10 (citing Ex. 2057 ¶¶ 121–131); PO Resp. 39–40); *see, e.g.*, Ex. 2057, 119 (citing Ex. 2096, 91; Ex. 2097, 4)).

Patent Owner also disputes Petitioner's assertion that Exhibit 2101 contains inadmissible hearsay evidence. PO Opp. Mot. Exclude 11. According to Patent Owner, Ms. Weber's Declaration testimony demonstrates that Exhibit 2101 falls within the business records exception to hearsay, as set forth in FRE 803(6): it is a scientific report, was stored on Regeneron servers, and bears facial indications of trustworthiness (written on Regeneron letterhead and dated and signed by Dr. Koehler-Stec, a study director and Regeneron employee). *Id.* (citing Ex. 2049, 24–26). Patent Owner notes that Petitioner does not challenge the foundation laid for the business records exception, and does not identify any condition of FRE 803(6) that has not been met. *Id.*

Patent Owner relies upon Exhibit 2049 (the purported testimony of "Ms. Weber") as authenticating Exhibit 2101 and demonstrating that it falls within the business records exception. PO Opp. Mot. Exclude 11. However,

there is no Exhibit 2049[11] entered into evidence in this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon.

Rule 803(6) allows business records to be admitted "if witnesses testify that the records are integrated into a company's records and relied upon in its day to day operations." *Air Land Forwarders, Inc. v. United States*, 172 F.3d 1338, 1342 (Fed. Cir. 1991) (quoting *Matter of Ollag Constr. Equip. Corp.*, 665 F.2d 43, 46 (2d Cir. 1981). Absent any such authenticating witness foundation, we cannot conclude that Exhibit 2101 falls within the Business Records exception of FRE 803(6), and we grant Petitioner's motion to exclude Exhibit 2101 as containing inadmissible hearsay.

c. Exhibit 2122

Petitioner next argues that Exhibit 2122, a confidential (filed under seal), non-public excerpt of clinical study protocol VGFT-OD-0605, should be excluded under FRE 402, 403, and 802. *See* Pet. Mot. Exclude 11. Petitioner first argues that Exhibit 2122 is irrelevant non-prior art under FRE 402 and unfairly prejudicial under FRE 403. *Id.* Petitioner argues that Patent Owner's sealed filing of Exhibit 2122 confirms it was not publicly available, and therefore does not demonstrate the POSA's knowledge or a prior art teaching. *Id.* Petitioner contends that any probative value of the

[11] Nor can we find a corresponding Exhibit 2049, or readily discern an exhibit that could reasonably be construed as providing the evidence of the missing Exhibit 2049, in the related IPR2022-01226, which was argued at the same time as the present *inter partes* review.

Exhibit is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder. *Id.*

Petitioner also argues that the reliance of Patent Owner's expert, Dr. Do, to assert as true the statements made in Exhibit 2122 constitutes impermissible hearsay evidence. Pet. Mot. Exclude 11–12 (citing Ex. 2056 ¶ 116).

Patent Owner argues, *inter alia*, that Ms. Weber's testimony makes clear that Exhibit 2122 falls within FRE 803(6), the business records exception to the rule against hearsay: it is a clinical study protocol, stored in Regeneron's regulatory archive, and bears facial indicia of trustworthiness (Regeneron protocol headers and file path information on each page). PO Opp. Mot. Exclude 12 (citing Ex. 2048 ¶ 3; Ex. 2049, 24–26).

Patent Owner again relies on an Exhibit (Ex. 2048) to support the assertion that Exhibit 2122 falls within the Business Records exception of FRE 803(6). Again, however, no such Exhibit 2048 is present in the record of this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon. *See Air Land*, 172 F.3d at 42. In the absence of any such authentication, we consequently grant Petitioner's motion to exclude Exhibit 2122 as impermissible hearsay under FRE 803.

d. Exhibit 2103 and Exhibit 2104

Petitioner contends that these Exhibits are confidential (filed under seal), non-public documents purported to be a research collaboration agreement and email chain and should be excluded under FRE 402, 403, and 802. Pet. Mot. Exclude 12. Petitioner argues that Exhibits 2103 and 2104

should be excluded as irrelevant non-prior art under FRE 402 and unfairly prejudicial under FRE 403. *Id.* Petitioner also argues that the Exhibits are hearsay under FRE 801, and should be excluded. *Id.*

Patent Owner responds that, although Patent Owner does not use Exhibits 2103 and 2104 as prior-art, and because non-prior art may be relevant, Petitioner's argument lacks merit for the same reasons as discussed with respect to Exhibit 2101. PO Opp. Mot. Exclude 12; *see supra* Section III.A.4.b.

Patent Owner additionally argues that Jeffrey Spada, Associate Director, eDiscovery and Litigation Support at Regeneron Pharmaceuticals, Inc., authenticated these documents in his sworn declaration and during his deposition. PO Opp. Mot. Exclude 12 (citing Ex. 2343 ¶¶ 1–3; Ex. 2349, 13–14, 15–16, 16–18, 20, 21). According to Patent Owner, Mr. Spada's testimony establishes that Exhibits 2103 and 2104 fall within FRE 803(6), the business records exception to the rule against hearsay: they are a Regeneron research collaboration agreement and an email chain regarding the same, stored in the custodial files of George Yancopoulos, the inventor of the '681 patent, and bear facial indicia of trustworthiness. *Id.* at 12–13 (citing Ex. 2343 ¶¶ 1–3; Ex. 2349, 13–14, 15–16, 16–18, 20, 21).

In its Response, Patent Owner offers the Exhibits as part of its argument that the amino acid sequence of VEGF Trap-Eye was not publicly available before EYLEA's FDA approval in November 2011. *See* PO Resp. 25. Specifically, Patent Owner points to Exhibits 2103 and 2104 as evidence that Patent Owner imposed restrictions on its research collaborators receiving VEGF Trap samples for experimentation purposes. *Id.* at 25–26 (citing Ex. 2103 § 5 Agreement; Ex. 2104).

We agree with Patent Owner that Ex. 2103 and 2104 are relevant to Patent Owner's argument that persons of ordinary skill in the art would not have had access to the VEGF Trap-Eye sequence at the time of invention. As such, we conclude that they are relevant under FRE 402 and 403.

We have reviewed the Declaration and relevant foundational testimony of Mr. Spada, and conclude that he has satisfactorily established that Exhibits 2103 and 2104 fall within the business records exception of FRE 803(6) as a record normally kept in the course of a regularly conducted business activity.[12] We therefore deny Petitioner's motion to exclude Exhibits 2103 and 2104.

e. Exhibits 2298 and 2299

Petitioner next argues that Exhibit 2298, a confidential (filed under seal), non-public document alleged to be a clinical study agreement between Vitreoretinal Consultants and Patent Owner, should be excluded because Patent Owner does not cite to Exhibit 2298 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–

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[12] Federal Rule of Evidence 803(6) states that:

> Records of regularly conducted activity. A memorandum, report, record, or data compilation, in any form, of acts, events, conditions, opinions, or diagnoses, made at or near the time by, or from information transmitted by, a person with knowledge, if kept in the course of a regularly conducted business activity, and if it was the regular practice of that business activity to make the memorandum, report, record or data compilation, all as shown by the testimony of the custodian or other qualified witness, unless the source of information or the method or circumstances of preparation indicate lack of trustworthiness.

*See Shu-Hui Chen v. Bouchard*, 347 F.3d 1299, 1308 n.2 (Fed. Cir. 2003)

402. Pet. Mot. Exclude 13. Similarly, Petitioner contends that Exhibit 2299, a confidential (filed under seal), non-public compilation of the VIEW protocol signature pages, should be excluded because it was not publicly available, and does not represent a person of ordinary skill in the art's knowledge or a prior art teaching. *Id.* at 13–14. Petitioner also contends that Patent Owner also fails to cite Exhibit 2299 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–402. *Id.* at 13.

Petitioner additionally argues that Exhibit 2299 is inadmissible as hearsay evidence because the papers are out-of-court statements offered for the truth of the matter asserted, i.e., the alleged confidentiality restrictions in place as of July 2007 regarding VEGF Trap-Eye. Pet. Mot. Exclude 13.

Patent Owner responds that Dr. Brown relies on Exhibit 2298 in his Declaration, and that declaration paragraph is cited in Patent Owner's Response. PO Opp. Mot. Exclude 13 (citing PO Resp. 25 (citing Ex. 2055 ¶ 67)).

With respect to Exhibit 2299, Patent Owner contends that Dr. Brown's and Ms. Weber's testimony establish that Exhibit 2299 falls within FRE 803(6), the Business Records exception to the hearsay rule. PO Opp. Mot. Exclude 14. According to Patent Owner, the Exhibit was generated in the ordinary course of regularly conducted business activity (i.e., a clinical investigation), was stored by Regeneron in its regulatory archives and by Dr. Brown's practice at Iron Mountain, and bears facial indications of trustworthiness (dated signatures by Dr. Brown's partner on every page), all as confirmed by individuals with knowledge. *Id.* (citing Ex. 1022, 62–63).

In his Declaration, Dr. Brown testifies that:

> [M]y institution, Vitreoretinal Consultants of Houston, signed a Clinical Study Agreement to conduct a clinical study entitled "A Randomized, Double Masked, Active Controlled Phase III Study of the Efficacy, Safety, and Tolerability of Repeated Doses of Intravitreal VEGF Trap in Subjects with Neovascular Age-Related Macular Degeneration" concerning Protocol number VGFT-OD-0605, which required my institution/practice to maintain information disclosed by Regeneron or generated as a result of the study in confidence and also limited our use of such information only for the purposes of the study. Ex. 2298 ¶ 6. In addition to the clinical study agreement, when our group/institution was provided the protocol for the VIEW trial, the document was clearly marked with a confidentiality legend and required that the clinical investigator sign the protocol and agree to be bound by its limitations on use and disclosure. Ex. 2299.

Ex. 2055 ¶ 67. Patent Owner relies upon this testimony as demonstrating that the amino acid sequence of VEGF Trap-Eye (the claimed SEQ ID NO:1 and SEQ ID NO:2) was not known to the artisan of ordinary skill, and that the clinical users of the drug were subject to confidentiality restrictions. *See* PO Resp. 25–26. As such, we find that the evidence adduced in these Exhibits is relevant to Patent Owner's arguments.

With respect to Petitioner's argument that Exhibit 2099 constitutes inadmissible hearsay evidence, and as we have explained above, we can find no evidence of an Exhibit 2048 or 2049, or of Ms. Weber's testimony, in Patent Owner's exhibits of record in this *inter partes* review. However, we find that the testimony of Dr. Brown is sufficient to authenticate the Exhibit and to establish that it falls within the Business Records exemption of FRE 803(6). Therefore, we find that Exhibits 2298 and 2299 are admissible.

Petitioner's motion to exclude Exhibits 2298 and 2299 is consequently denied.

f. Portions of Exhibits 2055–57, and 2059

Finally, Petitioner argues that Patent Owner's expert declaration testimony corresponding to the Challenged Exhibits should also be excluded. Pet. Mot. Exclude 14 (citing *Wi-LAN Inc. v. Sharp Elecs. Corp.*, 992 F.3d 1366, 1374 (Fed. Cir. 2021). Petitioner contends that Patent Owner has adduced no evidence that any of the challenged Exhibits are documents upon which a person of ordinary skill in the art would "reasonably rely" in forming an opinion on the subject matter at issue, thus warranting exclusion of portions of the declarations of Dr. Do (Ex. 2056 ¶ 116), Dr. Klibanov (Ex. 2057 ¶¶ 76, 78–79, 82, 86, 120–21, 123–28), Dr. Brown (Ex. 2055 ¶ 67), and Dr. Manning (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117).

Patent Owner responds that Petitioner's motion fails to identify which declaration paragraphs correspond to which exhibits, or to explain how or why the experts' use of any particular exhibit is allegedly improper. PO Opp. Mot. Exclude 14. Patent Owner contends that Petitioner's assertions lack particularity and do not satisfy Petitioner's burden on a motion to exclude. *Id.*

Patent Owner also argues that Petitioner's original objections to evidence failed to identify the portions of the expert declarations that it now moves to exclude with any particularity, instead asserting only that the FRE 703 objection applies to each of Exhibits 2048, 2049, 2050, and 2052 in their entirety. PO Opp. Mot. Exclude 15 (citing Pet. Mot. Exclude 3; and

citing *Nippon Suisan Kaisha Ltd. v. Pronova Biopharma Norge AS*, PGR2017-00033, 2019 WL 237114, at *23–24 (PTAB Jan. 16, 2019).

As we explained above, we dismiss Petitioner's motion to exclude the Financial Exhibits and the Marketing Exhibits as moot. We consequently also dismiss as similarly moot, Petitioner's motion to exclude Dr. Manning's related testimony. (Exhibit 2059 ¶¶ 11, 28–29, 43, 47–117).

Because we have denied Petitioner's motion to exclude the Sequence Exhibits, we also deny Petitioner's motion to exclude the related portions of Dr. Klibanov's testimony (Ex. 2057 ¶¶ 76, 78, 79, 82, and 86). Similarly, because we deny Petitioner's motion to exclude Exhibits 2098, we deny Petitioner's motion to exclude the related testimony of Dr. Klibanov with respect to that Exhibit (Ex. 2057 ¶ 120).

We have also explained why we deny Petitioner's motion to exclude Exhibit 2299. We therefore also deny Petitioner's motion to exclude the related foundational testimony of Dr. Brown (Ex. 2055 ¶ 67).

We grant Petitioner's motion to exclude the unauthenticated Exhibit 2101 as inadmissible hearsay evidence, as explained above. We therefore also exclude the related portions of Dr. Klibanov's testimony that rely upon that evidence relating to the Regeneron study (Ex. 2057 ¶¶ 123–128).

Finally, we also grant Petitioner's motion to exclude Exhibit 2122 under FRE 803. We therefore also exclude the related testimony of Dr. Do (Ex. 2056 ¶ 116).

5. Summary

For the reasons we have explained in the preceding sections, we dismiss as moot Petitioner's motion to exclude the Financial Exhibits

(Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, and 2282–85) and Marketing Exhibits (Exs. 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278) as well as Dr. Manning's related testimony (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117).

We deny, for the reasons explained above, Petitioner's motion to exclude the Sequence Exhibits (Exs. 2079, 2080 2084, and 2085) as well as Exhibits 2098, 2103, 2104, 2228, and 2229. We similarly deny Petitioner's motion to exclude the portions of Patent Owner's expert's testimony related to these Exhibits, *viz.*, that of Dr. Klibanov (Ex. 2057 ¶¶ 76, 78, 79, 82, 86, 120).

We grant Petitioner's motion to exclude Exhibits 2101 and 2122. We also grant Petitioner's motion to exclude the related portions of Dr. Klibanov's and Dr. Do's testimony relying upon those Exhibits (Ex. 2057 ¶¶ 123–128 and Ex. 2056 ¶ 116, respectively).

*B. Patent Owner's Motion to Exclude*

Patent Owner moves to exclude Exhibits 1058, 1020, 1087, 1167, 1124, 1150, and 1151, and related portions of Exhibits 1102, 1103, 1107, and 1115. PO Mot. Exclude 1, 10. We consider each of Patent Owner's arguments in turn.

a. Ex. 1058

Patent Owner argues that Ex. 1058 should be excluded as evidence. PO Mot. Exclude 2. Exhibit 1058 (Rosenfeld) forms a partial basis for Petitioner's Ground 5 contentions that the challenged claims are unpatentable as obvious over the cited prior art. *See* Pet. 13.

Patent Owner argues that: (1) Ex. 1058 is not authenticated and irrelevant under FRE 401-403, 802, and 901. PO Mot. Exclude 2–9.

As we explain below, we conclude that the challenged claims in this *inter partes* review are anticipated by Dixon and therefore unpatentable (Ground 1). Because we reach this conclusion, we do not reach Petitioner's contentions that the claims are obvious on the basis of Ground 5. Nor does our analysis rely upon, or cite to, Exhibit 1058. We consequently dismiss as moot Patent Owner's motion to exclude Exhibit 1058.

b. Exhibits 1020, 1087, 1167, and related portions of Exhibits 1102, 1103, 1107, and 1115

Patent Owner next urges us to exclude Exhibits 1020, 1087, and 1167 on the basis that none of these Exhibits were cited in the Petition or the Petitioner's Reply. PO Mot. Exclude 10. Similarly, Patent Owner seeks to exclude the related portions of Petitioner's expert testimony not cited in the pleadings:

(i) Ex. 1002 ¶¶ 30–42, 46–47, 53–63, 65–69, 71–82, 101, 109–112, 114, 119, 122–125, 129–131, 133–134, 137, 313-–331, 335–346, 356–372, 377–389, 393, and 396;

(ii) Ex. 1003 ¶¶ 31–43;

(iii) Ex. 1107 ¶¶ 6–48, 51–64, 66–71, 78–86, 92–96, and 101–27;

(iv) Ex. 1115 ¶¶ 21, 23–59.

*Id.* Patent Owner states that it timely objected to each of these uncited exhibits and expert declaration paragraphs. *Id.* Patent Owner contends that these uncited exhibits and testimony were not relied upon by Petitioner and should therefore be excluded as irrelevant. *Id.* at 11.

Petitioner responds that Patent Owner's contention that multiple portions of at least Exhibits 1002, 1107, and 1115 "were not cited in the

pleadings" is inaccurate. Pet. Opp. Mot. Exclude 8–9 (quoting PO Mot. Exclude 10). Petitioner asserts that its Reply does in fact rely upon at least paragraph 73 of Exhibit 1002 to rebut Regeneron's assertion of "great uncertainty" regarding extended dosing in clinical practice prior to 2010. *Id.* at 9 (citing Pet. Reply 60, 22). Petitioner also contends that its Reply further relies on at least paragraphs 14–44, 51–57, and 102–126 of Exhibit 1107 to explain: (1) alleged shortcomings of the intrinsic record; (2) Patent Owner's representations to the U.S. Patent and Trademark Office; (3) the realities of the VIEW clinical trials; and (4) secondary consideration of non-obviousness analyses. *Id.* (citing Pet. Reply 5, 8, 23, 25, 8, 11). Petitioner argues that its Reply also relies on paragraphs 28–59 of Exhibit 1115 in its blocking patent discussion. *Id.* (citing Pet. Reply 23).

Petitioner additionally argues that the identified exhibits and expert testimony are a matter of public record, and the Board may have reason to consult any of these exhibits or take public notice of them. Pet. Opp. Mot. Exclude 9. Petitioner notes that Patent Owner has provided no legitimate justification for excluding this evidence altogether at this time. Petitioner argues that the Board can, in its discretion, assign weight to the evidence as appropriate, and as it has done in prior IPRs. *Id.* (citing, e.g., *Square, Inc. v. 4361423 Canada Inc.*, IPR2019-01649, Paper 43, 32–33 (PTAB Apr. 22, 2021).

Patent Owner replies that Petitioner does not deny that Exhibits 1020, 1087, 1167, and the challenged portions of Exhibits 1002, 1003, 1107, and 1115 not cited by Petitioner in its Opposition were not relied upon in any of its pleadings. Patent Owner contends that these Exhibits and portions of Exhibits should be excluded as being of no consequence in determining the

outcome of the proceeding. PO Reply Mot. Exclude 3–4 (citing *One World Techs., Inc. v. Chamberlain Grp., Inc.*, IPR2017-00126, Paper 56 at 16 (PTAB Oct. 24, 2018)).

We do not find Patent Owner's argument persuasive. To the extent that the challenged Exhibits and testimony are relied upon in this Final Written Decision, the Board is capable of assigning to them appropriate probative weight. *See, e.g.*, *Square, Inc. v. 4361423 Canada Inc.*, IPR2019-01649, Paper 43, 32-33 (PTAB Apr. 22, 2021). Moreover, Patent Owner alleges no prejudice by the inclusion of these Exhibits and testimony in the record of this *inter partes* review. Because Board proceedings favor inclusion in the public record, and because Patent Owner alleges no potential prejudice from inclusion of this evidence in the record, we deny Patent Owner's motion to exclude Exhibits 1020, 1087, and 1167 and the challenged paragraphs of Exhibits 1102, 1103, 1107, and 1115.

c. Exhibits 1124, 1150, and 1151

Patent Owner next seeks to exclude Exhibits 1124, 1150, and 1151. PO Mot. Exclude 14. These Exhibits consist of complaints and exhibits filed by the U.S. Department of Justice and Horizon Healthcare Services, Inc. against Patent Owner and were introduced by Petitioner to impeach the credibility of Patent Owner's commercial success expert, Dr. Manning. *See* Pet. Opp. Mot. Exclude 10–11. Patent Owner contends that these Exhibits are irrelevant, prejudicial, and inadmissible hearsay evidence under FRE 403 and FRE 803, 804, and 807. PO Mot. Exclude 12–14.

Dr. Manning's testimony relates to the commercial success of the compound recited in the challenged claims as objective evidence of non-

obviousness. As we explained above, we conclude in this Final Written Decision is anticipated by Dixon (Ground 1) and we do not reach Petitioner's obviousness Grounds 4–6. We therefore do not rely upon Dr. Manning's testimony as to objective indicia of non-obviousness. *See Cohesive Techs.,* 543 F.3d at 1364. Nor does our analysis rely upon, or cite to, the Exhibits challenged by Patent Owner. Consequently, we dismiss as moot, Patent Owner's motion to exclude Exhibits 1124, 1150, and 1151.

d. Summary

For the reasons set forth above, we dismiss Patent Owner's motion to exclude Exhibits 1058, 1124, 1150, and 1151. We deny Patent Owner's motion to exclude Exhibits 1020, 1087, 1167, and the related portions of Exhibits 1102, 1103, 1107, and 1115 cited by Patent Owner.

## IV. ANALYSIS

### *A. Claim Construction*

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006)

(citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Petitioner initially argues that the language of the preamble reciting "a method for treating" is not limiting upon the claims. Pet. 17–20. Petitioner additionally proposes constructions for the claim terms "initial dose," "secondary dose," and "tertiary dose." *Id.* at 24–25. Finally, Petitioner argues that the limitation reciting "wherein exclusion criteria for the patient include all of…." (the "exclusion criteria") are not entitled to patentable weight under the printed matter doctrine. *Id.* at 25–28.

Patent Owner disagrees, arguing that not only is the preamble limiting and requires "treating," but that the recited "method for treating" requires "a high level of efficacy." PO Resp. 8–19. Patent Owner further argues that the printed matter doctrine is inapplicable to the "exclusion criteria" limitation and that exclusion criteria are limiting upon the claims. *Id.* at 18–25. We address each of these arguments in turn.

1. Preamble

a. Petitioner's arguments

Petitioner argues the preamble is not limiting upon the claims. Pet. 17–18. Petitioner argues that: (1) the preamble is merely a statement of intended purpose and, therefore, not a limitation; and (2) the preamble provides no antecedent basis for any other claim element, and that any argument that "the patient" and "angiogenic eye disorder" claim terms find their respective meaning in the preamble is meritless. *Id.* at 20.

Alternatively, argues Petitioner, if the preamble is limiting, it should be given its plain and ordinary meaning, which does not require any specific efficacy requirement. *Id.* at 20–23.

b. Patent Owner's Response

Patent Owner responds that: (1) the preamble is limiting and requires "treating"; (2) the recited "method for treating" requires a high level of efficacy; and (3) the intrinsic record supports a high level of efficacy. PO Resp. 8–18.

Specifically, Patent Owner argues that where our reviewing court has found "method for treating" preambles to be limiting, they have consistently found that such claims require effective treatment. PO Resp. 9 (citing, e.g., *Sanofi Mature IP v. Mylan Labs. Ltd.*, 757 F. App'x 988, 992–94 (Fed. Cir. 2019); *Eli Lilly & Co. v. Teva Pharms. Int'l GMBH*, 8 F.4th 1331, 1340–43 (Fed. Cir. 2021)). Patent Owner disputes the Board's conclusion in the -00881 IPR that the claimed methods encompass ineffective administration, citing the '681 Specification's disclosure that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount." *Id.* (quoting Ex. 3001, 10). Patent Owner contends that the -00881 Decision's reliance on that passage is "contrary not only to the above precedent, but also the weight of evidence." *Id.* (citing Ex. 2056 ¶¶ 59–67; Ex. 2021, 192–193, 200). According to Patent Owner, a person of ordinary skill in the art would not look at this passage in isolation and, asserts that the remainder of the Specification "repeatedly characterizes the method as one that is useful for treating angiogenic eye disorders in patients." *Id.* at 9–10 (quoting Ex. 3001, 19).

Patent Owner argues further that the claimed method for treating requires a high level of efficacy. PO Resp. 10. According to Patent Owner, the method of the '681 patent was groundbreaking because it maintained initial gains with less frequent "tertiary doses." *Id.* at 12 (citing Ex. 1001, col. 2, ll. 7–24). Patent Owner contends that, contrary to Petitioner's suggestion that this high level of efficacy lacks support, every exemplification of the claimed Q8 dosing regimen in the '681 patent specification shows the regimen achieving and maintaining a high level of efficacy in the treated population. *Id.* at 14 (citing Pet. 22; also citing, e.g., Ex. 1001, Examples 4, 5).

Patent Owner points to Shams[13], an abandoned patent publication, which discloses an extended dosing regimen for Lucentis that meets the operative steps of the '681 patent claims (Q8 or longer tertiary dosing), where study subjects gained vision during monthly loading doses but lost those gains during tertiary maintenance dosing. PO Resp. 13 (citing Ex. 2022, 30–32, 40–42, 44–45, 46–47, 48–49, 561; Ex. 1030, 7–9, Fig. 1C). Patent Owner asserts that, by expressly recognizing that the PIER dosing regimen left an unmet need in the art, the '681 Specification makes clear that achieving and maintaining a high level of efficacy is the whole point of the claimed methods. *Id.*

Patent Owner argues that a person of ordinary skill in the art would not have required non-inferiority data for every angiogenic eye disorder to understand, from the disclosures of the '681 patent, that VEGF Trap would be similarly effective across angiogenic eye disorders. PO Resp. 14 (citing

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[13] Shams (US 2007/0190058 A1, August 16, 2007) ("Shams") (Ex. 2024).

Pet. 2, 22 n.7; Ex. 2001 ¶¶ 37–38). Patent Owner contends that, once VEGF Trap was shown to be non-inferior to Lucentis in treating wet AMD, a skilled artisan would have expected it to also be highly effective for other angiogenic eye disorders. *Id.* at 15.

Patent Owner also points to the prosecution history of the '681 patent, in which Patent Owner overcame a double patenting rejection to the challenged claims by explaining that the "treatment protocol" encompassed by the claimed invention resulted in surprising efficacy, i.e., noninferiority to ranibizumab, despite less frequent dosing. PO Resp. 15 (citing Ex. 1017, 458–63, 484–86 (citing Ex. 1018); also citing *Fenner Invs., Ltd. v. Cellco P'ship*, 778 F.3d 1320, 1322–23 (Fed. Cir. 2015)).

Patent Owner argues that this evidence supports its contention that, as of 2011, a person of ordinary skill in the art would have understood that the claimed "method for treating," must provide highly effective treatment to the patient (on par with the standard-of-care at patent filing). PO Resp. 15–16 (citing Ex. 2001 ¶¶ 32–39; Ex. 2056 ¶¶ 98, 56–98).

c. Analysis

These same arguments were argued and addressed in the prior -00881 Decision. *See* Ex. 3001, 12–23. As an initial matter, we are not persuaded by Patent Owner's reliance on *Sanofi* and *Eli Lilly*. *See* PO Resp. 9. In *Sanofi*, a non-precedential decision, the Federal Circuit held that the preamble to the claims at issue, reciting "[a] method of increasing survival comprising administering to a patient in need thereof" was limiting upon the claims, in conformance with the court's prior decisions in *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) and *Rapoport v.*

*Dement*, 254 F.3d 1053 (Fed. Cir. 2001). *Sanofi*, 757 F. App'x at 992–93. Furthermore, the court held that, because the preamble was limiting, and recited a "method of increasing survival" the proposed claims would now clearly require "increasing survival." *Id.* at 994. The preamble to claim 1 of the '681 patent, however, recites no such "increase" with respect to efficacy, but merely recites "A method for treating an angiogenic eye disorder in a patient," and the remainder of the claim requires no specific efficacy requirement.

Nor does *Eli Lilly* support Patent Owner's position. In *Eli Lilly*, the court upheld the Board's conclusion that the preamble reciting "a method for treating headache in an individual" was limiting upon the claims. *Eli Lilly*, 8 F.4th at 1343. However, it noted, in upholding the Board's conclusion, the Board also "found that while the claims encompass a clinical result, they do not *require* such a result." *Id.* (emphasis added). We also find that the similar language of the preamble to challenged claim 1 of the '681 patent, although encompassing clinical efficacy, does not require it, let alone a "high degree of efficacy."

In the -00881 Decision, challenged claim 1 of US 9,254,338 B2 (the "'338 patent") recited preamble language identical to that recited in claim 1 of the '681 patent, *viz.*, "a method for treating an angiogenic eye disorder in a patient." *See* Ex. 1001, col. 21, ll. 40–41; Ex. 3001, 7. The Board found that this preamble was limiting upon the remainder of the claim. Ex. 3001, 18. Specifically, the Board found that:

> Here, the claims are directed to methods of administering, i.e., using, a VEGF antagonist for an intended purpose of "treating an angiogenic eye disorder in a patient." The Specification repeatedly characterizes the method as one for treating

> angiogenic eye disorders in patients. Apart from the preamble, the independent claims do not elsewhere recite or indicate any other use for the method steps comprising the administration of a VEGF antagonist. Thus, we determine that the preamble sets forth the essence of the invention—treating an angiogenic eye disorder in a patient.
>
> Additionally, we find that the preamble provides antecedent basis for claim terms "the patient" recited in the body of each independent claim, and "angiogenic eye disorders" recited in dependent claims 6, 7, 18, and 20. Indeed, without the preamble, it would be unclear to whom the doses of VEGF are administered.
>
> Thus, …in view of the evidence of record, namely, the claim language and the written description of the '338 patent, we find that the preambles of method claims 1 and 14 are limiting insofar as they require "treating an angiogenic eye disorder in a patient."

*Id.* at 17–18 (citations omitted). We adopt this same reasoning here and find that the preamble of claim 1 reciting "[a] method for treating an angiogenic eye disorder in a patient" is limiting.

We do not find persuasive, however, Patent Owner's argument that the preamble's recitation of a "method for treating" requires a high level of efficacy. In the -00881 Decision, the Board rejected Patent Owner's similar argument because it required improperly importing limitations into the claims. *See* Ex. 3001, 22. Specifically, the Board found that:

> [W]hen the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount," and discloses that "a therapeutically effective amount can be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder,"

> or it may not. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

*Id.* at 21–22 (citation omitted). Furthermore, the Board found that:

> Patent Owner proposes that the claims require not only achieving a therapeutically effective result, but more specifically, achieving a "high level of efficacy that was noninferior to the standard of care by the time the patent was filed in 2011." In the Sur-reply, Patent Owner describes a "highly effective treatment for angiogenic eye disorders" as "one that is on par to Lucentis or off-label Avastin and can produce visual acuity gains, not just slow vision losses." The Specification refers to "a high level of efficacy" in one instance, i.e., in the "Background" section. The Specification does not describe there, or elsewhere that "treating," in the context of the claims or in the art, requires achieving a "high level of efficacy" or providing results "on par to Lucentis or off-label Avastin."

*Id.* at 22 (citations omitted).

We adopt the same reasoning here, and find that, for the purposes of this Decision, the evidence of record and the Specification support construing the preamble's recitation of a "method for treating a patient with an angiogenic eye disorder" as meaning administering a compound, i.e., the recited VEGF antagonist, to such patient for the purpose of improving or providing a beneficial effect in their angiogenic eye disorder. We find that, as in *Eli Lilly*, although the claims "encompass a clinical result, they do not require such a result." *Eli Lilly*, 8 F.4th at 1343. We consequently reject

Patent Owner's argument that the preamble to the challenged claims requires a "high level of efficacy," as proposed by Patent Owner. *See* Ex. 3001, 22.

2. "Initial dose," "Secondary Dose," and "Tertiary Dose"

Petitioner next contends that a person of ordinary skill in the art would understand each of these claim terms as expressly defined in the '681 patent's Specification. Pet. 24. The Specification defines the claim terms as follows:

> The terms "initial dose," "secondary doses," and "tertiary doses," refer to the temporal sequence of administration of the VEGF antagonist Thus, the "initial dose" is the dose which is administered at the beginning of the treatment regimen (also referred to as the "baseline dose") ; the "secondary doses" are the doses which are administered after the initial dose; and the "tertiary doses" are the doses which are administered after the secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of dosing regimens, but will generally differ from one another in terms of frequency of administration.

Ex. 1001, col. 3 ll. 34–44. Petitioner also notes that the Specification further explains that "the immediately preceding dose" means "in a sequence of multiple administrations, the dose of VEGF antagonist which is administered to a patient prior to the administration of the very next dose in the sequence with no intervening doses." Pet. 24 (citing Ex. 1001, col. 3, ll. 54–59; Ex. 1002 ¶¶ 44–45).

We adopt Petitioner's proposed construction of the claim terms "initial dose," "secondary dose," and "tertiary dose." Petitioner proposes adoption of the definitions expressly set forth in the Specification of the '681 patent, *viz.*, that the initial dose is the dose "administered at the beginning of

the treatment regimen," and is followed by the secondary doses that are "administered after the initial dose," and the tertiary doses are "administered after the secondary doses" and may be distinguished from the secondary doses "in terms of frequency of administration." Ex. 1001, col. 3, ll. 36–44.

Patent Owner does not expressly dispute Petitioner's construction, other than to argue that, by 2011, a person of ordinary skill in the art would have understood "initial" and "secondary" doses to correspond to loading doses and "tertiary" doses to correspond to maintenance doses. PO Resp. 11–12 (citing Ex. 2026 ¶¶ 39–40; Ex. 2001 ¶¶ 47–49).

We do not find persuasive Patent Owner's argument that the definition of these terms requires a high, or otherwise defined, degree of efficacy. As we stated in the -00881 Decision:

> Based on those express definitions in the Specification, we do not find cause to construe the terms differently. In particular, we do not find that the Specification requires the "tertiary doses" to maintain any efficacy gain achieved after the initial and secondary doses, or that the term suggests any specific level of efficacy. *The Specification unequivocally states that "[t]he terms 'initial dose,' 'secondary doses,' and 'tertiary doses,' refer to the temporal sequence of administration of the VEGF antagonist."*

Ex. 3001, 25 (emphasis added). We see no need or reason to upend this construction now, and we adopt Petitioner's proposed definition of the claim terms "initial dose," "secondary doses," and "tertiary doses" as the express definition provided by the '681 Specification.

3. The exclusion criteria

The "exclusion criteria" limitation of challenged claim 1 recites:

[W]herein exclusion criteria for the patient include all of:

(1) active intraocular inflammation;

(2) active ocular or periocular infection;

(3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 58–62.

a. Petitioner's arguments

Petitioner argues that the "exclusion criteria" are entitled to no patentable weight under the printed matter doctrine. Pet. 25.

Petitioner points to the two-part analysis set forth in *Praxair Distrib., Inc. v. Mallinckrodt Hosp. Prods. IP Ltd.*, 890 F.3d 1024, 1032 (Fed. Cir. 2018). Under this analysis we first determine whether the claim limitation in question is directed to printed matter. i.e., "if it claims the content of information." *Praxair*, 890 F.3d 1032 (citing *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015). In the second step, we determine whether the printed matter is functionally related to its "substrate," i.e., whether the printed material is "interrelated with the rest of the claim." *Id.* Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850).

Petitioner first argues that the exclusion criteria (i.e., preexisting conditions) represent informational content regarding the patient. Pet. 26. Petitioner argues that the challenged claims recite no active step of applying (or assessing the patient for) the exclusion criteria and consequently is "informational content" constituting a "mental step/printed material element." *Id.* at 27. Petitioner asserts that, even if application of the "exclusion criteria" could be inferred, the challenged claims do not dictate

that any procedural step be taken, or that any alteration be made to the claimed dosing regimen. *Id.*

Turning to the second step of the *Praxair* analysis, Petitioner contends that there is no functional relationship between the exclusion criteria and the rest of the claim (i.e., the operative steps of administering a VEGF antagonist to treat an angiogenic eye disorder). Pet. 27. Specifically, Petitioner argues that neither the presence nor absence of any exclusion criteria dictates any changes to the actual claimed dosing steps—i.e., the operative steps remain the same. *Id.* Therefore, argues Petitioner, because the "exclusion criteria" are "directed to mental steps" that "attempt to capture informational content," and lack a functional relationship to the other steps of the claimed treatment method, the exclusion criteria should be "considered printed matter lacking patentable weight." *Id.* (quoting *Praxair*, 890 F.3d at 1033).

b. Patent Owner's Response

Patent Owner contends that the exclusion criteria are entitled to patentable weight. PO Resp. 18. According to Patent Owner, the exclusion criteria are not mere "informational content," and the POSA would understand that they are not optional when practicing the claimed methods. *Id.* at 19 (citing Ex. 2056 ¶ 100). Rather, argues Patent Owner, practicing the challenged claims requires actually applying the recited criteria—i.e., assessing a patient for the conditions listed as exclusion criteria, and administering treatment only to a patient who does not have the recited conditions. *Id.* Patent Owner contends that the plain meanings of the words "exclusion" and "criteria" mandate that patients having the listed conditions

(i.e., the "criteria") are actually "excluded" from treatment. *Id.* at 20 (citing Ex. 2062, 4, 7; Ex. 2056 ¶ 109). Consequently, Patent Owner argues, only patients who are cleared of the exclusion criteria may be treated according to the claimed methods. *Id.*

Patent Owner asserts that the '681 Specification confirms that the exclusion criteria are mandatory. PO Response 20. Patent Owner points to Example 4 of the Specification, which describes 37 exclusion criteria known to have been used in Regeneron's Phase III VIEW clinical trials; numbers 18, 19, and 20 on that list correspond, respectively, to the exclusion criteria of the claims, and were employed in Example 4. *Id.* (citing Ex. 1001, cols. 10–12, ll. 25–62; Ex. 2056 ¶ 107). Patent Owner asserts that Example 4's description is consistent with how the VIEW study exclusion criteria were actually applied: as non-optional criteria that limited the treatment population. *Id.* at 21 (citing Ex. 2056 ¶¶ 103–104, 108).

Patent Owner asserts that both parties' experts confirm that the POSA would understand that the exclusion criteria are mandatory. PO Resp. 21. Patent Owner points to the testimony of Petitioner's expert Dr. Albini, who states that "clinical trial investigators are required to apply each of the exclusion criteria." *Id.* (citing Ex. 1002 ¶¶ 93, 203, 251; Ex. 2323, 105–109). Patent Owner notes that its expert, Dr. Do, agrees. Ex. 2056 ¶¶ 108, 105, 109). Patent Owner contends that the mandatory nature of the exclusion criteria distinguishes them from contraindications printed on a drug label, which a physician may choose to employ, or not. *Id.* (citing Ex. 2056 ¶ 110; Ex. 2323, 103). Contraindications, argues Patent Owner, are "symptom[s], circumstance[s], etc., which tend[] to make a particular course of (remedial) action inadvisable" however it is ultimately at the

clinician's discretion whether to follow them or not. *Id.* at 22 (citing Ex. 2062, 3).

Patent Owner contends that the challenged claims differ markedly from the "printed matter" claims in *Praxair*, which were expressly directed to the provision of "information" or a "recommendation," with no requirement that the "information" or "recommendation" change the scope or practice of the claims. PO Resp. 22 (citing *Praxair*, 890 F.3d at 1029–30*)*. In contrast, asserts Patent Owner, the challenged claims do not recite the provision of information, but instead define which patients are treated by the claimed methods, i.e., patients having an angiogenic eye disorder, and not having any of the exclusion criteria. *Id.* (citing Ex. 1001, claim 1; Ex. 2323, 104–105).

Turning to the second part of the *Praxair* test, Patent Owner argues that the exclusion criteria bear a functional relationship to the claim. PO Resp. 23. Patent Owner asserts that the exclusion criteria define the patient population for treatment, and so define how (i.e., upon whom) the treatment steps are to be performed; ignoring the exclusion criteria would result in a different (broader) group of patients would be treated. PO Resp. 23 (citing PO Prelim. Resp. 40). According to Patent Owner, claim terms defining the population of patients to be treated with a claimed method are limiting. *Id.* (citing, e.g., *Rapoport*, 254 F.3d at 1058–60; *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1356–57 (Fed. Cir. 2014); *Jansen*, 342 F.3d at 1333–34; *GlaxoSmithKline LLC v. Fibrogen, Inc.*, IPR2016-01318, 2017 WL379248, *3 (PTAB Jan. 11, 2017); *Praxair*, 890 F.3d at 1035).

Patent Owner also contends that the exclusion criteria also require that the medical provider take specific action—assessing the patient for the

exclusion criteria, then administering treatment only to a patient who is determined not to have the excluded conditions. *Id.* (citing Ex. 2056 ¶¶ 101, 105). As an instance of this, Patent Owner points again to Example 4 of the '681 Specification, which discloses that subjects underwent assessment at screening, and that patients who were found to have one of the listed exclusion criteria were excluded from treatment. *Id.* at 23–24 (citing Ex. 2056 ¶¶ 102–104, 108; Ex. 1001, col. 12, ll. 33–62). Patent Owner argues that such assessments are a routine part of clinical practice as well. *Id.* at 24 (citing Ex. 1002 ¶¶ 98, 350; Ex. 2323, 122, 72–82, 92; Ex. 2056 ¶¶ 105, 109).

c. Petitioner's Reply and Patent Owner's Sur-Reply

Petitioner replies that, contrary to Patent Owner's argument, "assessing a patient for the conditions listed as Exclusion Criteria" is not among the claimed steps. Pet. Reply 9. Petitioner points to the District Court's finding in the parallel *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) (the "district court proceedings") that the claimed exclusion criteria in Patent Owner's related US 10,888,601 and US 11,253,572 patents' (the "'601 and '572 patents") claims lack patentable weight, and observing that "[e]ven under Regeneron's 'assess and exclude' approach, a patient either never starts the method (and hence the method doesn't change); or, if doctors screened for the information and found no infection or inflammation, the same method proceeds." *Id.* (quoting Ex. 1112, 34–35). Petitioner asserts that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.* (citing Ex. 1112, 34–35 (citing IPR2022-01226, Institution Decision,

Paper 22, 15 (PTAB Jan. 11, 2023)). Therefore, argues Petitioner, the exclusionary criteria are strictly informational, without requiring the practitioner to act, or refrain from acting, in a specified manner, and not functionally related to the practice of the claimed method. *Id.*

Petitioner also disputes Patent Owner's contention that unlike contraindications printed on a drug label, a skilled artisan would not treat exclusion criteria as optional in clinical practice. Pet. Reply (citing PO Resp. 21). Petitioner points out that Patent Owner's expert, Dr. Do, admits that she "may proceed with the intravitreal injection despite the presence of one of these conditions." *Id.* at 10 (citing Ex. 2056 ¶¶ 158, 110; Ex. 1112, 33. According to Petitioner, Dr. Do also admits that "in the context of a clinical trial, if a patient has one or more of the exclusion criteria, they would not be included in clinical trial," thereby forfeiting treatment, whereas in her own practice she would "exclude the patient from treatment, at least temporarily." *Id.* (citing (Ex. 1109, 149) (Ex. 2056 ¶ 158). Petitioner contends that nothing in the '681 specification shows that the claimed exclusion criteria are mandatory outside of a clinical trial setting. *Id.* (citing Ex. 1107 ¶ 65).

With respect to the second part of the *Praxair* test, Petitioner contends that, even if the exclusion criteria were mandatory, they still would not be functionally related to the rest of the claims. Pet. Rely 11. Petitioner notes Patent Owner's argument that the exclusion criteria "define the patient population for treatment," but contends that the mental step of deciding not to treat a patient is unpatentable because "[o]nce the information is detected, no … treatment is given." *Id.* (quoting PO Resp. 23; Petition 26) (citation omitted).

Patent Owner responds that, with respect to Dr. Do's testimony, treating physicians can administer aflibercept in any number of ways, according to their medical judgment, but such administration will only practice the method of the challenged claims if it meets every claim limitation, including application of the exclusion criteria. PO Sur-Reply 8 (citing Ex. 2056 ¶ 158). Patent Owner adds that both parties' experts also agree that applying the exclusion criteria requires the active step of patient assessment to identify a treatment-eligible patient. *Id.* (citing Ex. 2323, 72–79).

Patent Owner argues again that the exclusion criteria define and limit the population of patients eligible for treatment. PO Sur-Reply 9. According to Patent Owner, to be eligible for the claimed treatment method, a patient must have an angiogenic eye disorder and must not have any of the recited excluded conditions. *Id.* Patent Owner contends that, by Petitioner's logic, no population-defining limitation for a method-of-treatment claim could be entitled to patentable weight, because patients who fall outside the defined population will not be treated as claimed. *Id.*

d. Analysis

We are persuaded by Petitioner's argument that the exclusion criteria are not limiting upon the claims. In *Praxair*, our reviewing court held that the printed matter doctrine is not limited to literal printed matter, but is also applicable when a claim limitation "claims the content of information" absent an adequate functional relationship. *Praxair*, 890 F.3d at 1032 (quoting *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015)). "Claim limitations directed to the content of information and lacking a requisite

functional relationship are not entitled to patentable weight because such information is not patent eligible subject matter under 35 U.S.C. § 101." *Id.* (citing *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1064 (Fed. Cir. 2010)).

If a claim limitation is directed to printed matter, the next step in the *Praxair* analysis is to determine whether the printed matter is functionally related to its "substrate." *Praxair*, 890 F.3d at 1032. Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850). However, "[w]here the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." *Id.* (quoting *In re Ngai*, 367 F.3d 1336, 1339 (Fed. Cir. 2004)).

More specifically, printed matter is functionally related to its substrate when the language changes not mere thoughts or outcomes, but provides action steps that the method requires. *See C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1381 (Fed. Cir. 2020) (holding that the test for printed matter is whether it "merely informs people of the claimed information, or whether it instead interacts with the other elements of the claim to … cause a specific action in a claimed process."); *see also Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) (stating that language "is only a statement of purpose and intended result" where its "expression *does not result in a manipulative difference in the steps of the claim*") (emphasis added).

In the case presently before us, there is little question that the exclusion criteria are directed to informational content. Specifically, the limitation in question expressly states that the "exclusion criteria for the

patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks." This list of conditions relays direct information to the practitioner of the claimed method as to the nature of the exclusion criteria, much in the manner of the listing of contraindications included with the packaging of any other drug. The exclusion criteria are certainly analogous to elements of claim 1 in *Praxair*, in which a practitioner of the claimed "method of providing pharmaceutically acceptable nitric oxide gas" provided information [to the medical provider]:

> [T]hat, in patients with preexisting left ventricular dysfunction, inhaled nitric oxide may increase pulmonary capillary wedge pressure (PCWP), leading to pulmonary edema, the information of (ii) being sufficient to cause a medical provider considering inhaled nitric oxide treatment for a plurality of neonatal patients who (a) are suffering from a condition for which inhaled nitric oxide is indicated, and (b) have pre-existing left ventricular dysfunction, to elect to avoid treating one or more of the plurality of patients with inhaled nitric oxide in order to avoid putting the one or more patients at risk of pulmonary edema.

*Praxair*, 890 F.3d at 1028–29. These limitations of claim 1 of *Praxair* (quoted above) and the exclusion criteria of the present challenged claims both provide information to the practitioner of the respective claimed methods concerning criteria to assess risks that may be incurred when practicing the method with a patient.

With respect to the second step of the *Praxair* analysis, however, we do not find that the exclusion criteria of the challenged claims are functionally related to the rest of the claim. The claims do not expressly recite any positive step to be performed (or a negative step *not* to be performed) should a patient meet the exclusion criteria. Patent Owner

attempts to distinguish the challenged claims from those of *Praxair* by arguing that the latter claims "were expressly directed to 'providing information' or a 'recommendation'" to the medical provider, which the medical provider was free to ignore. *See* PO Resp. 22. However, an individual practicing the method of the challenged claims would be similarly free to ignore the conditions of the exclusionary criteria and still be practicing the claimed method.

To be clear, and contrary to Patent Owner's argument, there are no positive or negative limitations in the challenged claims that *require* a person of ordinary skill in the art to act or not act in a certain way to practice the recited steps of the claimed method. As such, the information provided by the exclusionary criteria can be considered to be optional information, in that there is no direction to the practitioner to perform, or not perform, any specific step based upon the provided criteria. Thus, the exclusionary criteria are strictly informational, without requiring the practitioner to act, or refrain from acting, in a specified manner, and not functionally related to the practice of the claimed method.

Furthermore, *Rapoport* does not support Patent Owner's case. In *Rapoport*, an appeal from an interference proceeding before the Board, our reviewing court held that the Board was correct in interpreting "treatment of sleep apneas" as being limited to treatment of the underlying sleep apnea disorder, i.e., reducing the frequency and severity of the apnea episodes during sleep, and not additionally to treatment of anxiety secondary to sleep apnea. *Rapoport*, 254 F.3d at 1059–60. The court found that Board was correct in interpreting the language of the '681 Specification as distinctly limiting the construction of the disputed claim terms to the treatment only of

sleep apneas and not to secondary symptoms, such as anxiety. *Id.* Such is not the case in the present *inter partes* review. Patent Owner is not trying to expand the pool of eligible patients to include those with additional, related conditions, but argues that, by listing the exclusion criteria, the '681 patent is requiring the practitioner to actively exclude a set of patients. But, as we explain below, the language of the challenged claims does not support Patent Owner's arguments that the claims expressly or even implicitly *require* any action on the part of the practitioner based upon the exclusion criteria.

Patent Owner's reliance upon *Jansen* is similarly unavailing. The question before the Federal Circuit in *Jansen* was whether a preamble reciting "[a] method for treatment of sleep apneas comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof to a patient in need of such treatment" was limiting upon the claim. *Jansen*, 342 F.3d at 1329, 1333–34. The court found that the preamble was limiting because it was "a statement of the intentional purpose for which the method must be performed." *Id.* The court did not find, as Patent Owner argues, that the preamble expressly limited the population of patients, or which patients should be excluded. *Id.*

In the present case, although the '681 Specification describes the use of the exclusion criteria in a clinical trial (Example 4), as we have explained, the exclusion criteria purportedly relate to the method of treatment, but propose no discrete manipulative difference in the steps by which the method, as practiced, should be altered by applying the exclusion criteria. *See Bristol-Myers*, 246 F.3d at 1376.

In the parallel district court proceedings, the district court, acknowledging our Institution Decision in the present *inter partes* review, arrived at the same conclusion with respect to essentially identical exclusion criteria limitations in Patent Owner's related '601 and '572 patents. Ex. 1112. Noting that the claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice," the district court found that:

> The language does not require any action step to be taken as a consequence. Nothing has "transform[ed] the process of taking the drug" aflibercept in the claimed method—the "actual method" found in the underlying independent claim, e.g., 2 mg of aflibercept, on the stated dosing schedule, remains the same.

*Id.* at 34–35 (citing *King Pharms., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010) (holding that when claim language did not change the underlying treatment method, it deserved no patentable weight).

The district court noted that, even under Patent Owner's "assess and exclude" approach, a patient either never starts the method (and hence the method doesn't change) or, if doctors screened for the information and found no infection or inflammation, the method proceeds as claimed. Ex. 1112, 35. The district court concluded that this confirms that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.*

The Board made a similar point at oral argument concerning the same exclusion criteria in the related IPR2022-01226[14]:

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[14] Oral arguments in both the present *inter partes* review and IPR2022-01225 were heard sequentially and before the same panel on October 25, 2023. *See* Hearing Tr. 1.

> MS. DURIE: Well, I think you're right that it is flipped sides of the same coin, but I think it is important that what the exclusion criteria do is say, you do not have this condition. And therefore, you are eligible for treatment and the steps of the method may proceed.
>
> It is no different from any other criteria that is used to determine patient eligibility. And there is an entire body of case law that says determining that patients are eligible for treatment can be something that has patentable weight.
>
> ….
>
> JUDGE NEW: I would flip that around and say, wait a minute. The exclusion criteria say to a patient: you are not eligible for this treatment. We are not going to treat you. And therefore, the practice of the method is irrelevant.
>
> MS. DURIE: I think that argument could be used with any criteria that is used to determine patient eligibility. I would say it determines that a patient is eligible by saying, you have been screened. You do not have any of these conditions. You have not had active infection in the last two weeks. Therefore, the treatment may proceed.

Hearing Tr. 64.

In the district court proceedings, the court continued:

> Claims that had an actual active step based on the exclusion criteria to be analogous to the Praxair claim 9 situation would ***require*** that patients lacking ocular inflammation or infection participate in a modified method (such as a different drug, dose, or schedule); or ***require*** ongoing treatment to stop—but that would only happen if inflammation or infection arises while the method is underway, and [Patent Owner] insists its exclusion criteria are directed to pre-screening before the method even starts.

Ex. 1112, 35 (emphases in original). The court concluded that because "there is no requirement to take new action [or to take no action] that flows from the 'wherein the exclusion criteria for a patient include…' information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight." *Id.* at 37. We agree.

As the district court recognized, we are not bound by its decision (nor it by ours) because "the PTAB properly may reach a different conclusion based on the same evidence," for the Board and the district courts function under different evidentiary standards and burdens of proof. *See* Ex. 1112, 34 (citing *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293–94 (Fed. Cir. 2017). However, as the Federal Circuit recognized, "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

Such is the case in this instance. We find that the exclusion criteria recite informational content that does not result in a manipulative difference in the steps of the claim, and are therefore not functionally related to the claim. We consequently conclude that the exclusion criteria of the challenged claims are not entitled to patentable weight under the printed matter doctrine.

*B. A Person of Ordinary Skill in the Art*

Petitioner contends that a person of ordinary skill in the art would have: (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field. Pet. 28. Petitioner asserts that such a

person would typically have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders, including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists. *Id.* at 28–29 (citing Ex. 1002 ¶¶ 27–29; Ex. 1003 ¶¶ 21–25).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Response. Because we find Petitioner's definition to be consistent with the level of skill in the art (*see, e.g.*, Exs. 1006, 1020), we adopt Petitioner's definition.

### *C. Ground 1: Anticipation under 35 U.S.C. § 102 of claims 1, 3–11, 13, 14, 16–24, and 26 by Dixon (Ex. 1006)*

Claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are challenged as unpatentable under 35 U.S.C. § 102 as being anticipated by Dixon. Pet. 48–52.

#### 1. Overview of Dixon

Dixon was published in October, 2009, and is prior art to the '681 patent. Ex. 1006, 1573. Dixon discloses that a new drug for the treatment of age-related macular degeneration ("AMD") is aflibercept ("VEGF Trap-Eye"), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2. *Id.* Abstr. Dixon discloses that VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD. *Id.*

Dixon discloses that, structurally, VEGF Trap-Eye is a fusion protein consisting of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment. Ex. 1006, 1575, Fig. 1. Dixon also discloses the PrONTO, CLEAR-IT-1, CLEAR-IT-2, and VIEW 1/VIEW 2 clinical trials. *Id.* at 1574–76, Ex. 1002 ¶ 74. Dixon identifies "[d]esirable attributes for emerging therapies for neovascular AMD include higher visual improvement rates and decreased dosing intervals" as a motivation for the "development of new drugs for neovascular AMD . . . focused on both improving efficacy and extending duration of action," Ex. 1006, 1574, 1577; Ex. 1002 ¶ 78.

Dixon further discloses results from the phase II clinical trial CLEAR-IT-2, which included four monthly doses (at weeks 0, 4, 8 and 12) followed by *pro re nata* ("PRN," "p.r.n.," or "prn") administration. Ex. 1006, 1576. Dixon reports that CLEAR-IT-2 subjects treated with that regimen exhibited mean improvement in visual acuity of nine letters and a mean decrease in retinal thickness of 143 μm. *Id.*; Ex. 1002 ¶¶ 79–80. Dixon further reports that "patients dosed at 2.0 mg during the initial monthly dosing period required 1.6 injections on average during the p.r.n. dosing phase." Ex. 1006, 1577. Dixon discloses that, in the CLEAR-IT-2 trial:

> Two groups received monthly doses of either 0.5 or 2.0 mg for 12 weeks (at weeks 0, 4, 8 and 12) and three groups received quarterly doses of either 0.5, 2.0 or 4.0 mg for 12 weeks (at weeks 0 and 12). Following this fixed dosing period, patients were treated with the same dose of VEGF Trap-Eye on a p.r.n. basis. Criteria for re-dosing included an increase in central retinal thickness of ≥ 100 μm by OCT, a loss of ≥ 5 ETDRS letters in conjunction with recurrent fluid by OCT, persistent fluid as indicated by OCT, new onset classic neovascularization, new or persistent leak on FA or new macular subretinal hemorrhage.

*Id.* at 1576. Dixon also discloses that "[p]atients initially treated with 2.0 or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) and 5.4 ($p < 0.085$) Early Treatment Diabetic Retinopathy Study ("ETDRS") letters with 29 and 19% gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." *Id.*

Dixon also describes the then-ongoing VIEW 1/VIEW 2 phase III clinical trials. Ex. 1006, 1576. Dixon discloses that, with respect to the VIEW 1 trial:

> This non-inferiority study will evaluate the safety and efficacy of intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses), compared with 0.5 mg of ranibizumab administered every 4 weeks. After the first year of the study, patients will enter a second year of p.r.n. dosing evaluation. The VIEW 2 study has a similar study design.

*Id.* (internal citations omitted).

2. Challenged independent claims 1 and 14

In the -00881 Decision, we determined that independent claims 1 and 14 of the '338 patent were unpatentable under 35 U.S.C. § 102 as anticipated by Dixon. For the convenience of the reader, we present a claim chart comparing independent claim 1 of the present challenged claims and claim 1 of the '338 patent in the -00881 Decision:

| **IPR2022-01225<br>US 10,130,681 B2<br>Claim 1** | **IPR2021-00881<br>US 9,254,338 B2<br>Claim 1 (unpatentable)** |
|---|---|
| 1. A method for treating an angiogenic eye disorder in a patient, | 1. A method for treating an angiogenic eye disorder in a patient, |

| | |
|---|---|
| said method comprising sequentially administering to the patient<br><br>a single initial dose of a VEGF antagonist,<br><br>followed by one or more secondary doses of the VEGF antagonist,<br><br>followed by one or more tertiary doses of the VEGF antagonist; | said method comprising sequentially administering to the patient<br><br>a single initial dose of a VEGF antagonist,<br><br>followed by one or more secondary doses of the VEGF antagonist,<br><br>followed by one or more tertiary doses of the VEGF antagonist; |
| wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and<br><br>wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose; | wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and<br><br>wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose; |
| wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component<br><br>comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2. | wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2. |

| | |
|---|---|
| wherein exclusion criteria for the patient include all of:<br>(1) active intraocular inflammation;<br>(2) active ocular or periocular infection;<br>(3) any ocular or periocular infection within the last 2 weeks. | |

As is evident from the chart above, challenged claim 1 of the present Petition and claim 1 of the '338 patent are identical, with the sole exception in the '681 patent of the additional limitation reciting the exclusion criteria. Similarly, challenged claim 14 of the present Petition and claim 14 of the '338 patent are identical, with the exception of the same exclusion criteria limitation added in the '681 patent.

Because, in the -00881 Decision, we concluded that claim 1 of the '338 patent is anticipated by Dixon, we incorporate here by reference our reasoning in the -00881 Decision with respect to the corresponding limitations of claim 1 of the '681 patent. *See* -00881 Decision, 26–46.

Briefly, in the -00881 Decision, we concluded that the preponderance of the evidence, including Dixon's express teaching that aflibercept and VEGF Trap-Eye have the "same molecular structure" demonstrated that Dixon inherently disclosed the claimed amino acid sequence of VEGF Trap-Eye (aflibercept). *See* Ex. 3001, 32–40. The Board found that the disclosures of Dixon, the prosecution history, and Patent Owner's own documents, demonstrated that aflibercept and VEGF Trap-Eye were the

same well-characterized single drug, rather than, as Patent Owner suggested, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye." *Id.* at 39.

Patent Owner makes essentially the same arguments in the present *inter partes* review (*see* PO Resp. 28–35) and, in view of the evidence of record, and our reasoning in the -00881 Decision, it fares no better than before. Of particular note is Patent Owner's argument that it's publications and Dixon, consistently refer to "VEGF Trap- Eye" as an ophthalmology drug and aflibercept as an oncology product. PO Resp. 35 (citing Ex. 2057 ¶¶ 39, 106–107; Ex. 2044, 101). Patent Owner points to Dr. Albini's testimony that it was "certainly possible" that a skilled artisan, reading Dixon could have concluded that VEGF Trap-Eye and aflibercept were different products. *Id.* (citing Ex. 2021, 342–343, 334–335). Patent Owner asserts that "this is fatal to Petitioner's inherency assertion." *Id.*

We disagree, and add that we addressed this issue extensively in the -00881 Decision. *See* Ex. 3001, 32–40. Dixon discloses that:

> VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure, but there are substantial differences between the preparation of the purified drug product and their formulations. Both aflibercept and VEGF Trap-Eye are manufactured in bioreactors from industry standard Chinese hamster ovary cells that overexpress the fusion protein. However, VEGF Trap-Eye undergoes further purification steps during manufacturing to minimize risk of irritation to the eye. VEGF Trap-Eye is also formulated with different buffers and at different concentrations (for buffers in common) suitable for the comfortable, non-irritating, direct injection into the eye.

Ex. 1006, 1575. Dixon thus teaches that the VEGF-antagonist, the active ingredient, in aflibercept and VEGF Trap-Eye are the same molecule (i.e., have the same molecular structure) but that the two medicaments are

thereafter formulated differently in that VEGF Trap undergoes further purification steps and uses different buffers appropriate for intraocular injection.

Furthermore, with respect to Dr. Albini's testimony as to whether a person of ordinary skill in the art "concluded that VEGF Trap-Eye and aflibercept were different products," Patent Owner mischaracterizes Dr. Albini's response:

> Q. Okay. Okay. So is it possible that the hypothetical person of ordinary skill in the art reading about a Phase 1 study of aflibercept, an oncology -- the oncology product in AMD and then separately a Phase 1 study of VEGF Trap-Eye in AMD may have reasonably concluded that these are different products?
>
> ….
>
> A. As I've already testified, I think it's certainly possible. But again, I think that a POSA would know that the molecule for treating eye disease that would be relevant to this patent would be the molecule in the CLEAR-IT-1 trial.

Ex. 2022, 342–343.

As Dr. Albini testifies, Dixon makes the distinction between the formulations containing the claimed VEGF receptor antagonist in terms of purification steps and buffers, but is clear on the point that the VEGF receptor antagonist in both formulations has the same molecular structure as that recited in the claims. *See also* Ex. 3001, 36–39 (concluding that Patent Owner's own documents demonstrate that VEGF Trap-Eye is its drug being used in the VIEW1 and VIEW 2 studies disclosed by Dixon).

Moreover, as Petitioner points out, Dixon also expressly discloses in its Abstract that "[o]ne promising new drug is aflibercept (VEGF Trap-Eye)," showing that persons of ordinary skill in the art knew VEGF Trap-

Eye and aflibercept, the molecular sequence of which was reported in the 2006 WHO index,[15] to refer to the same molecule as that recited in the challenged claims. (*See, e.g.*, Pet. 49; Ex. 1002 ¶¶ 83, 102, 152).

As we stated in the related IPR2021-00880, in which Patent Owner made the same arguments:

> Finally, as the above discussion and common sense strongly suggest, a drug that is reported in late Phase III clinical testing on human subjects is going to be a well-characterized single drug, rather than, as Patent Owner suggests, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye."

IPR2021-00880, Paper 89 at 58.

We incorporate by reference and adopt the reasoning of the -00881 Decision in the present case, and conclude that the preponderance of the evidence demonstrates that Dixon inherently discloses the "VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2," also known as aflibercept or VEGF Trap-Eye, as recited in challenged claims 1 and 4.

For the reasons explained in Section IV.A.3.d above, the exclusion criteria are entitled to no patentable weight. Because independent challenged claims 1 and 14 are otherwise identical to claims 1 and 14 of the '338 patent of the -00881 Decision, we conclude, for the same reasons set

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[15] "Aflibercept" in 20(2) WHO DRUG INFORMATION 118–19 (2006) (WHO index") (Ex. 1113).

forth in the -00881 Decision, that Petitioner has demonstrated, by a preponderance of the evidence, that challenged claims 1 and 14 of the '681 patent are unpatentable as being anticipated by Dixon.

3. Challenged dependent claims 3–11, 13, 16–24, and 26

Each of challenged claims 3–11, 13, 16–24, and 26 are identical to dependent claims 3–11, 13, 16–24, and 26 of the '338 patent, which were all found to be unpatentable as anticipated by Dixon in the -00881 Decision. *Compare* Ex. 1001, claims *with* IPR2021-00881, Ex. 1001, claims. Consequently, the only difference between these claims in the present *inter partes* review and the -00881 IPR is the incorporation of the exclusion criteria into the dependent claims from independent claims 1 or 14. *See Monsanto Co. v. Syngenta Seeds, Inc.*, 503 F.3d 1352, 1357 (Fed. Cir. 2007) (holding that "[a] claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers" (quoting 35 U.S.C § 112 ¶ 4 (2000))).

We have explained, in Section IV.A.3. above, why we conclude that the exclusion criteria are not accorded patentable weight. We therefore incorporate by reference and adopt the Board's reasoning and conclusions from the -00881 Decision with respect to the challenged claims in this *inter partes* review, and we conclude, for the same reasons, that Petitioner has shown, by a preponderance of the evidence, that dependent claims 3–11, 13, 16–24, and 26 of the '681 patent are anticipated by Dixon, and unpatentable. Furthermore, because we conclude that the challenged claims are unpatentable as anticipated by Dixon, we do not reach additional Grounds 2–6 of the Petition.

## V. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has demonstrated by a preponderance of the evidence, that challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are unpatentable as being anticipated by Dixon. Furthermore, Petitioner's Motion to Exclude Evidence is granted-in-part, denied-in-part and dismissed-in-part. Patent Owner's Motion to Exclude Evidence is denied-in-part and dismissed-in-part.

## VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that based on a preponderance of the evidence, claims 1, 3–11, 13, 14, 16–24 and 26 of the '681 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is granted in part, denied in part and dismissed in part; and

FURTHER ORDERED that Patent Owner's Motion to Exclude is denied in part and dismissed in part; and

FURTHER ORDERED that because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

| Claims | 35 U.S.C. § | References | Claims Shown Unpatentable[16] | Claims Not shown Unpatentable |
|---|---|---|---|---|
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Dixon | 1, 3–11, 13, 14, 16–24, 26 | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Adis | | |
| 1, 3–11, 13, 14, 16–24, 26 | 102 | Regeneron 2008 | | |
| 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon alone or in view of Papadopoulos and/or Wiegand | | |
| 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon in combination with Rosenfeld-2006, and if necessary, Papadopoulos patent and/or Wiegand | | |
| 1, 3–11, 13, 14, 16–24, 26 | 103 | Dixon in combination with Heimann- | | |

[16] As noted in Section III.A., we do not reach Petitioners' anticipation grounds based on Adis, Regeneron 2008, NCT-795, and NCT-377, or Petitioners' obviousness ground challenging claims 1, 3–11, 13, 14, 16–24 and 26 as we have determined that those claims are unpatentable based on the Dixon anticipation ground, as noted in the table.

| | | | | |
|---|---|---|---|---|
| | | 2007, and if necessary, Papadopoulos and/or Wiegand | | |
| **Overall Outcome** | | | 1, 3–11, 13, 14, 16–24, 26 | |

IPR2022-01225
Patent 10,130,681 B2

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# EXHIBIT 4

*Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*,
IPR2022-01226, Paper 101 (PTAB Jan. 9, 2024)

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Paper 101
Date: January 9, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

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IPR2022-01226[1]
Patent 10,888,601 B2

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Before JOHN G. NEW, SUSAN L. C. MITCHELL, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

# JUDGMENT
## Final Written Decision
## Denying in Part, Granting in Part, and Dismissing in Part Petitioner's Motion to Exclude Evidence, Denying in Part and Dismissing in Part Patent Owner's Motion to Exclude Evidence, Determining All Challenged Claims Unpatentable
*35 U.S.C. § 318(a)*

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[1] IPR2023-00533, *Celltrion, Inc. et al. v. Regeneron Pharms., Inc.*, and IPR2023-00566, *Samsung Bioepis Co., Ltd. v. Regeneron Pharms., Inc.*, have been joined with this *inter partes review*. *See* Papers 38, 39.

# I. INTRODUCTION

We have jurisdiction to hear this *inter partes* review under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioner Mylan Pharmaceuticals Inc. ("Petitioner") has established, by a preponderance of the evidence, that challenged claims 1–9, 34–39, 41–43, and 45 of Patent Owner Regeneron Pharmaceuticals, Inc.'s ("Patent Owner") U.S. Patent No. 10,888,601 B2 (Ex. 1001, the "'601 patent") are unpatentable. We also grant-in-part, deny-in-part, and dismiss-in part Petitioner's Motion to Exclude Evidence and deny-in part and dismiss-in-part Patent Owner's Motion to Exclude Evidence.

## *A. Procedural History*

On July 1, 2022, Petitioner filed its Petition (Paper 2, "Petition") seeking *inter partes* review of claims 1–9, 34–39, 41–43, and 45 of the '601 patent. Patent Owner timely filed a Preliminary Response. (Paper 13, "Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-Reply. Paper 17 ("Prelim. Reply"); Paper 19 ("Prelim. Sur-Reply"). On January 1, 2022, and pursuant to 35 U.S.C. § 314, we instituted *inter partes* review. Paper 22 ("Institution Decision" or "Dec.").

After institution of trial, Patent Owner filed a Response (Paper 44, "PO Resp."), to which Petitioner filed a Reply (Paper 60, "Pet. Reply"), and Patent Owner, in turn, filed a Sur-Reply (Paper 65, "PO Sur-Reply").

Both Petitioner (Paper 76) and Patent Owner (Paper 77) filed Motions to Exclude Evidence ("Pet. Mot. Exclude" and "PO Mot. Exclude,"

respectively) and filed Oppositions (Papers 82 and 80) to the opposing party's Motion to Exclude Evidence (respectively, "Pet. Opp. Mot. Exclude" and "PO Opp. Mot. Exclude"). Both parties also filed a Reply to their opponent's Opposition to their Motions to Exclude ("Pet. Reply Mot. Exclude," "PO Reply Mot. Exclude").[2] Paper 83, Paper 84.

## II. BACKGROUND

### *A. Real Parties-in-Interest*

Petitioner identifies Viatris Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, Johnson & Johnson, Biocon Biologics Inc., Biocon Limited, Biocon Biologics Limited, Biocon Biologics UK Limited, and Biosimilar Collaborations Ireland Limited as real parties-in-interest. Paper 99 at 2. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 97 at 2.

### *B. Related Matters*

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880, IPR2021-00881, IPR2022-01225 (PTAB), and *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.), as related matters. Paper 5, 2; Paper 6, 1. Patent Owner also identifies *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated before

[2] Papers 44, 60, and 76 of the record are the unredacted versions of these papers. Papers 45, 59, 78 are the respective redacted versions of record.

institution). Paper 5, 2–3. Petitioner further identifies the following as judicial or administrative matters that would affect, or be affected by, a decision in this proceeding: *Apotex Inc. v. Regeneron Pharmaceuticals, Inc.*, IPR2022-01524 (PTAB), *United States v. Regeneron Pharms., Inc.*, No. 1:20-cv-11217-FDS (D. Mass.), and *Horizon Healthcare Servs., Inc. v. Regeneron Pharms., Inc.*, No. 1:22-cv-10493-FDS (D. Mass.). Paper 6, 1–2.

Petitioner also identifies additional patents and patent applications that claim priority to the '601 patent, namely: US 9,254,338 B2; US 9,669,069 B2; US 10,857,205 B2; US 10,828,345 B2; US 10,130,681 B2; and US 11,253,572 B2; and US Appl. Ser. Nos. 17/072,417; 17/112,063; 17/112,404; 17/350,958; and 17/740,744. Paper 6, 2.

On March 22, 2023, this *inter partes* review was joined with IPR2023-00533, *Celltrion, Inc. v. Regeneron Pharms. Inc.* and IPR2023-00566, *Samsung Bioepis Co., Ltd.*, both of which also challenged claims 1–9, 34–39, 41–43, and 45 of the '601 patent. *See* Papers 38, 39. Petitioners in the joined *inter partes* reviews acted as "silent understudies" in the present proceeding, and did not participate actively in the present proceeding. A copy of this Final Written Decision will be entered in each of IPR2023-00532 and IPR2023-00566.

Of particular relevance to our decision in this proceeding is the Final Written Decision entered in IPR2021-00881 (the "-00881 IPR") on November 9, 2022. *See* IPR 2021-00881, Paper 94 (the "-00881 Decision," Ex. 3001). Both the '601 patent and US 9,254,338 B2 (the "'338 patent") at issue in IPR2021-00881 share a common specification. *Compare* Ex. 1001, *with* IPR2021-00881, Ex. 1001. In the -00881 Decision, the panel found that the challenged claims were unpatentable on at least one of the same

grounds asserted against the challenged claims in the present Petition. *See generally* Ex. 3001.

*C. The Asserted Grounds of Unpatentability*

Petitioner contends that claims 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable, based upon the following grounds:

| Ground | Claim(s) Challenged | 35 U.S.C. § | Reference(s)/Basis |
|---|---|---|---|
| 1 | 1–9, 34–39, 41–43, 45 | 102[3] | Dixon[4] |
| 1 | 1–9, 34–39, 41–43, 45 | 102 | Adis[5] |
| 3 | 1–9, 34–39, 41–43, 45 | 102 | Regeneron 2008[6] |

[3] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '601 patent issued has an effective filing date after that date, the AIA versions of §§ 102 and 103 apply.

[4] J.A. Dixon et al., *VEGF Trap-Eye for the Treatment of Neovascular Age-Related Macular Degeneration*, 18(10) EXPERT OPIN. INVESTIG. DRUGS 1573–80 (2009) ("Dixon") Ex. 1006.

[5] Adis R&D Profile, *Aflibercept: AVE 0005, AVE 005, AVE0005, VEGF Trap – Regeneron, VEGF Trap (R1R2), VEGF Trap-Eye*, 9(4) DRUGS R D 261–269 (2008) ("Adis") Ex. 1007.

[6] Press Release, *Regeneron and Bayer HealthCare Announce Encouraging 32-Week Follow-Up Results from a Phase 2 Study of VEGF Trap-Eye in Age-Related Macular Degeneration*, (April 28, 2008) ("Regeneron 2008") Ex. 1012.

| Ground | Claim(s) Challenged | 35 U.S.C. § | Reference(s)/Basis |
|---|---|---|---|
| 4 | 1–9, 34–39, 41–43, 45 | 102 | NCT-795[7] |
| 5 | 1–9, 34–39, 41–43, 45 | 103 | Dixon alone or in view of Papadopoulos[8] and/or Wiegand[9] |
| 6 | 1–9, 34–39, 41–43, 45 | 103 | Dixon in combination with Rosenfeld-2006[10], and if necessary, Papadopoulos patent and/or Wiegand |
| 7 | 1–9, 34–39, 41–43, 45 | 103 | Dixon in combination with Heimann-2007, and if necessary, Papadopoulos and/or Wiegand |

[7] ClinicalTrials.gov (archive), *Vascular Endothelial Growth Factor (VEGF)Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD) (VIEW1)*, *available at*: https://clinicaltrials.gov/ct2/history/NCT00509795?A=8&B=9&C=merged#StudyPageTop (last visited December 21, 2022) Ex. 1014.

[8] Papadopoulos et al. (US 7,374,758 B2, May 20, 2008) ("Papadopoulos") Ex. 1010.

[9] Wiegand et al. (US 7,531,173 B2, May 12, 2009) ("Wiegand") Ex. 1008.

[10] P.J. Rosenfeld et al., *Ranibizumab for Neovascular Age-Related Macular Degeneration*, 355 (14) N. ENGL. J. MED. 1419–31; Suppl. App'x 1–17 (2006) ("Rosenfeld") Ex. 1058.

Petitioner also relies upon the Declarations of Dr. Thomas A. Albini (the "Albini Declaration," Ex. 1002) and Dr. Mary Gerritsen (the "Gerritsen Declaration," Ex. 1003). Patent Owner relies upon the Declarations of Dr. Diana V. Do (the "Do Declaration," Ex. 2056), Dr. Alexander M. Klibanov (the "Klibanov Declaration," Ex. 2057), David M. Brown (the "Brown Declaration," Ex. 2055), and Dr. Richard Manning (the "Manning Declaration," Ex. 2059). We have reviewed the credentials of Petitioner's and Patent Owner's declarants, and consider each to be qualified to provide the opinions for which their testimony has been submitted.

*D. The '601 Patent*

The '601 patent is directed to methods for treating angiogenic eye disorders by sequentially administering multiple doses of a vascular epithelial growth factor ("VEGF") antagonist to a patient. Ex. 1001, Abstr. These methods include the administration of multiple doses of a VEGF antagonist to a patient at a frequency of once every 8 or more weeks, and are useful for the treatment of angiogenic eye disorders such as, *inter alia*, age related macular degeneration. *Id.*

In an exemplary embodiment, a single "initial dose" of VEGF antagonist ("VEGFT") is administered at the beginning of the treatment regimen (i.e., at "week 0"), two "secondary doses" are administered at weeks 4 and 8, respectively, and at least six "tertiary doses" are administered once every 8 weeks thereafter, i.e., at weeks 16, 24, 32, 40, 48, 56, etc.). Ex. 1001, cols. 2–3, ll. 63–2.

*E. Representative Claim*

Independent claim 34 is representative of the challenged claims, and recites:

> 34. A method for treating an angiogenic eye disorder in a patient in need thereof, said method comprising administering to the patient an effective sequential dosing regimen of a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
>
> wherein each secondary dose is administered 4 weeks after the immediately preceding dose; and
>
> wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component.

Ex. 1001, col. 24, ll. 4–19.[11]

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[11] For the purposes of this Decision, the terms "aflibercept" and "VEGF Trap-Eye" are used to refer to the same active VEGF antagonist that is recited in challenged claim 1 as "a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2." *See, e.g.*, Ex. 1006,

*F. Priority History of the '601 Patent*

The '601 patent issued from U.S. Application Ser. No. 16/397,267 (the "'267 application") filed on April 29, 2019, and claims the priority benefit of, *inter alia*, US Provisional Application Ser. No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

The claims of the '601 patent, including challenged claims 1–9, 34–39, 41–43, and 45 were allowed on November 12, 2020, and the patent issued on January 12, 2021. Ex. 1017, 5591; Ex. 1001, code (45).

## III. MOTIONS TO EXCLUDE EVIDENCE

Both parties have submitted Motions to Exclude Evidence (Papers 76, 77) and have also filed Oppositions (Papers 82, 80) and Replies (Papers 83, 84) to the opposing party's Motions to Exclude. We now consider each party's Motion to Exclude in turn.

*A. Petitioner's Motion to Exclude*

Petitioner moves to exclude Patent Owner's Exhibits 2037–2039, 2079, 2080, 2084, 2085, 2098, 2101, 2122, 2136, 2138–40, 2163, 2169, 2170, 2176, 2190, 2197, 2200, 2208, 2218, 2229, 2243, 2244, 2250, 2259, 2277–79, 2282–85, 2298, 2299, and portions of Exhibits 2055–57 and 2059. Pet. Mot. Exclude 1. We address each of Petitioner's arguments in turn.

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1575 ("VEGF Trap-Eye and aflibercept … have the same molecular structure").

1. Exhibits 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and portions of Exhibit 2059 (¶¶ 11, 28–29, 43, 47, 50–55, 60–61, 63–69, 72, 74–75, 78, 84, 108–09, 113–16, and attachments C1–C12, D1–D4, D7, and X2)

Petitioner argues that Patent Owner relies on the testimony of its expert, Dr. Manning, in support of its commercial success contentions. Pet. Mot. Exclude 1–2 (citing, e.g., PO Resp. 2, 41, 56–57; PO Sur-Reply 25–28). Petitioner asserts that Dr. Manning in turn relies on various documents purporting to reflect profit and loss statements for Patent Owner's product. *Id.* at 2 (citing Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and Ex. 2059 at Attachments C1–C12, D1–D4, D7, and X2 (collectively, the "Financial Exhibits")). Petitioner also argues for exclusion of portions of Dr. Manning's Declaration relating to this evidence, i.e., Ex. 2059 ¶¶ 11, 28–29, 43, 47, 50–55, 60–61, 63–69, 72, 74–75, 78, 84, 108–109, 113–116. *Id.* Petitioner states that it timely objected to the challenged Financial Exhibits. *Id.* (citing Papers 24, 49).

Petitioner seeks exclusion of the Financial Exhibits on the bases of: (1) FRE 1006 (compilations of sales data created for this proceeding, without production of the underlying business records); (2) FRE 901 (lack of authentication by a witness with personal knowledge); (3) FRE 801–03 (hearsay of records not within the business record exception); and FRE 702 (alleged unreliability of expert testimony). Pet. Mot. Exclude 2–5.

As Petitioner states, Patent Owner relies upon these Exhibits as objective secondary evidence of non-obviousness. *See, e.g.*, PO Resp. 55–57. However, and as we explain below, because we find that the challenged claims are anticipated by Dixon, we do not reach Patent Owner's arguments

that the claims are non-obvious (Grounds 5–7) or its contentions regarding secondary considerations of non-obviousness. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cor. 2008) (holding that "secondary considerations are not an element of a claim of anticipation"). Consequently, we dismiss Petitioner's motion to exclude the Financial Documents as moot.

2. Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, 2278, and portions of Exhibit 2059 (¶¶ 61, 73, 85, 88–94, 98, 99, 103)

Petitioner argues that Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278 (collectively, the "Marketing Exhibits") purport to be Patent Owner's supportive internal marketing materials and ATU survey data. Pet. Mot. Exclude 6. Petitioner contends that Patent Owner offers the Marketing Exhibits as evidence of the claimed methods commercial success and as secondary objective indicia of no-obviousness. Petitioner states that it timely objected to the challenged Marketing Exhibits. *Id.* (citing Papers 24, 49).

Petitioner urges us to exclude the Marketing Exhibits under FRE 403 because their probative value is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder.

As in Section III.A.1 above, we do not reach Patent Owner's arguments that the challenged claims are non-obvious (Grounds 5–7), because we conclude that they are anticipated by Dixon (Ground 1). *Cohesive Techs.*, 543 F.3d at 1364. We consequently dismiss Petitioner's motion to exclude the Marketing Exhibits as moot.

3. Exhibits 2079, 2080, 2084, and 2085

Petitioner argues that Exhibits 2079, 2080, 2084, and 2085 (the "Sequence Exhibits") are webpage printouts of the amino acid sequences of human VGFR1 and VEGFR2 that should be excluded under FRE 402 and FRE 403. Pet. Mot. Exclude 8. Petitioner contends that Patent Owner's expert, Dr. Klibanov, offers the Sequence Exhibits as evidence of variability in publicly available amino acid sequences of human VGFR1/2. *Id.* (citing, e.g., Ex. 2057 ¶¶ 76, 78, 79, 82, 86, and 87). Petitioner states that it timely objected to the Sequence Exhibits. *Id.* (citing Paper 48).

Petitioner argues that Exhibits 2079 and 2084 are webpage printouts dated February 28, 2023, that should be excluded as irrelevant non-prior art under FRE 402, and as unfairly prejudicial under FRE 403. Pet. Mot. Exclude 8–9. Petitioner asserts that Exhibits 2079 and 2084 indicate on their faces that they were both printed on February 28, 2023, twelve years after the alleged priority date of the challenged patent, and therefore have no bearing on the patentability of the challenged claims. *Id.* at 9. Petitioner also contends that Patent Owner fails to cite Exhibits 2079, 2080, 2084, and 2085 in its Preliminary Response, Response, or Sur-Reply, demonstrating that they do not have a tendency to make any fact of consequence more or less probable. *Id.* (citing *SK Innovation Co., Ltd. v. Celgard, LLC*, IPR2014-00679, Paper 58, 49 (PTAB September 25, 2015)).

Patent Owner responds that the data contained within the Sequence Exhibits antedates the priority date of the '601 patent, i.e., January 13, 2011. PO Opp. Mot. Exclude 8. Patent Owner asserts that Exhibits 2080 and 2085 indicate that they were publicly available as of January 11, 2011. *Id.* (citing Ex. 2080, 1; Ex. 2085, 1). Patent Owner argues that Exhibit 2079 provides

the same accession number or identifier, "P17948," and the same title, "VGFR1_HUMAN," and contains the same sequence information as Exhibit 2080, which Patent Owner asserts was publicly available before the priority date.. *Id.* (citing Ex. 2079, 9; Ex. 2080, 3). Patent Owner makes corresponding arguments for Exhibits 2084 and 2085. *Id.*

Petitioner disputes Patent Owner's contention that the information contained in Exhibits 2079 and 2084 was available, in the form of Exhibits 2080 and 2085, before the '601 patent's claimed priority date of January 13, 2011. Pet. Reply Mot. Exclude 3. Petitioner also contends that Exhibits 2079 and 2084 are duplicative of Exhibits 2080 and 2085 and should be excluded under FRE 403 as needlessly cumulative. *Id.* Furthermore, argues Petitioner, to the extent that they are not cumulative, they should be excluded because Patent Owner has provided no evidence that the information was available prior to January 13, 2011. *Id.* (citing *In re Lister*, 583 F.3d 1307, 1316 (Fed. Cir. 2009)).

Petitioner also asserts that, in arguing the relevance of the Sequence Exhibits, Patent Owner cites to a single sentence in the Response in which the four exhibits in question are among nine that are not themselves directly referenced, but merely cited in Dr. Klibanov's Declaration. Pet. Reply Mot. Exclude 4 (citing PO Resp. 27). Petitioner contends that, because this sentence is the only instance Patent Owner relies on for the Sequence Exhibits, they are not relevant to any issue before the Board and should be excluded under FRE 401 and 402. *Id.*

We are not persuaded by Petitioner's arguments. Exhibits 2079 and 2080 both identify the sequences for VGFR1 (accession no. P17948) presented in each as having the same accession number, P17948, and Exhibit

2080 expressly identifies the entry date of the sequence into the Uniprot protein sequence and functional information database as at least January 11, 2011, which antedates the claimed priority date of the '601 patent. Exhibit 2079 provides further identifying information of the sequence identified in the two Exhibits. The two Exhibits thus complement each other, each providing additional information about the other, and indicating an entry date of the sequence as prior to the priority date of the '601 patent. The same is true for Exhibits 2084 and 2085 with respect to VEGFR2 (accession no. P35968). Petitioner does not contest that the database was publicly available, and we conclude that the Exhibits are relevant prior art.

With respect to Petitioner's arguments that the Sequence Exhibits are unduly duplicative, we do not find that a pair of exhibits documenting the amino acid sequence of two proteins relevant to the claimed sequence is unduly cumulative, particularly given the complementary natures of Exhibit 2079 with Exhibit 2080, and Exhibit 2084 with Exhibit 2085. As to the extent of Patent Owner's reliance on the Sequence Exhibits, given the relevance of the Exhibits, we find this argument goes more to the weight of the evidence, rather than its admissibility. We consequently deny Petitioner's motion to exclude the Sequence Exhibits.

4. Exhibits 2098, 2101, 2122, 2298, and 2299

a. Exhibit 2098

Petitioner argues that Patent Owner does not cite Exhibit 2098 in its Preliminary Response, Response, or Sur-Reply, and that it is therefore not relevant to any contested issue in this proceeding. Pet. Mot. Exclude 9 (citing FRE 402). Petitioner also asserts that Exhibit 2098 is dated March

14, 2014, and Patent Owner filed it under seal. *Id.* at 10. As such, argues Petitioner, Exhibit 2098 was not publicly available prior art. *Id.* (citing *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1568–69 (Fed. Cir. 1988)).

Patent Owner responds that Exhibit 2098 was cited and relied on by Dr. Klibanov, Patent Owner's expert, and in Patent Owner's Response, through citation to the relevant paragraph of Dr. Klibanov's report. PO Opp. Mot. Exclude 9 (citing PO Resp. 39 (citing Ex. 2057 ¶ 120)). Patent Owner contends that it does not rely upon Exhibit 2098 as prior art, but rather to illustrate the inherent variability in the production of VEGF Trap-Eye, and that this variability was known in the prior art. *Id*. (citing PO Resp. 39–40 (citing Ex. 2057 ¶¶ 117–120); *see also id.* at 9 n.6 (citing Exs. 2096, 2097, 2099, 2100)).

We are not persuaded by Petitioner's argument that Exhibit 2098 should be excluded. Paragraphs 117–119 of the Klibanov Declaration are offered by Patent Owner to demonstrate that it was known in the prior art that synthesis of recombinant human proteins was known to be inherently variable. *See* Ex. 2057 ¶¶ 117–119 (citing e.g., Ex. 2096, 91; Ex. 2097, 4). Exhibit 2098, although not publicly-available prior art, is at least probative of the understanding of one of ordinary skill in the art and, in consequence, admissible. We therefore deny Petitioner's motion to exclude Exhibit 2098.

b. Exhibit 2101

Petitioner next urges us to exclude Exhibit 2101. Petitioner argues that Exhibit 2101, a non-public, internal, technical report, was not cited by Patent Owner in its Preliminary Response, Response, or Sur-Reply, and that

it is therefore not relevant to any contested issue in this proceeding under FRE 402. Pet. Mot. Exclude 10. Petitioner also argues that Exhibit 2101 should be excluded as irrelevant non-prior art. *Id.* (citing FRE 402).

Petitioner contends that Exhibit 2101 should also be excluded under FRE 801–803 as constituting inadmissible hearsay evidence. Pet. Mot. Exclude 10. According to Petitioner, Exhibit 2101 includes out-of-court statements of PO's in-house personnel, offered for the truth of the matters asserted therein. *Id.*

Patent Owner responds that it does not rely on Exhibit 2101 for its prior art teaching; rather, Patent Owner asserts, Exhibit 2101 illustrates the inherent variability in producing VEGF Trap-Eye, which was known in the prior art. PO Opp. Mot. Exclude 10 (citing Ex. 2057 ¶¶ 121–131; PO Resp. 39–40); *see, e.g.*, Ex. 2057 ¶ 119 (citing Ex. 2096, 91; Ex. 2097, 4).

Patent Owner also disputes Petitioner's assertion that Exhibit 2101 contains inadmissible hearsay evidence. PO Opp. Mot. Exclude 11. According to Patent Owner, Ms. Weber's Declaration testimony demonstrates that Exhibit 2101 falls within the business records exception to hearsay, as set forth in FRE 803(6): it is a scientific report, was stored on Regeneron servers, and bears facial indications of trustworthiness (written on Regeneron letterhead and dated and signed by Dr. Koehler-Stec, a study director and Regeneron employee). *Id.* (citing Ex. 2049, 24–26). Patent Owner notes that Petitioner does not challenge the foundation laid for the business records exception, and does not identify any condition of FRE 803(6) that has not been met. *Id.*

Patent Owner relies upon Exhibit 2049 (the purported testimony of "Ms. Weber") as authenticating Exhibit 2101 and demonstrating that it falls

within the business records exception. PO Opp. Mot. Exclude 11. However, there is no Exhibit 2049[12] entered into evidence in this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon.

Rule 803(6) allows business records to be admitted "if witnesses testify that the records are integrated into a company's records and relied upon in its day to day operations." *Air Land Forwarders, Inc. v. United States*, 172 F.3d 1338, 1342 (Fed. Cir. 1999) (quoting *Matter of Ollag Constr. Equip. Corp.*, 665 F.2d 43, 46 (2d Cir. 1981)). Absent any such authenticating witness foundation, we cannot conclude that Exhibit 2101 falls within the Business Records exception of FRE 803(6), and we grant Petitioner's motion to exclude Exhibit 2101 as containing inadmissible hearsay.

c. Exhibit 2122

Petitioner next argues that Exhibit 2122, a confidential (filed under seal), non-public excerpt of clinical study protocol VGFT-OD-0605, should be excluded under FRE 402, 403, and 802. *See* Pet. Mot. Exclude 11. Petitioner first argues that Exhibit 2122 is irrelevant non-prior art under FRE 402 and unfairly prejudicial under FRE 403. *Id.* Petitioner argues that Patent Owner's sealed filing of Exhibit 2122 confirms it was not publicly available, and therefore does not demonstrate a person of ordinary skill's

[12] Nor can we find a corresponding Exhibit 2049, or readily discern an exhibit that could reasonably be construed as providing the evidence of the missing Exhibit 2049, in the related IPR2022-01225, which was argued at the same item as the present *inter partes* review.

knowledge or a prior art teaching. *Id.* Petitioner contends that any probative value of the Exhibit is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder. *Id.*

Petitioner also argues that the reliance of Patent Owner's expert, Dr. Do, to assert as true the statements made in Exhibit 2122 constitutes impermissible hearsay evidence. Pet. Mot. Exclude 11–12 (citing Ex. 2056 ¶ 116).

Patent Owner argues, *inter alia*, that Ms. Weber's testimony makes clear that Exhibit 2122 falls within FRE 803(6), the business records exception to the rule against hearsay: it is a clinical study protocol, stored in Regeneron's regulatory archive, and bears facial indicia of trustworthiness (Regeneron protocol headers and file path information on each page). PO Opp. Mot. Exclude 12 (citing Ex. 2048 ¶ 3; Ex. 2049, 24–26).

Patent Owner again relies on an Exhibit (Ex. 2048) to support the assertion that Exhibit 2122 falls within the Business Records exception of FRE 803(6). Again, however, no such Exhibit 2048 or Exhibit 2049 is present in the record of this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon. *See Air Land*, 172 F.3d at 1342. In the absence of any such authentication, we consequently grant Petitioner's motion to exclude Exhibit 2122 as impermissible hearsay under FRE 803.

d. Exhibits 2298 and 2299

Petitioner next argues that Exhibit 2298, a confidential (filed under seal), non-public document alleged to be a clinical study agreement between Vitreoretinal Consultants and Patent Owner, should be excluded because

Patent Owner does not cite to Exhibit 2298 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–402. Pet. Mot. Exclude 12. Similarly, Petitioner contends that Exhibit 2299, a confidential (filed under seal), non-public compilation of the VIEW protocol signature pages, should be excluded because it was not publicly available, and does not represent a person of ordinary skill in the art's knowledge or a prior art teaching. *Id.* at 12–13. Petitioner also contends that Patent Owner also fails to cite Exhibit 2299 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–402. *Id.* at 13.

Petitioner additionally argues that Exhibit 2299 is inadmissible as hearsay evidence because the papers are out-of-court statements offered for the truth of the matter asserted, i.e., the alleged confidentiality restrictions in place as of July 2007 regarding VEGF Trap-Eye. Pet. Mot. Exclude 13.

Patent Owner responds that Dr. Brown relies on Exhibit 2298 in his Declaration, and that declaration paragraph is cited in Patent Owner's Response. PO Opp. Mot. Exclude 13 (citing PO Resp. 25 (citing Ex. 2055 ¶ 67)).

With respect to Exhibit 2299, Patent Owner contends that Dr. Brown's and Ms. Weber's testimony establish that Exhibit 2299 falls within FRE 803(6), the Business Records exception to the hearsay rule. PO Opp. Mot. Exclude 14. According to Patent Owner, the Exhibit was generated in the ordinary course of regularly conducted business activity (i.e., a clinical investigation), was stored by Regeneron in its regulatory archives and by Dr. Brown's practice at Iron Mountain, and bears facial indications of trustworthiness (dated signatures by Dr. Brown's partner on

every page), all as confirmed by individuals with knowledge. *Id.* (citing Ex. 1022, 62–63).

> In his Declaration, Dr. Brown testifies that:
>
> > [M]y institution, Vitreoretinal Consultants of Houston, signed a Clinical Study Agreement to conduct a clinical study entitled "A Randomized, Double Masked, Active Controlled Phase III Study of the Efficacy, Safety, and Tolerability of Repeated Doses of Intravitreal VEGF Trap in Subjects with Neovascular Age-Related Macular Degeneration" concerning Protocol number VGFT-OD-0605, which required my institution/practice to maintain information disclosed by Regeneron or generated as a result of the study in confidence and also limited our use of such information only for the purposes of the study. Ex. 2298 ¶ 6. In addition to the clinical study agreement, when our group/institution was provided the protocol for the VIEW trial, the document was clearly marked with a confidentiality legend and required that the clinical investigator sign the protocol and agree to be bound by its limitations on use and disclosure. Ex. 2299.

Ex. 2055 ¶ 67. Patent Owner relies upon this testimony as demonstrating that the amino acid sequence of VEGF Trap-Eye (the claimed SEQ ID NO:1 and SEQ ID NO:2) was not known to the artisan of ordinary skill, and that the clinical users of the drug were subject to confidentiality restrictions. *See* PO Resp. 25–26. As such, we find that the evidence adduced in these Exhibits is relevant to Patent Owner's arguments.

With respect to Petitioner's argument that Exhibit 2099 constitutes inadmissible hearsay evidence, and as we have explained above, we can find no evidence of an Exhibit 2048 or 2049, or of Ms. Weber's testimony, in Patent Owner's exhibits of record in this *inter partes* review. However, we find that the testimony of Dr. Brown is sufficient to authenticate the Exhibit and to establish that it falls within the Business Records exemption of FRE

803(6). Therefore, we find that Exhibits 2298 and 2299 are admissible. Petitioner's motion to exclude Exhibits 2298 and 2299 is consequently denied.

e. Portions of Exhibits 2055–57, and 2059

Finally, Petitioner argues that Patent Owner's expert declaration testimony corresponding to the Challenged Exhibits should also be excluded. Pet. Mot. Exclude 13–14 (citing *Wi-LAN Inc. v. Sharp Elecs. Corp.*, 992 F.3d 1366, 1374 (Fed. Cir. 2021)). Petitioner contends that Patent Owner has adduced no evidence that any of the challenged Exhibits are documents upon which a person of ordinary skill in the art would "reasonably rely" in forming an opinion on the subject matter at issue, thus warranting exclusion of portions of the declarations of Dr. Do (Ex. 2056 ¶ 116), Dr. Klibanov (Ex. 2057 ¶¶ 76, 78–79, 82, 86, 120–121, 123–128), Dr. Brown (Ex. 2055 ¶ 67), and Dr. Manning (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117). *Id.* at 14.

Patent Owner responds that Petitioner's motion fails to identify which declaration paragraphs correspond to which exhibits, or to explain how or why the experts' use of any particular exhibit is allegedly improper. PO Opp. Mot. Exclude 13. Patent Owner contends that Petitioner's assertions lack particularity and do not satisfy Petitioner's burden on a motion to exclude. *Id.* at 13–14.

Patent Owner also argues that Petitioner's original objections to evidence failed to identify the portions of the expert declarations that it now moves to exclude with any particularity, instead asserting only that the FRE 703 objection applies to each of Exhibits 2048, 2049, 2050, and 2052 in

their entirety. PO Opp. Mot. Exclude 14 (citing Pet. Mot. Exclude 3; and citing *Nippon Suisan Kaisha Ltd. v. Pronova Biopharma Norge AS*, PGR2017-00033, 2019 WL 237114, at *23–24 (PTAB Jan. 16, 2019).

As we explained above, we dismiss Petitioner's motion to exclude the Financial Exhibits and the Marketing Exhibits as moot. We consequently also dismiss, as similarly moot, Petitioner's motion to exclude Dr. Manning's related testimony. Ex. 2059 ¶¶ 11, 28–29, 43, 47–117.

Because we have denied Petitioner's motion to exclude the Sequence Exhibits, we also deny Petitioner's motion to exclude the related portions of Dr. Klibanov's testimony (Ex. 2057 ¶¶ 76, 78, 79, 82, and 86). Similarly, because we deny Petitioner's motion to exclude Exhibits 2098, we deny Petitioner's motion to exclude the related testimony of Dr. Klibanov with respect to that Exhibit (Ex. 2057 ¶ 120).

We have also explained why we deny Petitioner's motion to exclude Exhibit 2299. We therefore also deny Petitioner's motion to exclude the related foundational testimony of Dr. Brown (Ex. 2055 ¶ 67).

We grant Petitioner's motion to exclude the unauthenticated Exhibit 2101 as inadmissible hearsay evidence, as explained above. We therefore also exclude the related portions of Dr. Klibanov's testimony that rely upon that evidence relating to the Regeneron study (Ex. 2057 ¶¶ 123–128).

Finally, we also grant Petitioner's motion to exclude Exhibit 2122 under FRE 803. We therefore also exclude the related testimony of Dr. Do (Ex. 2056 ¶ 116).

5. Summary

For the reasons we have explained in the preceding sections, we dismiss as moot Petitioner's motion to exclude the Financial Exhibits (Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, and 2282–85) and Marketing Exhibits (Exs. 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278) as well as Dr. Manning's related testimony (Ex. 2059 ¶¶ 11, 28, 29, 43, 47–117).

We deny, for the reasons explained above, Petitioner's motion to exclude the Sequence Exhibits (Exs. 2079, 2080, 2084, and 2085) as well as Exhibits 2098, 2228, and 2229. We similarly deny Petitioner's motion to exclude the portions of Patent Owner's experts' testimony related to these Exhibits, *viz.*, that of Dr. Klibanov (Ex. 2057 ¶¶ 76, 78, 79, 82, 86, 120).

We grant Petitioner's motion to exclude Exhibits 2101 and 2122. We also grant Petitioner's motion to exclude the related portions of Dr. Klibanov's and Dr. Do's testimony relying upon those Exhibits (Ex. 2057 ¶¶ 123–128 and Ex. 2056 ¶ 116, respectively).

*B. Patent Owner's Motion to Exclude*

Patent Owner moves to exclude Exhibits 1058, 1009, 1015, 1020, 1087, 1108, 1167, 1124, 1150, and 1151 and related portions of Exhibits 1002, 1003, 1107, and 1115. PO Mot. Exclude 1, 10. We consider each of Patent Owner's arguments in turn.

1. Ex. 1058

Patent Owner argues that Exhibit 1058 should be excluded as evidence. PO Mot. Exclude 2. Exhibit 1058 (Rosenfeld) forms a partial

basis for Petitioner's Ground 5 contentions that the challenged claims are unpatentable as being obvious over the cited prior art. *See* Pet. 12.

Patent Owner argues that Exhibit 1058 is not authenticated and irrelevant under FRE 401–403, 802, and 901. PO Mot. Exclude 2–9.

As we explain below, we conclude that the challenged claims in this *inter partes* review are anticipated by Dixon and therefore unpatentable (Ground 1). Because we reach this conclusion, we do not reach Petitioner's contentions that the claims are obvious on the basis of Ground 5. Nor does our analysis rely upon, or cite to, Exhibit 1058. We consequently dismiss as moot Patent Owner's motion to exclude Exhibit 1058.

2. Exhibits 1009, 1015, 1020, 1087, 1108, 1167, and related portions of Exhibits 1002, 1003, 1107, and 1115

Patent Owner next urges us to exclude Exhibits 1009, 1015, 1020, 1087, 1108, and 1167 on the basis that none of these Exhibits were cited in the Petition or the Petitioner's Reply. PO Mot. Exclude 9. Similarly, Patent Owner seeks to exclude the related portions of Petitioner's expert testimony not cited in the pleadings:

(i) Ex. 1002 ¶¶ 30–47, 53–63, 65–68, 70–71, 75–82, 87–92, 98–99, 112, 114, 119, 121, 123, 130–133, 138–140, 142, 161, 164–66, 170–171, 173–174, 177–178, 180, 209–215, 225, 249–255, 285–291, 344–345, and 352–353;

(ii) Ex. 1003 ¶¶ 31–41;

(iii) Ex. 1107 ¶¶ 6–64, 66–71, 79–86, 92–93, 101, and 102–127;

(iv) Ex. 1115 ¶¶ 28–59.

*Id.* at 10, 15. Patent Owner states that it timely objected to each of these uncited exhibits and expert declaration paragraphs. *Id.* Patent Owner

contends that these uncited exhibits and testimony were not relied upon by Petitioner and should therefore be excluded as irrelevant. *Id.*

Petitioner responds that Patent Owner's contention that multiple portions of at least Exhibits 1002, 1107, and 1115 "were not cited in the pleadings" is inaccurate. Pet. Opp. Mot. Exclude 8–9 (quoting PO Mot. Exclude 10). Petitioner asserts that its Reply does in fact rely upon at least paragraph 73 of Exhibit 1002 to rebut Regeneron's assertion of "great uncertainty" regarding extended dosing in clinical practice prior to 2010. *Id.* at 9 (citing Pet. Reply 60, 22). Petitioner also contends that its Reply further relies on at least paragraphs 14–44, 51–57, and 102–126 of Exhibit 1107 to explain: (1) alleged shortcomings of the intrinsic record; (2) Patent Owner's representations to the U.S. Patent and Trademark Office; (3) the realities of the VIEW clinical trials; and (4) secondary consideration of non-obviousness analyses. *Id.* (citing Pet. Reply 5, 8, 23, 25, 8, 11). Petitioner argues that its Reply also relies on paragraphs 28–59 of Exhibit 1115 in its blocking patent discussion. *Id.* (citing Pet. Reply 23).

Petitioner additionally argues that the identified exhibits and expert testimony are a matter of public record, and the Board may have reason to consult any of these exhibits or take public notice of them. Pet. Opp. Mot. Exclude 9. Petitioner notes that Patent Owner has provided no legitimate justification for excluding this evidence altogether at this time. Petitioner argues that the Board can, in its discretion, assign weight to the evidence as appropriate, and as it has done in prior IPRs. *Id.* (citing, e.g., *Square, Inc. v. 4361423 Canada Inc.*, IPR2019-01649, Paper 43, 32–33 (PTAB Apr. 22, 2021).

Patent Owner replies that Petitioner does not deny that Exhibits 1009, 1015, 1020, 1087, 1108, and 1167 and the challenged portions of Exhibits 1002, 1003, 1107, and 1115 not cited by Petitioner in its Opposition were not relied upon in any of its pleadings. Patent Owner contends that these Exhibits and portions of Exhibits should be excluded as being of no consequence in determining the outcome of the proceeding. PO Reply Mot. Exclude 3–4 (citing *One World Techs., Inc. v. Chamberlain Grp., Inc.*, IPR2017-00126, Paper 56 at 16 (PTAB Oct. 24, 2018)).

We do not find Patent Owner's argument persuasive. To the extent that the challenged Exhibits and testimony are relied upon in this Final Written Decision, the Board is capable of assigning to them appropriate probative weight. *See, e.g.*, *Square*, IPR2019-01649, Paper 43, 32–33. Moreover, Patent Owner alleges no prejudice by the inclusion of these Exhibits and testimony in the record of this *inter partes* review. Because Board proceedings favor inclusion in the public record, and because Patent Owner alleges no potential prejudice from inclusion of this evidence in the record, we deny Patent Owner's motion to exclude Exhibits 1009, 1015, 1020, 1087, 1108, and 1167, and the challenged paragraphs of Exhibits 1102, 1103, 1107, and 1115.

3. Exhibits 1124, 1150, and 1151

Patent Owner next seeks to exclude Exhibits 1124, 1150, and 1151. PO Mot. Exclude 14. These Exhibits consist of complaints and exhibits filed by the U.S. Department of Justice and Horizon Healthcare Services, Inc. against Patent Owner and were introduced by Petitioner to impeach the credibility of Patent Owner's commercial success expert, Dr. Manning. *See*

Pet. Opp. Mot. Exclude 10–11. Patent Owner contends that these Exhibits are irrelevant, prejudicial, and inadmissible hearsay evidence under FRE 403 and FRE 803–804, and 807. PO Mot. Exclude 11–14.

Dr. Manning's testimony relates to the commercial success of the compound recited in the challenged claims as secondary objective evidence of non-obviousness. As we explained above, we conclude in this Final Written Decision is anticipated by Dixon (Ground 1) and we do not reach Petitioner's obviousness Grounds 5–7. We therefore do not rely upon Dr. Manning's testimony as to objective indicia of nonobviousness. Nor does our analysis rely upon, or cite to, the Exhibits challenged by Patent Owner. *Cohesive Techs.*, 543 F.3d at 1364. Consequently, we dismiss as moot Patent Owner's motion to exclude Exhibits 1124, 1150, and 1151.

f. Summary

For the reasons set forth above, we dismiss Patent Owner's motion to exclude Exhibits 1058, 1124, 1150, and 1151. We deny Patent Owner's motion to exclude Exhibits 1009, 1015, 1020, 1087, 1108, and 1167, and the related portions of Exhibits 1002, 1003, 1107, and 1115 cited by Patent Owner.

## IV. ANALYSIS

### *A. Claim Construction*

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of

ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Petitioner initially argues that the language of the preamble reciting "a method for treating" is not limiting upon the claims. Pet. 15–22. Petitioner also argues that the limitation reciting "wherein exclusion criteria for the patient include all of…." (the "exclusion criteria") of claims 9 and 36 are not entitled to patentable weight under the printed matter doctrine. *Id.* at 23–25. Petitioner, it its Reply Brief, further argues that the limitations of claims 5 and 6 establishing Best Corrected Visual Acuity ("BCVA") performance criteria also lack patentable weight. Pet. Reply 11–12. Finally, Petitioner additionally proposes constructions for the claim terms "initial dose," "secondary dose," and "tertiary dose." Pet. 22–23.

Patent Owner argues that: (1) the challenged claims require effective treatment; and (2) the exclusion criteria recited in challenged claims 9 and 36 are limiting upon the claims. PO Resp. 8–23. Patent Owner also challenges Petitioner contention that the limitations establishing BCVA criteria lack patentable weight. PO Sur-Reply 10–13.

On October 27, 2023, subsequent to oral argument, the Board authorized additional briefing by the parties on their proposed claim construction of the claim term "effective sequential dosing regimen," as recited in challenged claim 34. Both parties filed their proposed constructions ("Pet. CC" and "PO CC", Papers 94, 93) and Oppositions to the opposing party's construction ("Pet. CC Opp." and "PO CC Opp.", Papers 95, 96).

We address each of the parties' arguments in turn.

1. Construction of "effective amount" in the preambles of claims 1 and 10 and "effective sequential dosing regimen" in the preamble of claim 34)

a. Petitioner's arguments

Petitioner argues the preamble is not limiting upon the claims. Pet. 15–16. Petitioner argues that: (1) the preamble is merely a statement of intended purpose and, therefore, not a limitation; and (2) the preamble provides no antecedent basis for any other claim element. *Id.* at 15–16, 18. Alternatively, argues Petitioner, if the preamble is limiting, it should be given its plain and ordinary meaning, which does not require any specific efficacy requirement. *Id.* at 18–22.

b. Patent Owner's Response

Patent Owner acknowledges the Board's finding in its Institution Decision that the preamble of the challenged claims require "treating an angiogenic eye disorder in a patient." PO Resp. 9–10 (citing Dec. 10; also citing Ex. 2056 ¶ 81). Patent Owner contends that the challenged claims further require that the "method for treating" actually be effective, asserting

that challenged claims 1, 2 and 5–9 expressly state that the claimed method requires administering an "effective amount of aflibercept which is 2 mg" for the treatment of wet AMD. *Id.* at 10 (citing Ex. 1001, col. 21, ll. 43–44, 47–48, 55–67; Ex. 2056 ¶¶ 83, 85). Patent Owner asserts that claims 34–39, 41–43, and 45 of the '601 patent similarly state that the claimed method requires administering an "effective sequential dosing regimen" for treatment of an angiogenic eye disorder. *Id.* (citing Ex. 1001, col. 24, ll. 6, 20–32, 35–43, 46–47); Ex. 2056 ¶¶ 84–85).

Patent Owner points to the Board's Final Written Decision in the related -00881 IPR, in which the Board recognized that including efficacy language, e.g., "effective amount," in the body of the claims signals that the method must actually be effective (i.e., result in a beneficial effect) in a given patient. PO Resp. 10 (citing Ex. 3001, 20). According to Patent Owner, the language "effective sequential dosing regimen" in claim 34 and its dependents signals the same. *Id.* at 10–11. Patent Owner therefore asserts that, contrary to Petitioner's assertion, administration of aflibercept in the claimed doses and frequency is not sufficient to practice the claimed method. *Id.* at 11. Rather, argues Patent Owner, the challenged claims expressly require that the patient receive effective treatment. *Id.* (citing Pet. 61 n.10; Ex. 2056 ¶¶ 82–85).

Patent Owner asserts that the '601 Specification confirms that effective treatment of an angiogenic eye disorder is the essence of the claimed invention. PO Resp. 11 (citing Ex. 1001, col. 1, ll. 25–27, also citing *id.* at col. 2, ll. 3–5, 29–30, col. 7, ll. 27–30). Patent Owner notes that the '601 Specification also discloses that the inventor "surprisingly discovered that beneficial therapeutic effects can be achieved" with the

claimed method. *Id.* (quoting Ex. 1001, col. 2, ll. 11–17; also citing Ex. 2056 ¶¶ 86–87). Patent Owner argues that a critical aspect of the invention is efficacy is further confirmed by the Specification's disclosure that there was a need in the art for "efficac[ious]" extended dosing regimens, immediately following the Specification's reference to a prior unsuccessful trial in which extended dosing of Lucentis was not effective. *Id.* (citing Ex. 1001, col. 1, ll. 61–67; Ex. 2024). Patent Owner therefore argues that a person of ordinary skill in the art, reading the claims recital of "effective" treatment, in view of the Specification, would understand the claims to require such effective treatment. *Id.* at 12 (citing Ex. 2056 ¶¶ 81–87).[13]

c. Petitioner's Reply and Patent Owner's Sur-Reply

Petitioner replies that Patent Owner's proposed "effectively treating" construction would require, as concluded by the -00881 Decision, "improperly importing limitations into the claims." Pet. Reply 3 (quoting Ex. 3001, 22). Petitioner contends that Patent Owner does not dispute that efficacy is not literally written in the claims. *Id.* Petitioner points out that the '601 Specification nowhere defines or guides how a skilled artisan should ascertain, measure, or differentiate "effectively treating." *Id.* Nor, argues Petitioner, does Patent Owner proffer an actual construction in its Response. *Id.*

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[13] Patent Owner also rebuts Petitioner's allegations that Patent Owner's proposed construction poses "enablement, written description, and definiteness problems" for the challenged claims. PO Resp. 12–15. We need not reach either Petitioner's or Patent Owner's response in this respect to arrive at an appropriate claim construction.

Petitioner responds that, in the -00881 Decision, the Board recognized that "including efficacy language, e.g., 'effective amount,' in the body of the claims…signals that the method must actually be effective." Pet. Reply 3 (citing Ex. 3001, 20) (alteration in original). However, Petitioner notes, the Board made clear that it was not suggesting "any categorical rule regarding a requirement for therapeutic effectiveness based upon the inclusion or omission of that claim phrase alone." *Id.* (quoting Ex. 3001, 20 n.11).

Petitioner contends that, during prosecution of the '601 patent, Patent Owner and its experts proposed claim construction of "effectively treating" as meaning "noninferior," "statistically noninferior," or "comparable." Pet. Reply 4. Petitioner asserts that Patent Owner, and its expert, Dr. Do, advance the proposed construction of "effectively treating, " with no explanation for what that means, or how it comports with the challenged dependent claims that recite visual acuity limitations ranging from losing less than 15 letters to gaining more than 15 letters. *Id.* at 4–5.

Petitioner also argues that Patent Owner's two experts, Dr. Do and Dr. Brown, offer contradictory testimony as to which patients received the claimed method of treatment: Dr. Do testified that "the 5.6 percent of patients who lost 15 or more letters on the 2Q8 arm, they did not practice the claimed method of treatment because they did not achieve and maintain a high level of efficacy comparable to that seen with Lucentis [i.e., ranibizumab]." Pet. Reply 5 (quoting Ex. 1109, 97) (alteration in original). But, argues Petitioner, Dr. Brown, when asked whether patients in the VEGF Trap-Eye 8-week dosing arm received treatment that was "non-inferior to ranibizumab," testified that "everyone in the cohort met non-inferiority." *Id.* (citing Ex. 1110, 52).

Petitioner asserts that Dr. Do's opinion that "effective" treatment means "far more than the mere loss of 15 or fewer letters" also contradicts the intrinsic record. Pet. Reply 5 (quoting Ex. 2056 ¶ 79). Petitioner points out that challenged dependent claim 3 recites a method for treating "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score." *Id.* (citing Ex. 1001, claim 3). Petitioner argues that the scope of Claim 1 must therefore include cases "wherein the patient loses less than 15 letters" as "effective treatment." *Id.* at 6. Petitioner contends that the Board should discount Dr. Do's testimony because it "is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history." *Id.* (quoting *Phillips*, 415 F.3d at 1318; and citing (Ex. 1107 ¶¶ 11–30, 45–48).

Patent Owner responds that, contrary to Petitioner's position, the preamble is limiting and requires efficacy. PO Sur-Reply 2. Patent Owner asserts that every challenged claim expressly requires effective treatment and thus disputes Petitioner's assertion that "efficacy is not literally written in the claims." *Id.* (quoting Pet. Reply 3). According to Patent Owner, the evidence of record shows that, as of 2011, a skilled artisan would have understood "effective treatment" to mean treatment comparable to or on par with standard-of-care, i.e., monthly Lucentis or Avastin. *Id.* at 2 (citing PO Resp. 11–12).

Patent Owner points to Petitioner's expert, Dr. Albini's testimony that his pre-2011 treatment goal for patients with angiogenic eye disorders was aligned with PO's construction:

> Q: [W]ithin a given patient, you would hope that your PRN [as-needed] dosing of that patient got them efficacy that

was as good as they personally would get with monthly dosing of Lucentis; is that right?

A: That's correct.

PO Sur-Reply 3 (quoting Ex. 2347, 127) (alterations in original). Patent Owner contends that this meant visual acuity gains, not losses, and not merely achieving the clinical trial endpoint of loss of ≤ 15 letters on ETDRS. *Id.* (citing PO Resp. 3–4; Ex. 2056 ¶¶ 78–79). Patent Owner therefore asserts that its construction does not require "importing limitations into the claims." *Id.* at 4.

Patent Owner accuses Petitioner of ignoring the claim term "effective," rather than proposing a claim term for it. PO Sur-Reply 4 (citing Pet. Reply 2–3). Patent Owner contends that Petitioner's reliance upon the Board's claim construction ruling in IPR2021-00881 similarly disregards the differences between the language of the respective claims. *Id.* (citing, e.g., *Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) ("holding that "[i]t is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous")).

Patent Owner also disputes Petitioner's contention that Patent Owner's construction is "contradictory". PO Sur-Reply 4 (citing Pet. Reply 3–5). Patent Owner contends that Petitioner conflates expert testimony concerning randomized clinical trials conducted on a population basis (and their population-based outcome measures) with testimony concerning treatment of individual patients. *Id.* at 4–5. Patent Owner argues that it is undisputed between the parties that the challenged claims are directed to treating "a patient." *Id.* at 5 (citing Ex. 1107 ¶ 40) (emphasis omitted). According to Patent Owner, both parties' experts agree that a person of

ordinary skill in the art would not use statistical non-inferiority or clinical-trial-based outcome measures when assessing individual-patient efficacy. *Id.* (citing Ex. 2347, 127). Patent Owner also contends that both parties' experts agree that those of ordinary skill in the art would have understood effective treatment to mean treatment on par with monthly administration of Lucentis (or Avastin). *Id.* (citing Ex. 2347, 127).

Patent Owner argues further that its expert, Dr. Do, explained that the colloquial use of the term "non-inferior" in connection with an individual patient means "comparable to," or "on par with" treatment with monthly Lucentis or Avastin. PO Sur-Reply 5 (citing Ex. 1109, 15–16, 22–24, 24–30, 34, 42; Ex. 2056 ¶ 78). Patent Owner notes that Dr. Brown agreed with Dr. Do's construction, and also agreed that one does not measure statistical non-inferiority when treating an individual patient. *Id.* at 5–6 (citing Ex. 2055 ¶¶ 104–105; Ex. 1110, 50). Patent Owner also notes that Dr. Albini also agreed that clinicians using anti-VEGF agents pre-2011 sought efficacy "as good as" what the patient would achieve with monthly Lucentis. *Id.* at 6 (citing Ex. 2347, 127).

Patent Owner argues that its construction is consistent with the intrinsic record. PO Sur-Reply 6. According to Patent Owner, Petitioner quotes from the prosecution history of the '601 patent, but omits that Patent Owner highlighted vision gains achieved with Q8 dosing. *Id.* (citing Pet. Reply 4; Ex. 2331, 290).

d. Related argument regarding "administering to the patient an effective sequential dosing regimen"

Relatedly, and subsequent to hearing oral argument in this *inter partes* review, the Board invited the parties to submit additional briefing upon their proposed construction of the claim term "effective sequential dosing regimen," as recited in challenged claim 34. Paper 91. As authorized, both parties submitted briefs (respectively "Pet. CC" (Paper 94) and "PO CC" (Paper 93)) as well as Oppositions to the opposing party's brief (respectively "Pet. CC Opp." (Paper 95) and "PO CC Opp." (Paper 96)). We now turn to these arguments.

e. Petitioner's and Patent Owner's claim constructions

Petitioner points to its Petition, which states that claim 34 defines "an effective sequential dosing regimen as [the regimen] having the recited steps." Pet. CC 1 (citing Pet. 53 n.8, 61 n.10) (alteration in original). Petitioner argues that the steps follow the framework of "a single initial dose … followed by one or more secondary doses … followed by one or more tertiary doses," and that the '601 Specification ties this regimen to efficacy. *Id.* (alterations in original). Petitioner asserts that Patent Owner's proposed construction improperly relies on extrinsic evidence to rewrite claim 34 as requiring "effective treatment" to import a "standard-of-care, *i.e.,* monthly Lucentis or Avastin" claim meaning, which contradicts the intrinsic evidence. *Id.* (citing PO Resp. 3; Ex. 1002 ¶¶ 52, 153).

Petitioner points to the testimony of Dr. Albini, who opined that "no particular level of efficacy is required by any of the covered methods for treating." Pet. CC 1 (quoting Ex. 1107 ¶ 13). Rather, stated Dr. Albini, the goal is "inhibiting the angiogenic-promoting properties of VEGF." *Id.* at 1–

2 (citing Ex. 1107 ¶ 109). Petitioner notes that the '601 Specification calls this "an effective strategy for treating angiogenic eye disorders," discloses a wide range of clinical outcomes. *Id.* at 2 (quoting Ex. 1001, col. 1, ll. 54–56, Table 1, Table 2; also citing Ex. 1018, 2542).

Petitioner argues that, just as challenged claim 1 recites administering with an "effective amount" of the drug, defining the dose with the phrase "which is," claim 34 recites an "effective sequential dosing regimen of" drug doses, defining that regimen by what follows after "of." Pet. CC 2 (quoting Ex. 1001, claim 1, claim 34). According to Petitioner, challenged claim 34's dependent claims confirm that the manipulative steps in the "effective" regimen sequence framework (initial, secondary, tertiary) never change based on clinical outcomes or standards. *Id.* Rather, argues Petitioner, those claims narrowly define the types of doses administered. *Id.* (citing Ex. 1001, claim 35, claim 38, claim 41).

Petitioner points to Dr. Do's testimony to illustrate why an "effective … regimen" requires only this framework. Pet. CC 2. Petitioner states that when Dr. Do applied the "effective sequential dosing regimen" to claim that Eylea satisfied this element, she offered no proof of clinical performance—only the existence of the regimen steps. *Id.* (citing Ex. 2056 ¶ 135). Petitioner asserts that neither Dr. Do nor Dr. Brown could consistently delineate how or when a patient was in an "ineffective" regimen versus one with a "high level of efficacy," that was noninferior to the "standard of care," which was "Lucentis or Avastin," which undermines Patent Owner's proposed construction. *Id.* at 2–3 (citing Ex. 1109, 104–110, 121–126; Ex. 1110, 39; Ex. 2036, 81).

Petitioner contends that the '601 Specification states that the alleged need that the "present invention" purportedly solved was the regimen. Pet. CC 3 (citing Ex. 1001, col. 1, ll. 64–67 ("there remains a need in the art for new administration regimens for angiogenic eye disorders, especially those which allow for less frequent dosing while maintaining a high level of efficacy"); also citing *id.* at col. 1, ll. 64–67; col. 4, ll. 48–50, col. 3, ll. 30–41, col. 2, ll. 1–31, col. 3, ll. 42–44). Petitioner argues that, in define a "therapeutically effective" amount, the Specification broadly included doses that produced any "detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder," or "inhibits, prevents, lessens, or delays the progression of an angiogenic eye disorder." *Id.* at 3–4 (citing Ex. 1001, col. 6, ll. 60–65).

Petitioner contends that the '601 Specification's more general discussion of efficacy also does not impose thresholds on par with Lucentis or Avastin, or employs the phrase "standard of care." Pet. CC 4 (citing Ex. 1001, col. 7, ll. 26–43). Rather, the Specification discloses that "[g]enerally, the methods of the present invention demonstrate efficacy within 104 weeks of the initiation of the treatment regimen," with "efficacy" arising when, "from the initiation of treatment, the patient exhibits a loss of 15 or fewer letters on the" ETDRS visual acuity chart. *Id.* (citing Ex. 1001, col. 7, ll. 30–40). Petitioner also notes that the Specification describes gains of one or more letters from initiating treatment as "embodiments" of the invention. *Id.* (citing Ex. 1001, col. 7, ll. 40–43).

Petitioner argues that none of these outcomes or benefits measured according to metrics found in the Examples warrant exclusion from the meaning of an "effective … regimen," or even Patent Owner's "effective

treatment" alternative. Pet. CC 4. Petitioner contends that this is especially so when, as Dr. Albini explained, the Specification proposes that "'beneficial therapeutic effects can be achieved in patients suffering from angiogenic eye disorders by administering a VEGF antagonist,' and not that such effects must be achieved." *Id.* (citing Ex. 1002 ¶ 48 (quoting Ex. 1001, col. 2, ll. 11–17)).

Petitioner notes that Patent Owner relies upon Example 4 and the Specification's "high level of efficacy" language to try to justify importing its standard-of-care meaning. Pet. CC 4. Petitioner asserts that the latter phrase appears after "especially those…," signaling that high efficacy is a desirable embodiment, not the entire invention. *Id.* at 4–5 (citing Ex. 1001, col. 1, ll. 64–67). However, argues Petitioner, the Specification expressly warns that the claims' scope is limited "only by the appended claims," not the embodiments disclosed. *Id.* at 5 (quoting Ex. 1001, col. 3, ll. 9–13).

Finally, Petitioner argues that, during prosecution of this patent family, Patent Owner called Heier-2012's[14] results "unexpected." Pet. CC 5 (citing PO Resp. 55 n.21 (citing Ex. 2331, 288–91)). According to Petitioner, Heier-2012's primary efficacy metric was the comparative percentage of patients losing < 15 letters compared to ranibizumab, which Dr. Do allegedly insisted is not the standard of care. *Id.* (citing Ex. 1018, 2542; Ex. 2056 ¶¶ 64, 69, 79). Petitioner contends that Patent Owner's construction thus excludes an embodiment the Specification calls "efficac[ious]." *Id.* (citing Ex. 1001, col. 7, ll. 36–40).

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[14] J.S. Heier, *Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-related Macular Degeneration*, 119(12) OPHTHALMOL. 2537–48 (2012) ("Heier-2012") Ex. 1018.

Patent Owner responds that Petitioner's proposed construction invites error by asking the Board to ignore an express claim term. PO CC Opp. 1. Patent Owner contends that an "effective sequential dosing regimen" requires efficacy, and that to find otherwise would distort claim 34 to encompass sequential administration of minute doses of VEGF antagonist—resulting in a regimen that no one of skill in the art would deem "effective." *Id.* Patent Owner argues that the weight of the evidence of record shows that a person of ordinary skill in the art would only view the "effective sequential dosing regimen" of the '601 patent as effective if it maintained the treatment efficacy reflected in the standard-of-care, i.e., monthly Lucentis. *Id.* (citing PO Resp. 3–6, 41–43; PO Sur-Reply 2–6).

Patent Owner again contends that Petitioner's proposed construction renders an express claim term meaningless. For example, if the "effective sequential dosing regimen" requires nothing but sequential dosing, challenged claim 34 would encompass administering infinitesimal quantities of VEGF antagonist, incapable of achieving any treatment efficacy. PO CC Opp. 2. Patent Owner contends that both parties' experts agree that a person of ordinary skill in the art would not understand the '601 Specification's reference to "efficacy" to provide a clear definition for the claimed methods for treating. *Id.* (citing Ex. 2021, 177–181; Ex. 2056 ¶¶ 66, 78–79). Patent Owner contends that it is undisputed that no one portion of the Specification defines this phrase, and it must therefore be interpreted in context and given the meaning that a skilled artisan would have ascribed to it in 2011. *Id.* at 2–3 (citing, e.g., *Aventis Pharms. Inc. v. Amino Chems. Ltd.*, 715 F.3d 1363, 1373–74 (Fed. Cir. 2013)).

Patent Owner argues that although Petitioner points to various passages from the '601 Specification, it fails to provide any proposed construction or evidence for how a person of ordinary skill in the art would have understood the intrinsic record to inform the recited "effective sequential dosing regimen" limitation. PO CC Opp. 3. According to Patent Owner, the testimony of both parties' experts testimony supports Patent Owner' contention that a skilled artisan would have expected the "effective sequential dosing regimen" to provide efficacy on par with standard-of-care treatment, i.e., monthly Lucentis. *Id.* at 4 (citing PO Resp. 3–4, 41, 43; PO Sur-Reply 3–4; Ex. 2347, 127). Conversely, argues Patent Owner, no person of ordinary skill in the art would have viewed an extended dosing regimen that was inferior to the standard-of-care as "effective" for treating angiogenic eye disorders. *Id.* (citing PO Resp. 41–43; PO Sur-Reply 2–6).

Finally, Patent Owner argues that to the extent that the Board finds that the challenged claims require some non-zero level of efficacy other than that advanced by Patent Owner, it will be a new construction, neither advocated nor addressed by either party, and consequentially prejudicial to Patent Owner. PO CC Opp. 5. Patent Owner makes essentially the same arguments in its proposed claim construction brief that it does in its Response and Sur-Reply. *See* PO CC 1–5.

f. Analysis

We addressed similar arguments in the prior -00881 Decision. *See* Ex. 3001, 12–23. The difference in this case is that the challenged claims of the '601 patent recite the claim term "effective" in its preamble, e.g., "intravitreally administering, to said patient, an effective amount of

aflibercept" (claim 1, claim 10, claim 18); and "administering to the patient an effective sequential dosing regimen of a single initial dose of a VEGF antagonist…." (claim 34).

Petitioner contends that the preamble is not limiting upon the claims, but if it is limiting, the language of the claims is such that "no particular level of efficacy is required by any of the covered methods for treating," but rather that the goal of the invention is "inhibiting the angiogenic-promoting properties of VEGF." *See* Pet. 15–16, 18; Pet. CC 1 (quoting Ex. 1107 ¶¶ 13, 109). Patent Owner contends that the use of the claim term "effective" requires that the administered doses of the VEGF receptor antagonist demonstrate a high level of efficacy, one that is comparable to that achieved by monthly doses of certain other VEGF receptor antagonists, i.e., Lucentis and off-label Avastin. *See, e.g.*, PO Resp. 11–13, 41–43.

As an initial matter, we have previously addressed whether the preamble is limiting upon the claims in, *inter alia*, the -00881 Decision. In that Decision, we explained that:

> [T]he claims are directed to methods of administering, i.e., using, a VEGF antagonist for an intended purpose of "treating an angiogenic eye disorder in a patient." *See* Claims 1 and 14, Ex. 1001, 23:2–3; 24:3–4. The Specification repeatedly characterizes the method as one for treating angiogenic eye disorders in patients. *See, e.g., id.* at 1:18–20, 63–66, 2:23–27; 3:19–20; 5:11–13. Apart from the preamble, the independent claims do not elsewhere recite or indicate any other use for the method steps comprising the administration of a VEGF antagonist. Thus, we determine that the preamble sets forth the essence of the invention—treating an angiogenic eye disorder in a patient.

Ex. 3001, 17–18. We concluded that:

> [I]n view of Federal Circuit case law regarding statements of intended purpose in claims directed to method of using compositions, and in view of the evidence of record, namely, the claim language and the written description of the '338 patent, we find that the preambles of method claims 1 and 14 are limiting insofar as they require "treating an angiogenic eye disorder in a patient."

*Id.* at 18. The similar language of the challenged claims of the '601 patent, and our reasoning in the related -00881 Decision, compel the same conclusion here, i.e., that the preamble is limiting upon the claims.

We also addressed in the -00881 Decision whether the claims required, as Patent Owner argued, any degree of efficacy. Then, as now, Patent Owner argued that "treating" an angiogenic eye disorder requires achieving "a high level of efficacy, on par with the prevailing standard-of-care at the time of filing." Ex. 3001, 19 (quoting IPR2021-00881, Paper 41 at 13 (PO Resp.)). In our -00881 Decision, we reasoned that:

> [W]e find instructive the Specification's discussion [which is identical to that of the '601 patent] regarding the "Amount of VEGF Antagonist Administered." In that discussion, the Specification explains,
>
> > The amount of VEGF antagonist administered to the patient in each dose is, *in most cases*, a therapeutically effective amount. As used herein, the phrase "therapeutically effective amount" means a dose of VEGF antagonist that results in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or a dose of VEGF antagonist that inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder.
>
> (emphasis added). That description, along with the absence of the phrase "therapeutically effective" in the claims,11 signals for us the inventors' intention to not limit the claims to the

> administration of doses that ultimately prove to be therapeutically effective in a given patient. Instead, the Specification describes administration of VEGF antagonist doses for treating angiogenic eye disorder in a manner that encompasses doses that result in disclosed improvements and benefits, referred to as "therapeutically effective amounts," and doses that do not. Indeed, as guidance, the Specification discloses that "a therapeutically effective amount *can* be from about 0.05 mg to about 5 mg," without any guarantee that any particular dosage regimen administered within that range of dosage amounts will necessarily be "therapeutically effective," and without limiting the treatment methods based upon such results.

Ex. 3001, 20 (citations omitted, emphases added).

However, in the present *inter partes* review, the challenged claims *do* recite that the dose administered should be an "effective amount" (claims 1 and 10) or "an effective sequential dosing regimen" (claim 34). The question squarely presented, then, is whether the use of the claim term "effective," which is not present in the challenged claims of the -00881 IPR, requires, as Patent Owner contends, a "high level of efficacy" comparable to that of Lucentis or off-label Avastin. *See* PO Resp. 3–6, 41–43; PO Sur-Reply 2–6.

We conclude that they do not. In the case of challenged independent claims 1 and 10, the language of the claims expressly define what constitutes an "effective amount." Claim 1 recites:

> A method for treating age related macular degeneration patient in need thereof, comprising intravitreally administering, to said patient, an effective amount of aflibercept *which is* 2 mg approximately every 4 weeks for the first three months, followed by 2 mg approximately once every 8 weeks or once every 2 months.

Ex. 1001, claim 1 (emphasis added). Claim 10 uses virtually identical language. In other words, claims 1 and 10 expressly recite and define an

effective dose as "2 mg approximately every 4 weeks for the first three months, followed by 2 mg approximately once every 8 weeks or once every 2 months." The claims are silent with respect to any additional metric of required efficacy of this effective amount, requiring only the amount delivered at the prescribed intervals.

This is consistent with the disclosures of the '601 Specification. The Specification defines the claim term "therapeutically effective amount" thus:

> As used herein, the phrase "therapeutically effective amount" means a dose of VEGF antagonist that results in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or a dose of VEGF antagonist that inhibits, prevents, lessens, or delays the progression of an angiogenic eye disorder. In the case of an anti-VEGF antibody or a VEGF receptor-based chimeric molecule such as VEGFR1R2-FcΔC1(a) [e.g., aflibercept], a therapeutically effective amount can be from about 0.05 mg to about 5 mg.

Ex. 1001, cols. 6–7, ll. 58–1. The Specification then lists a range of therapeutically effective amounts of VEGF receptor antagonists ranging between 0.5 mg and 5 mg. *Id.* at col. 7, ll. 2–19. In other words, "an effective amount" is defined by the Specification as the *amount* of VEGF receptor antagonist that, when administered in the claimed method, will "result[] in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *Id.* at col. 6, ll. 61–65.

A person of ordinary skill in the art would thus understand that "an effective amount" is defined by the language of the claims as the amount of VEGF receptor antagonist that will cause the disclosed effects. Nothing in the language of the claims, or in the disclosures of the '601 Specification, expressly requires determining a degree of efficacy, rather, the claims are

directed to a prescribed regimen of drug administration. We conclude that a person of ordinary skill, understanding the disclosures of the Specification, would understand that the amounts of VEGF receptor antagonist recited in the claims and disclosed in the Specification constitute a "therapeutically effective amount" without additionally requiring a "high level of efficacy" comparable to that achieved by monthly doses of Lucentis or Avastin.

Furthermore, our -00881 Decision came to a similar conclusion, rejecting Patent Owner's similar argument because it required improperly importing limitations into the claims. *See* Ex. 3001, 22. Specifically, the Board found that:

> [W]hen the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount," and discloses that "a therapeutically effective amount can be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder," or it may not. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

*Id.* at 21–22 (citation omitted, second alteration in original). Furthermore, the Board found that:

> Patent Owner[] proposes that the claims require not only achieving a therapeutically effective result, but more

> specifically, achieving a "high level of efficacy that was noninferior to the standard of care by the time the patent was filed in 2011." In the Sur-reply, Patent Owner describes a "highly effective treatment for angiogenic eye disorders" as "one that is on par to Lucentis or off-label Avastin and can produce visual acuity gains, not just slow vision losses." The Specification refers to "a high level of efficacy" in one instance, i.e., in the "Background" section. The Specification does not describe there, or elsewhere that "treating," in the context of the claims or in the art, requires achieving a "high level of efficacy" or providing results "on par to Lucentis or off-label Avastin."

*Id.* at 22 (citations omitted).

With respect to challenged independent claim 34, we arrive at a conclusion similar to that concerning claims 1 and 10. Claim 34 does not expressly recite "an effective amount which is…" as do claims 1 and 10, but recites only "an effective sequential dosing regimen." For the same reasons that we have explained above, we construe this to refer to a sequential dosing regimen administered at the intervals recited in the claim, with the dosage amount being within the range (0.5–5.0 mg) disclosed in the '601 Specification that will "result[] in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *See* Ex. 1001, col. 6, ll. 60–65.

Our reviewing court's decision in *Eli Lilly and Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331 (Fed. Cir. 2021) supports our reasoning that the challenged claims do not require a "high level of efficacy" as Patent Owner argues. In *Eli Lilly*, the court upheld the Board's conclusion that the preamble of the claims at issue reciting "a method for treating headache in an individual" was limiting upon the claims. *Eli Lilly*, 8 F.4th at 1335, 1343.

The *Eli Lilly* claims also recited "administering to the individual an effective amount," similar to the language of the challenged claims of the present *inter partes* review. *Id.* at 1335. The court approvingly noted, in upholding the Board's conclusion, that the Board "found that while the claims encompass a clinical result, they do not *require* such a result." *Id.* at 1343. We also find that the similar language of the preamble to the challenged claims of the '601 patent, and the recitation of an "effective amount" or "an effective sequential dosing regimen," although encompassing clinical efficacy, does not *require* it, let alone a "high degree of efficacy."

Patent Owner argues that, without requiring a degree of efficacy, challenged claim 34 would encompass administering infinitesimal quantities of VEGF antagonist, incapable of achieving any treatment efficacy. *See* PO CC Opp. 2. We disagree. Challenged claims 1 and 10 expressly recite what constitutes an effective dose. With respect to challenged claim 34, as we have explained above, the '601 Specification sets forth a series of exemplary dosage ranges that would constitute a "therapeutically effective amount" generally being encompassed with the range of 0.5–5.0 mg of aflibercept. A person of ordinary skill in the art, reading the claims in light of the Specification would understand that these therapeutically effective amounts are those that would be expected to produce the results described by the Specification, *viz.*, "a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *See* Ex. 1001, col. 6, ll. 60–65.

Finally, Patent Owner argues that if "the Board finds that the challenged claims require some non-zero level of efficacy other than that

advanced by Patent Owner, it will be a new construction, neither advocated nor addressed by either party." PO CC Opp. 5. We do not do so here because we do not require *any* degree of efficacy to be imported into the claims. Rather, we construe the claim terms "effective amount" in challenged claims 1 and 10 to be the amount (2 mg) recited in the claims administered at the recited dosage intervals. We construe the claim term "effective sequential dosing regimen" of claim 34 to mean "administration of a VEGF receptor inhibitor at the recited dosage intervals and in the amount disclosed by the Specification (i.e., 0.5–5.0 mg) as being therapeutically effective."

2. The exclusion criteria

The "exclusion criteria" limitation of challenged claims 9 and 36 recites: "wherein exclusion criteria for the patient include (1) active intraocular inflammation; or (2) active ocular or periocular infection." *See, e.g.*, Ex. 1001, col. 21, ll. 65–67.

a. Petitioner's arguments

Petitioner argues that the "exclusion criteria" are entitled to no patentable weight under the printed matter doctrine. Pet. 23.

Petitioner points to the two-part analysis set forth in *Praxair Distrib., Inc. v. Mallinckrodt Hosp. Prods. IP Ltd.*, 890 F.3d 1024, 1032 (Fed. Cir. 2018). Pet. 23. Under this analysis we first determine whether the claim limitation in question is directed to printed matter. i.e., "if it claims the content of information." *Praxair*, 890 F.3d 1032 (citing *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015). In the second step, we determine

whether the printed matter is functionally related to its "substrate," i.e., whether the printed material is "interrelated with the rest of the claim." *Id.* Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850).

Petitioner first argues that the exclusion criteria (i.e., preexisting conditions) represent informational content regarding the patient. Pet. 24. Petitioner argues that the challenged claims recite no active step of applying (or assessing the patient for) the exclusion criteria and consequently is "informational content" constituting a "mental step/printed material element." *Id.* Petitioner asserts that, even if application of the "exclusion criteria" could be inferred, the challenged claims do not dictate that any procedural step be taken, or that any alteration be made to the claimed dosing regimen. *Id.*

Turning to the second step of the *Praxair* analysis, Petitioner contends that there is no functional relationship between the exclusion criteria and the rest of the claim (i.e., the operative steps of administering a VEGF antagonist to treat an angiogenic eye disorder). Pet. 24–25. Specifically, Petitioner argues that neither the presence nor absence of any exclusion criteria dictates any changes to the actual claimed dosing steps—i.e., the operative steps remain the same. *Id.* Therefore, argues Petitioner, because the "exclusion criteria" are "directed to mental steps" that "attempt to capture informational content," and lack a functional relationship to the other steps of the claimed treatment method, the exclusion criteria should be "considered printed matter lacking patentable weight." *Id.* (quoting *Praxair*, 890 F.3d at 1033).

b. Patent Owner's Response

Patent Owner contends that the exclusion criteria are entitled to patentable weight. PO Resp. 15. According to Patent Owner, the exclusion criteria are not mere "informational content," and a skilled artisan would understand that they are not optional when practicing the claimed methods. *Id.* at 16 (citing Ex. 2056 ¶¶ 95–99). Rather, argues Patent Owner, practicing the challenged claims requires actually applying the recited criteria—i.e., assessing a patient for the conditions listed as exclusion criteria, and administering treatment only to a patient who does not have the recited conditions. *Id.* Patent Owner contends that the plain meanings of the words "exclusion" and "criteria" mandate that patients having the listed conditions (i.e., the "criteria") are actually "excluded" from treatment. *Id.* at 20 (citing Ex. 2062, 4, 7; Ex. 2056 ¶ 109). Consequently, Patent Owner argues, only patients who are cleared of the Exclusion Criteria may be treated according to the claimed methods. *Id.*

Patent Owner asserts that the '601 Specification confirms that the exclusion criteria are mandatory. PO Resp. 17. Patent Owner points to Example 4 of the Specification, which describes 37 exclusion criteria known to have been used in Regeneron's Phase III VIEW clinical trials; numbers 18, 19, and 20 on that list correspond, respectively, to the recited exclusion criteria of the claims, and were employed in Example 4. *Id.* (citing Ex. 1001, cols. 10–12, ll. 50–32; Ex. 2056 ¶¶ 91, 96). Patent Owner asserts that Example 4's description is consistent with how the VIEW study exclusion criteria were actually applied: as non-optional criteria that limited the treatment population. *Id.*

Patent Owner asserts that both parties' experts confirm that a person of ordinary skill in the art would understand that the exclusion criteria are mandatory. PO Resp. 17. Patent Owner points to the testimony of Petitioner's expert Dr. Albini, who states that "clinical trial investigators are required to apply each of the exclusion criteria." *Id.* (quoting Ex. 2330 ¶¶ 93, 203, 251; Ex. 2323, 105–109). Patent Owner notes that its expert, Dr. Do, agrees with Dr. Albini's testimony. *Id.* at 18 (citing Ex. 2056 ¶¶ 97, 98). Patent Owner contends that the mandatory character of the exclusion criteria distinguishes them from contraindications printed on a drug label, which a physician may choose to employ or not. *Id.* (citing Ex. 2056 ¶ 99; Ex. 2323, 103). Contraindications, argues Patent Owner, are "symptom[s], circumstance[s], etc., which tend[] to make a particular course of (remedial) action inadvisable" however it is ultimately at the clinician's discretion whether to follow them or not. *Id.* (citing Ex. 2062, 3) (alteration in original).

Patent Owner contends that the challenged claims differ markedly from the "printed matter" claims in *Praxair*, which were expressly directed to the provision of "information" or a "recommendation," with no requirement that the "information" or "recommendation" change the scope or practice of the claims. PO Resp. 18 (citing *Praxair*, 890 F.3d at 1029–30*)*. In contrast, asserts Patent Owner, the challenged claims do not recite the provision of information, but instead define which patients are treated by the claimed methods, i.e., patients having an angiogenic eye disorder, and not having any of the Exclusion Criteria. *Id.* at 19 (citing Ex. 1001, cols. 21, ll. 65–67, col. 24, ll. 22–24; Ex. 2323, 104–105, 123).

Turning to the second part of the *Praxair* test, Patent Owner argues that the exclusion criteria bear a functional relationship to the claim. PO Resp. 19. Patent Owner asserts that the exclusion criteria define the patient population for treatment, and so define how (i.e., upon whom) the treatment steps are to be performed; ignoring the exclusion criteria would result in a different (broader) group of patients would be treated. *Id.* According to Patent Owner, claim terms defining the population of patients to be treated with a claimed method are limiting. *Id.* (citing, e.g., *Rapoport v. Dement*, 254 F.3d 1053, 1058–60 (Fed. Cir. 2001); *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1356–57 (Fed. Cir. 2014); *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333–34 (Fed. Cir. 2003); *GlaxoSmithKline LLC v. Fibrogen, Inc.*, IPR2016-01318, 2017 WL379248, at *3 (PTAB Jan. 11, 2017); *Praxair*, 890 F.3d at 1035).

Patent Owner also contends that the exclusion criteria also require that the medical provider take specific action—assessing the patient for the Exclusion Criteria, then administering treatment only to a patient who is determined not to have the excluded conditions. PO Resp. 20 (citing Ex. 2056 ¶ 90). As an instance of this, Patent Owner points again to Example 4 of the ’601 Specification, which discloses that subjects underwent assessment at screening, and that patients who were found to have one of the listed exclusion criteria were excluded from treatment. *Id.* (citing Ex. 2056 ¶¶ 91–96, 108; Ex. 1001, col. 12, ll. 56–64, 41–48). Patent Owner argues that such assessments are a routine part of clinical practice as well. *Id.* at 24 (citing Ex. 1002 ¶ 98; Ex. 2323, 122, 72–82, 92, 99–100, 123).

Patent Owner also argues that the doctrine of claim differentiation also supports the conclusion that the exclusion criteria of challenged claims 9 and 36 are limiting. PO Resp. 22. Patent Owner contends that claims of a patent are presumed to have a difference in scope, particularly where the "the absence of such difference in meaning and scope would make a claim superfluous." *Id.* (quoting *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998)).

Specifically, Patent Owner contends that the exclusion criteria are the sole difference between Claims 9 and 36 and the claims from which they depend (Claims 8 and 35, respectively). PO Resp. 22. According to Patent Owner, the doctrine of claim differentiation supports finding that the recited exclusion criteria limitation narrows the scope of challenged claims 9 and 36 compared to claims 8 and 35, from which they depend, by restricting the population of patients who may be treated according to the claimed methods. *Id.* (citing, e.g., *Littlefuse, Inc. v. Mersen USA EP Corp.*, 29 F.4th 1376, 1380 (Fed. Cir. 2022)).

c. Petitioner's Reply and Patent Owner's Sur-Reply

Petitioner replies that, in addition to the Board's preliminary finding that the exclusion criteria lack patentable weight, the district court in the parallel *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) (the "district court proceedings") arrived at the same conclusion in its *Markman* order that the exclusion criteria in the '601 patent's claims 9 and 36 claims lack patentable weight. Pet. Reply 7.

Petitioner also disputes Patent Owner's contention that unlike contraindications printed on a drug label, a skilled artisan would not treat the

exclusion criteria as optional in clinical practice. Pet. Reply 8 (citing PO Resp. 18). Petitioner points out that Patent Owner's expert, Dr. Do, acknowledges that a person of ordinary skill in the art "could, in his or her discretion," elect to perform an injection on a patient who presents with intraocular inflammation." *Id.* (Ex. 2056 ¶ 99; Ex. 1107 ¶ 65).

Petitioner argues that, under *Praxair*, claims 9 and 36 are "informational" because they ask doctors merely to think about the question instead of changing the dosing method. Pet. Reply 8 (citing Ex. 1112, 30–31). Petitioner asserts that the dose, drug, and schedule that the '601 patent recites does not change based on the outcome of reading, knowing, or thinking about any patient inflammation/infection information. *Id.* (citing Ex. 1112, 31). Furthermore, contends Petitioner, the exclusion criteria language does not require the practitioner to take any action at all. Rather, argues Petitioner, if the exclusion criteria are met, the method will not be practiced at all; the claimed steps of dosing 2 mg aflibercept on the regimen schedule recited in challenged independent claims 1 and 34 remains unaltered. *Id.* at 8–9 (citing Ex. 1112, 32, 33).

Consequently, argues Petitioner, the mental step of deciding not to treat a patient is unpatentable because "[o]nce the information is detected, no … treatment is given." Pet. Reply 9 (citing *INO Therapeutics LLC v. Praxair Distrib. Inc.*, 782 F. App'x 1001, 1008 (Fed. Cir. 2019)) (alteration in original). Petitioner points to the district court's *Markman* order, which found that "[e]ven under Regeneron's 'assess and exclude' approach, a patient either never starts the method (and hence the method doesn't change); or, if doctors screened for the information and found no infection or inflammation, the same method proceeds." *Id.* at 9–10 (quoting Ex. 1112,

35). The district court also found that "[t]his distinguishes the claims here from *Praxair* claim 9, where the method was required to start, then it could be modified based on the information." *Id.* at 10 (quoting Ex. 1112, 32). Petitioner also points to our Institution Decision's preliminary conclusion that "there is no direction to the practitioner to perform, or not perform, any specific step based upon the provided criteria." *Id.* (quoting Dec. 15).

Patent Owner responds that although Petitioner cites Dr. Do's testimony on physician discretion in clinical practice, this has no bearing on whether the exclusion criteria are mandatory when practicing the challenged claims. Patent Owner acknowledges that treating physicians can administer aflibercept in any number of ways within their medical judgment, but such administration will only practice claims 9 and 36 if it meets every limitation, including by applying the exclusion criteria. PO Sur-Reply 7 (citing, e.g., Ex. 2056 ¶ 99). Patent Owner points out that both parties' experts agree that applying the exclusion criteria requires the active step of patient assessment to identify a treatment-eligible patient. *Id.* at 7–8 (citing Ex. 2323, 72–79).

Patent Owner also argues that the evidence of record supports its contention that a skilled artisan would understand that the exclusion criteria must be applied, not merely considered. PO Sur-Reply 8. Patent Owner asserts that there is no discretionary or informational component to Claims 9 and 36. *Id.*

Patent Owner contends that the exclusion criteria also define the treatment-eligible patient population, and that if the exclusion criteria were ignored, the method would treat a different (broader) group of patients. PO Sur-Reply 8. Consequently, argues Patent Owner, the exclusion criteria bear a functional relationship to the rest of the claim and should be accorded

patentable weight. *Id.* Patent Owner contends that, by Petitioner's logic, no population-defining limitation for a method-of-treatment claim could be entitled to patentable weight, because patients who fall outside the defined population will not be treated as claimed. *Id.* at 9.

d. Analysis

We are persuaded by Petitioner's argument that the exclusion criteria are not limiting upon the claims. In *Praxair*, our reviewing court held that the printed matter doctrine does not apply only to literal printed matter, but, rather, is applicable when a claim limitation "claims the content of information." *Praxair*, 890 F.3d at 1032 (quoting *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015)). "Claim limitations directed to the content of information and lacking a requisite functional relationship are not entitled to patentable weight because such information is not patent eligible subject matter under 35 U.S.C. § 101." *Id.* (citing *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1064 (Fed. Cir. 2010)).

If a claim limitation is directed to printed matter, the next step in the *Praxair* analysis is to determine whether the printed matter is functionally related to its "substrate." *Praxair*, 890 F.3d at 1032. Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *In re DiStefano*, 808 F.3d at 850). However, "[w]here the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." *Id.* (quoting *In re Ngai*, 367 F.3d 1336, 1339 (Fed. Cir. 2004)) (alteration in original).

More specifically, printed matter is functionally related to its substrate when the language changes not mere thoughts or outcomes, but provides

action steps that the method requires. *See C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1381 (Fed. Cir. 2020) (holding that the test for printed matter is whether it "merely informs people of the claimed information, or whether it instead interacts with the other elements of the claim to … cause a specific action in a claimed process."); *see also Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) (holding that language "is only a statement of purpose and intended result" where its "expression *does not result in a manipulative difference in the steps of the claim*") (emphasis added).

In the case presently before us, there is little question that the exclusion criteria are directed to informational content. Specifically, the limitation in question expressly states that the "exclusion criteria for the patient include (1) active intraocular inflammation; or (2) active ocular or periocular infection." This listing of conditions relays direct information to the practitioner of the patent as to the nature of the exclusion criteria, much in the manner of the listing of contraindications included with the packaging of any other drug. The exclusion criteria are analogous to claim 1 in *Praxair*, in which the practitioner of the claimed "method of providing pharmaceutically acceptable nitric oxide gas" included providing information [to the medical provider]:

> [T]hat, in patients with preexisting left ventricular dysfunction, inhaled nitric oxide may increase pulmonary capillary wedge pressure (PCWP), leading to pulmonary edema, the information of (ii) being sufficient to cause a medical provider considering inhaled nitric oxide treatment for a plurality of neonatal patients who (a) are suffering from a condition for which inhaled nitric oxide is indicated, and (b) have pre-existing left ventricular dysfunction, to elect to avoid treating one or more of the plurality

> of patients with inhaled nitric oxide in order to avoid putting the one or more patients at risk of pulmonary edema.

*Praxair*, 890 F.3d at 1028–29. These limitations of claim 1 of *Praxair* (quoted above) and the exclusion criteria of the present challenged claims both provide information to the practitioner of the respective claimed methods concerning criteria to assess risks that may be incurred when practicing the method with a patient.

However, we do not find that the exclusion criteria of the challenged claims are functionally related to the rest of the claim. The claims do not expressly recite any positive step to be performed (or a negative step *not* to be performed) should a patient meet the exclusion criteria. Patent Owner attempts to distinguish the challenged claims from those of *Praxair* by arguing that the latter claims "were expressly directed to 'providing information' or a 'recommendation'" to the medical provider, which the medical provider was free to ignore. *See* PO Resp. 18. However, an individual practicing the method of the challenged claims would be similarly free to ignore the conditions of the exclusionary criteria and still be practicing all of the steps of the claimed method.

To be clear, and contrary to Patent Owner's position, we find that there are no positive or negative limitations in the challenged claims that *require* a person of ordinary skill in the art to act or not act in a certain way to practice the claimed method. As such, the information provided by the exclusionary criteria can be considered to be optional information, in that there is no direction to the practitioner to perform, or not perform, any specific step based upon the provided criteria. Thus, the exclusionary criteria are strictly informational, without requiring the practitioner to act, or

refrain from acting, in a specified manner, and not functionally related to the practice of the claimed method.

Furthermore, *Rapoport* does not support Patent Owner's case. In *Rapoport*, an appeal from an interference proceeding before the Board, our reviewing court held that the Board was correct in interpreting "treatment of sleep apneas" as being limited to treatment of the underlying sleep apnea disorder, i.e., reducing the frequency and severity of the apnea episodes during sleep, and not additionally to treatment of anxiety secondary to sleep apnea. *Rapoport*, 254 F.3d at 1059–60. The court found that Board was correct in interpreting the language of the patent's Specification as distinctly limiting the construction of the disputed claim terms to the treatment only of sleep apneas and not to secondary symptoms, such as anxiety. *Id.* Such is not the case in the present *inter partes* review. Patent Owner is not trying to expand the pool of eligible patients to include those with additional, related conditions, but arguing that, by listing the exclusion criteria, challenged claims 9 and 36 of the '601 patent is requiring the practitioner to actively exclude a set of patients. But, as we explain below, the language of the challenged claims does not support Patent Owner's arguments that the claims expressly, or even implicitly, *require* any action on the part of the practitioner.

Patent Owner's reliance upon *Jansen* is similarly unavailing. The question before the Federal Circuit in *Jansen* was whether a preamble reciting "[a] method for treatment of sleep apneas comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof to a patient in need of such treatment ...." was limiting upon the claim. *Jansen*, 342 F.3d 1329,

1333–34 (alteration in original). The court found that the preamble was limiting because it was "a statement of the intentional purpose for which the method must be performed." *Id.* The court did not find, as Patent Owner argues, that the preamble expressly limited the population of patients, or which patients should be excluded. *Id.*

In the present case, although the '601 Specification describes the use of the exclusion criteria in a clinical trial (Example 4), as we have explained, the exclusion criteria purportedly relate to the method of treatment, but propose no discrete manipulative steps by which the method, as practiced, should be altered by applying the exclusion criteria. *See Bristol-Myers*, 246 F.3d at 1376.

In the parallel district court proceedings, the district court, acknowledging our Institution Decision in the present *inter partes* review, arrived at the same conclusion with respect to identical exclusion criteria limitations in Patent Owner's '601 and '572 patents. Ex. 1112. Noting that the claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice," the district court found that:

> The language does not require any action step to be taken as a consequence. Nothing has "transform[ed] the process of taking the drug" aflibercept in the claimed method—the "actual method" found in the underlying independent claim, e.g., 2 mg of aflibercept, on the stated dosing schedule, remains the same.

*Id.* at 34–35 (citing *King Pharms., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010) (holding that when claim language did not change the underlying treatment method, it deserved no patentable weight)) (emphasis omitted, alteration in original).

The district court noted that, even under Patent Owner's "assess and exclude" approach, a patient either never starts the method (and hence the

method doesn't change) or, if doctors screened for the information and found no infection or inflammation, the method proceeds as claimed. Ex. 1112, 35. The district court concluded that this confirms that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.*

The Board made a similar point at oral argument:

> MS. DURIE: Well, I think you're right that it is flipped sides of the same coin, but I think it is important that what the exclusion criteria do is say, you do not have this condition. And therefore, you are eligible for treatment and the steps of the method may proceed.
>
> It is no different from any other criteria that is used to determine patient eligibility. And there is an entire body of case law that says determining that patients are eligible for treatment can be something that has patentable weight.
>
> ….
>
> JUDGE NEW: I would flip that around and say, wait a minute. The exclusion criteria say to a patient: you are not eligible for this treatment. We are not going to treat you. And therefore, the practice of the method is irrelevant.
>
> MS. DURIE: I think that argument could be used with any criteria that is used to determine patient eligibility. I would say it determines that a patient is eligible by saying, you have been screened. You do not have any of these conditions. You have not had active infection in the last two weeks. Therefore, the treatment may proceed.

Paper 98 ("Hearing Tr.") 64.

In the district court proceedings, the court continued:

> Claims that had an actual active step based on the exclusion criteria to be analogous to the Praxair claim 9 situation would ***require*** that patients lacking ocular inflammation or infection participate in a modified method (such as a different drug, dose, or schedule); or ***require*** ongoing treatment to stop—but that would only happen if inflammation or infection arises while the method is underway, and [Patent Owner] insists its exclusion criteria are directed to pre-screening before the method even starts.

Ex. 1112, 35 (emphases in original). The court concluded that because "there is no requirement to take new action [or to take no action] that flows from the 'wherein the exclusion criteria for a patient include…' information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight. *Id.* at 37. We agree.

As the district court recognized, we are not bound by its decision (nor it by ours) because "the PTAB properly may reach a different conclusion based on the same evidence," for the Board and the district courts function under different evidentiary standards and burdens of proof. *See* Ex. 1112, 33–34 (citing *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293–94 (Fed. Cir. 2017)). However, as the Federal Circuit recognized, "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

Such is the case in this instance. We find that the exclusion criteria recite informational content that does not does not result in a manipulative difference in the steps of the claim, and are therefore not functionally related to the claim.

Finally, Patent Owner argues that, under the doctrine of claim differentiation, claims are presumed to have a difference in their scope, and that the exclusion criteria, by excluding certain patients from the method,

further restrict the scope of the claims from which they depend. PO Resp. 22. We find that Patent Owner's argument begs the question by assuming, *a priori*, that the exclusion criteria are entitled to patentable weight because, Patent Owner argues, they restrict the scope of the claims. We disagree with Patent Owner's position because, as we have explained, we find that the limitations do *not* limit the claim, because they require no action (or inaction) on the part of the practitioner of the claimed method, but are informational in nature. Consequently, the exclusion claims of challenged claims 9 and 36 do not alter the scope of the claims from which they depend because they have no patentable weight.

We consequently conclude that the exclusion criteria of the challenged claims are not entitled to patentable weight under the printed matter doctrine.

3. The Best Corrected Visual Acuity limitations

Dependent challenged claims 5 and 6 recite limitations concerning the Best Corrected Visual Acuity requirements (the "BCVA limitation") for the claimed method. Claim 5 is exemplary and recites "wherein the patient gains at least 15 letters of Best Corrected Visual Acuity (BCVA) score." Ex. 1001, col. 21, ll. 55–56.

a. Petitioner's argument

In its Reply Brief, Petitioner argues that the BCVA limitation does not change the manipulative steps of the claims, and should therefore also be construed to have no patentable weight. Pet. Reply 11 (citing Ex. 1112, 38–39).

Petitioner argues that Patent Owner acknowledges that there is no change that doctors can make to the claimed regimen to ensure a particular BCVA score is achieved. Pet. Reply 11 (citing PO Resp. 26). Petitioner analogizes challenged claims 5 and 6 to the claims at issue in *Bristol-Myers*, in which the additional claim elements involved tumor regression and reducing patient toxicity, whereas the dosing schedule remained the same. *Id.* (citing *Bristol-Myers*, 246 F.3d at 1375–76). Petitioner notes that the Federal Circuit explained that the added claim language reflected "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim." Therefore, the court concluded, the language was not limiting on the claim. *Id.* (quoting *Bristol-Myers*, 246 F.3d at 1376; also citing *Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018); *King Pharms.*, 616 F.3d at 1277–79 (holding that adding test score outcomes to a method where patient blood AUC and other test measurements did not change the manipulative steps of the claim were non-limiting); also citing Ex. 1112, 37–39).

b. Patent Owner's position

Patent Owner first argues that The Board should disregard Petitioner's argument that the BCVA limitations lack patentable weight, because it exceeds the proper scope of a Reply Brief. PO Sur-Reply 10 (citing USPTO, *Consolidated Trial Practice Guide* at 45 (Nov. 2019)).

Patent Owner also argues that nothing about the BCVA limitations constitutes printed matter or mental steps. PO Sur-Reply 10. Patent Owner notes that, in a related proceeding, *Apotex Inc. v. Regeneron Pharms., Inc.*, IPR2022-01524 (PTAB Mar. 10, 2023), the Board considered and rejected

this argument, finding that such visual acuity gain limitations (or "results limitations") "must be given patentable weight." *Id.* (quoting *Apotex*, IPR2022-01524, Paper 9 at 18).

Specifically, Patent Owner asserts that, in *Apotex*, the Board found that the limitation reciting "wherein the patient achieves a gain in visual acuity within 52 weeks following the initial dose" was limiting upon the challenged claims. PO Sur-Reply 11 (citing *Apotex*, IPR2022-01524, Paper 9 at 18). Patent Owner notes that, in so finding, the Board considered, but did not find persuasive, the same case law Petitioner relies on in its Reply Brief, and found that the BCVA limitations aligned more closely with those held patentable in *Los Angeles Biomedical Research Inst. at Harbor-UCLA Med. Center v. Eli Lilly & Co.*, 849 F.3d 1049 (Fed. Cir. 2017). *Id.* (citing *Apotex*, IPR2022-01524, Paper 9 at 16–18). According to Patent Owner, the Board noted that, similarly to the claims in *LA Biomed*, the challenged claims were "directed to administering a pharmaceutical (aflibercept) to patients in need thereof, at a specified regimen and dosage, where a result of that treatment is expressly recited in the body" of the claims. *Id.* (quoting *Apotex*, IPR2022-01524, Paper 9 at 16).

Patent Owner contends that the BCVA limitations of challenged claims 5 and 6, like those addressed in *Apotex* and *LA Biomed*, are standalone limitations that "demand[] efficacy." PO Sur-Reply 12 (citing *Apotex*, IPR2022-01524, Paper 9 at 17; *LA Biomed*, 849 F.3d at 1061) (alteration in original). Patent Owner asserts that it is undisputed between the parties that the claims' requirement that "the patient gains at least 15 letters of [BCVA]" is not met unless the patient receiving the dosing regimen does, in fact, experience the required visual acuity gain. *Id.* (citing

Ex. 2347, 99–102). It is similarly undisputed, argues Patent Owner, that this gain does not occur in every patient. *Id.* (citing Ex. 2347, 100–101; Ex. 2323, 156). Accordingly, Patent Owner contends, the BCVA limitation gives the challenged claims "meaning and purpose" by adding an additional condition for success. *Id.* (citing *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002)).

Patent Owner thus distinguishes the BCVA limitations from the unpatentable recitations of efficacy in *Bristol-Myers* and *Copaxone*, which were not standalone limitations, but preambles, and which were duplicative of other claim elements. PO Sur-Reply 12–13 (citing *Bristol-Myers*, 246 F.3d at 1375; *Copaxone*, 906 F.3d at 1022–23).

c. Analysis

As an initial matter, we decline to heed Patent Owner's urging that we disregard Petitioner's arguments as being improperly first raised in the Reply Brief. *See* PO Sur-Reply 10. Whether the BCVA limitations are limiting upon the claims is certainly relevant to our construction of the challenged claims in this *inter partes* review, and as long as Patent Owner has received notice of, and had an opportunity to be heard with respect to, a proposed claim construction (even one raised *sua sponte* by the Board) Patent Owner's procedural rights under the Administrative Procedures Act are not violated. *Qualcomm Inc. v. Intel Corp.*, 6 F.4th 1256, 1265 (Fed. Cir. 2021). In this instance, Patent Owner received notice of Petitioner's proposed construction in its Reply Brief, and had an opportunity to be heard, both in its Sur-Reply Brief and at oral argument. *See, e.g.*, PO Sur-Reply 10–13; Hearing Tr. 66–68. Furthermore, the issue having been raised by

Petitioner's Reply Brief, Patent Owner could also have requested authorization for additional briefing upon the issue, which it did not. Consequently, we look to the merits of the parties' competing claim constructions.

Nevertheless, and as we explain in Section IV.C.4.b, iii below, we need not reach the question of whether the BCVA limitations of claims 5 and 6 are limiting, because we conclude that Dixon inherently discloses the BCVA limitations.

4. "Initial dose," "Secondary Dose," and "Tertiary Dose"

Petitioner next contends that a person of ordinary skill in the art would understand each of these claim terms as expressly defined in the '681 patent's Specification. Pet. 22. The Specification defines the claim terms as follows:

> The terms "initial dose," "secondary doses," and "tertiary doses," refer to the temporal sequence of administration of the VEGF antagonist Thus, the "initial dose" is the dose which is administered at the beginning of the treatment regimen (also referred to as the "baseline dose") ; the "secondary doses" are the doses which are administered after the initial dose; and the "tertiary doses" are the doses which are administered after the secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of dosing regimens, but will generally differ from one another in terms of frequency of administration.

Ex. 1001, col. 3, ll. 42–52. Petitioner also notes that the Specification further explains that "the immediately preceding dose" means "in a sequence of multiple administrations, the dose of VEGF antagonist which is administered to a patient prior to the administration of the very next dose in

the sequence with no intervening doses." Pet. 22 (citing Ex. 1001, col. 3, ll. 62–67; Ex. 1002 ¶¶ 44–45).

Patent Owner does not dispute Petitioner's construction.

We adopt Petitioner's proposed construction of the claim terms "initial dose," "secondary dose," and "tertiary dose." Petitioner proposes adoption of the definitions expressly set forth in the Specification of the '681 patent, *viz.*, that the initial dose is the dose "administered at the beginning of the treatment regimen," and is followed by the secondary doses "secondary doses" are "administered after the initial dose," and the tertiary doses are "administered after the secondary doses" and may be distinguished from the secondary doses "in terms of frequency of administration." Ex. 1001, col. 3, ll. 42–52.

*B. A Person of Ordinary Skill in the Art*

Petitioner contends that a person of ordinary skill in the art would have: (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field. Pet. 25–26. Petitioner asserts that such a person would typically have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders, including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists. *Id.* at 26 (citing Ex. 1002 ¶¶ 27–29; Ex. 1003 ¶¶ 21–25).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Response. Because we find Petitioner's definition to be consistent with the level of skill in the art (*see, e.g.*, Exs. 1006, 1020), we adopt Petitioner's definition.

### *C. Ground 1: Anticipation under 35 U.S.C. § 102 of claims 1–9, 34–39, 41–43, 45 by Dixon (Ex. 1006)*

Claims 1–9, 34–39, 41–43, and 45 of the '601 patent are challenged by Petitioner as unpatentable under 35 U.S.C. § 102 as being anticipated by Dixon. Pet. 43–50.

#### 1. Overview of Dixon

Dixon was published in October 2009, and is prior art to the '601 patent. Ex. 1006, 1573. Dixon discloses that a new drug for the treatment of age-related macular degeneration ("AMD") is aflibercept ("VEGF Trap-Eye"), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2. *Id.* at Abstr. Dixon discloses that VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD. *Id.*

Relevantly, Dixon discloses that, structurally, VEGF Trap-Eye is a fusion protein consisting of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment. Ex. 1006, 1575, Fig. 1. Dixon also discloses the PrONTO, CLEAR-IT-1, CLEAR-IT-2, and VIEW 1/VIEW 2 clinical trials. *Id.* at 1574–76, Ex. 1002 ¶ 74. Dixon identifies "[d]esirable attributes for emerging therapies for neovascular AMD include higher visual improvement rates and decreased dosing intervals" as a

motivation for the "development of new drugs for neovascular AMD . . . focused on both improving efficacy and extending duration of action," Ex. 1006, 1574, 1577; Ex. 1002 ¶ 78.

Dixon also describes the then-ongoing VIEW 1/VIEW 2 phase III clinical trials. Ex. 1006, 1576. Dixon discloses that, with respect to the VIEW 1 trial:

> This non-inferiority study will evaluate the safety and efficacy of intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses), compared with 0.5 mg of ranibizumab administered every 4 weeks. After the first year of the study, patients will enter a second year of p.r.n. dosing evaluation. The VIEW 2 study has a similar study design.

*Id.* (internal citations omitted).

2. Petitioner's arguments

a. Challenged claims 1 and 34

Petitioner presents the following tables summarizing its argument that the challenged independent claims are anticipated by Dixon:

For claim 1:

| Claim 1 | Dixon |
|---|---|
| A method for treating age related macular degeneration in a patient in need thereof, | "VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and Phase II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD." (Ex. 1006, 1573, 1577).<br>Phase 2 patients "treated with 2.0 mg or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p<0.0001$) and 5.4 ($p < 0.085$) ETDRS letters with 29 and 19% |

| | |
|---|---|
| | gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576).<br>"Two Phase III studies in wet AMD [VIEW1/VIEW2] are currently under way and seek to compare monthly ranibizumab to monthly or bimonthly VEGF Trap-Eye." (*Id.*, 1577–78). |
| comprising intravitreally administering, to said patient, | "The safety, tolerability and biological activity of intravitreal VEGF Trap-Eye in treatment of neovascular AMD was evaluated in the two-part Clinical Evaluation of Anti-angiogenesis in the Retina-1 (CLEAR-IT-1) study." (*Id.*). |
| an effective amount of aflibercept which is 2 mg | Patients treated with monthly loading doses of 2.0 mg followed by PRN dosing "achieved mean improvements of 9.0…ETDRS letters with 29%...gaining… ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576). Patients in this arm also displayed mean decreases in retinal thickness of 143 µM compared to baseline. (*Id.*)<br>"One promising new [angiogenesis inhibiting] drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." (*Id.*, 1573 (Abstract)).<br>"VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure." (*Id.*, 1575). |
| approximately every 4 weeks for the first 3 months, followed by 2 mg approximately once every 8 weeks or once every 2 months. | "[Phase 3] will evaluate the safety and efficacy of . . . 2.0 mg at an 8 week dosing interval (following ***three monthly doses***)." (Ex. 1006, 1576 (emphasis added)). |

Pet. 43–45. For claim 34:

| Claim 34 | Dixon |
|---|---|
| A method for treating an angiogenic eye disorder in a patient in need thereof, | "VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and Phase II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD." (Ex. 1006, 1573, 1577).<br>Phase 2 patients "treated with 2.0 mg or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p<0.0001$) and 5.4 ($p < 0.085$) ETDRS letters with 29 and 19% gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576).<br>"Two Phase III studies in wet AMD [VIEW1/VIEW2] are currently under way and seek to compare monthly ranibizumab to monthly or bimonthly VEGF Trap-Eye." (*Id.*, 1577–78). |
| said method comprising administering to the patient an effective sequential dosing regimen of a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist | "[Phase 3] will evaluate the safety and efficacy of . . . 2.0 mg at an 8 week dosing interval (***following three monthly doses***)." (Ex. 1006, 1576 (emphasis added)). In other words, an "initial dose" at day 0, "secondary doses" at weeks 4 and 8; and "tertiary doses" of every 8 weeks beginning at week 16 (i.e., doses at weeks 0, 4, 8, 16, 24, 32, 40, and 48). |
| wherein each secondary dose is administered 4 weeks after the | (*Id.*). (i.e., the doses at weeks 0, 4, 8). |

| | |
|---|---|
| immediately preceding dose; and | |
| wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose; | (*Id.*). (i.e., the doses at weeks 16, 24, 32, 40, and 48). |
| wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component. | VEGF Trap-Eye is "a fusion protein of binding domains of VEGF receptors-1 and -2 attached to the Fc fragment of human IgG." (Ex. 1006, 1576 (Fig.1)).<br>"VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure." (*Id.*, 1575). |

Pet. 45–46.

b. Challenged claims 2, 8, 42, and 43

Petitioner argues that these dependent claims further claim neovascular (wet) AMD or AMD. Pet. 46. Petitioner points to Dixon's disclosure of administering VEGF Trap-Eye to patients with neovascular AMD. *Id.* (citing Ex. 1006, 1573, 1576 ("~1200 patients with neovascular AMD"); Ex. 1002 ¶¶ 158–160, 184–186).

c. Challenged claims 3 and 4

Claims 3 and 4 recite "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected

Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score." Pet. 47.

Petitioner asserts that Dixon discloses that in phase 2 "[p]atients initially treated with 2.0 … mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) … ETDRS [BCVA] letters with 29[%] … gaining … ≥ ~15 ETDRS letters at 52 weeks."[15] Pet. 47 (citing Ex. 1006, 1576) (alterations in original). According to Petitioner, a gain of ≥ ~15 ETDRS BCVA letters necessarily encompasses a loss of less than 15 letters. *Id.* (citing Ex. 1002 ¶ 162). Petitioner also contends that Dixon discloses that for phase 3 (VIEW) "the primary outcome will be the proportion of patients who maintain vision at week 52 (defined as a loss of < 15 ETDRS letters)." *Id.* (citing Ex. 1006, 1576; Ex. 1002 ¶ 162).

Petitioner additionally argues that the claimed visual acuity measures do not distinguish the claimed dosing regimens from prior art disclosing the same regimens. Pet. 47. Claim 1 (from which claims 3 and 4 depend) covers the dosing regimen used in the VIEW trial; the same dosing regimen was disclosed in Dixon. *Id.* (citing Ex. 1002 ¶ 163). Petitioner argues that "because the prior art methods in their 'normal and usual operation … perform the function which [PO] claims in [the '601 patent], then such [patent] will be considered, to have been anticipated by the [prior art].'" *Id.* at 47–48 (quoting *King Pharms.*, 616 F.3d at 1276 (quoting *In re*

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[15] We note here that, similar to challenged claims 5 and 6, claims 3 and 4 appear to recite the BCVA limitations that we concluded in Section IV.A.3.c *supra* are not eligible to be accorded patentable weight. However, because Petitioner does not make this argument with respect to claims 3 and 4, we set forth Petitioner's arguments on the merits as presented in its Petition.

*Ackenbach*, 45 F.2d 437, 439 (C.C.P.A. 1930)) (alteration in original); and citing *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1380 (Fed. Cir. 2005).

d. Challenged claims 5 and 6

Challenged claims 5 and 6 recite "wherein the patient gains at least 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score."

Petitioner argues that Dixon discloses that in phase 2 "[p]atients initially treated with 2.0…mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$)…ETDRS [BCVA] letters with 29[%]…gaining…≥ ~15 ETDRS letters at 52 weeks." N Pet. 48 (citing Ex. 1006, 1576; Ex. 1002 ¶ 167).

Petitioner additionally contends that, as with claims 3 and 4, Dixon discloses that the same VIEW clinical trial regimen with the same drug now claimed in claim 1, from which claims 5 and 6 depend, and thus that Dixon necessarily anticipates these claims. Pet. 48 (citing Ex. 1002 ¶¶ 168–69; *King Pharms.*, 616 F.3d at 1276; *Perricone*, 432 F.3d at 1380.

e. Claim 7

With respect to claim 7, which recites "wherein approximately every 4 weeks comprises approximately every 28 days or approximately monthly," Petitioner argues that Dixon discloses "[Phase 3] will evaluate the safety and efficacy of…2.0 mg at an 8 week dosing interval (following three monthly

doses)." Pet. 48–49 (citing Ex. 1006, 1576; Ex. 1002 ¶¶ 154–157) (alterations in original).

f. Challenged claims 9 and 36

Claims 9 and 36 recite "wherein exclusion criteria for the patient include (1) active intraocular inflammation; or (2) active ocular or periocular infection." Pet. 49. Patent Owner contends that the recited exclusion criteria are entitled no patentable weight, an argument with which we agree, as we explain in Section IV.A.2.d above. *Id.* Consequently, we do not reach Petitioner's additional arguments with respect to these claims.

g. Challenged claim 35

Claim 35 limits the claimed method of claim 34 to "aflibercept." Petitioner argues again that Dixon discloses that "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure," and are therefore the same molecule. Pet. 49 (citing Ex. 1006, 1575). Petitioner also points to Dixon's disclosure that "[o]ne promising new [angiogenesis inhibiting] drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." *Id.* (citing Ex. 1006, 1573 (Abstr.); Ex. 1002 ¶ 172) (emphasis omitted, second alteration in original).

h. Challenged claims 37 and 38

Claims 37 and 38 recite "intraocular administration" and "intravitreal administration." Petitioner contends that intravitreal administration is a subset of intraocular administration and refers to administration directly into

the vitreous chamber of the eye. Pet. 50 (citing Ex. 1002 ¶¶ 69, 179; Ex. 1001, col. 2, ll. 47–50). Petitioner also notes that Dixon discloses that the VIEW studies will evaluate "the safety and efficacy of intravitreal VEGF Trap-Eye." *Id.* (citing Ex. 1006, 1576).

i. Challenged claims 39, 41, and 45

Claims 39, 41, and 45 recite "recite "2 mg" of VEGF antagonist. Petitioner asserts that Dixon discloses the use of 2.0 mg VEGF Trap-Eye doses with the VIEW dosing regimen. Pet. 50 (citing Ex. 1006, 1576 ("2.0 mg at an 8 week dosing interval (following three monthly doses")); Ex. 1002 ¶¶ 181–183). According to Petitioner, Dixon explains that the 2 mg intravitreal dose "allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity as it will be rapidly bound to VEGF and inactivated." *Id.* (citing Ex. 1006, 1575).

3. Patent Owner's Response

Patent Owner first argues, again, that because Petitioner's references do not disclose any efficacy data for the claimed method for treating, either expressly or inherently, the claims are not anticipated. PO Resp. 23 (citing, e.g., *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1055 (Fed. Cir. 2010); *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, No. 18-1043-KAJ, slip op. at 37 (D. Del. Aug. 10, 2020)). Patent Owner argues further that, because the recited method for treating is not the necessary result of carrying out the disclosures set forth in Dixon, Petitioner cannot show this limitation is inherently present. *Id.* at 23–24.

Patent Owner also argues that Dixon discloses only prospective studies "designed to evaluate the efficacy and safety of VEGF Trap-Eye" administered according to a specified dosing regimen. PO Resp. 24 (citing Ex. 1013, 1). According to Patent Owner, Dixon does not disclose the high level BCVA gains required by the method of Claims 5 and 6. *Id.* (citing Ex. 1001, col. 21, ll. 55–59; Ex. 2056 ¶¶ 36, 39, 42, 44; Ex. 2323, 197–202, 208). Nor, argues Patent Owner, does Dixon otherwise disclose "any data showing that the claimed Q8 dosing regimen would effectively treat." *Id.* (citing Ex. 2056 ¶¶ 36, 39, 42, 44; Ex. 2323, 197–202).

Patent Owner next argues that the visual acuity gains required by the BCVA limitations of challenged claims 5 and 6 do not necessarily result from the disclosures of the prior art. PO Resp. 25–29.

Patent Owner next contends that, even if a person of ordinary skill in the art knew how to make VEGF Trap-Eye, due to the inherent variability in protein production, such a skilled artisan would not necessarily produce a version of the protein that could treat an angiogenic eye disorder according to the claimed dosing regimen. PO Resp. 29 (citing Ex. 2057 ¶¶ 116–119; Ex. 2096, 90–91). According to Patent Owner, variations in fusion protein production may result in misfolding, aggregation, truncation due to proteolytic cleavage, and/or various changes in covalent post-translational modifications, which can affect the stability and biological activity of recombinant proteins. *Id.* (citing Ex. 2057 ¶¶ 118–119; Ex. 2097, 3–4). Patent Owner argues that for glycoproteins, changes in host cell and culture conditions were known to greatly affect the pattern and extent of post-translational glycosylation of the expressed protein. *Id.* (citing Ex. 2057 ¶ 121). Patent Owner contends that the presence and quantity of sialic acid

residues incorporated post-translationally into a protein were known to affect "absorption, serum half-life, and clearance from the serum, as well as the physical, chemical and immunogenic properties of the respective glycoprotein." *Id.* at 29–30 (citing Ex. 2057 ¶ 122 (quoting Ex. 2099, 1)).

Patent Owner argues that given the variability of manufacturing therapeutic biologics, knowing how to make VEGF Trap-Eye would not necessarily result in a protein that effectively treated an angiogenic eye disorder according to the claimed method. PO Resp. 30 (citing Ex. 2099 ¶ 131; also citing *Rapoport*, 254 F.3d at 1063; *Galderma Labs., L.P. v. Teva Pharms. USA, Inc.*, 799 F. App'x 838, 845–46 (Fed. Cir. 2020)).

Patent Owner argues further that the disclosed dosing regimen will not necessarily result in treating angiogenic eye disorders in some patients. PO Resp. 31. According to Patent Owner, even if VEGF Trap-Eye were made correctly, properly purified, and formulated, administration according to the disclosed regimen will not necessarily result in an effective treatment for all patients with angiogenic eye disorders. *Id.* Petitioner's expert posits that if the claims require efficacy, they require "a loss of 15 or fewer letters on the ETDRS visual acuity chart." *Id.* (citing Ex. 1002 ¶ 52). Patent Owner does not agree that a regimen resulting in vision loss would be considered effective treatment by 2011, nevertheless, it maintains that Petitioner has not shown inherency even under that standard.

Patent Owner argues that, because administration of VEGF Trap-Eye under the claimed dosing regimen will not *necessarily* result in effectively treating a patient with angiogenic eye disease, Petitioner cannot demonstrate inherency. PO Resp. 31 (citing, e.g., *Galderma*, 799 F. App'x at 846; *Rapoport*, 254 F.3d at 1063).

Finally, Patent Owner argues that, with respect to Petitioner's argument that its references anticipate the challenged claims because "anticipation does not require actual performance" and "proof of efficacy is not required," Supreme Court precedent that experimental uses (like the prospective VIEW trials) do not constitute prior art should apply with equal force to printed publications that disclose such experimental uses. PO Resp. 33 (citing *City of Elizabeth v. Am. Nicholson Pavement Co.*, 97 U.S. 126, 134–35 (1877)). Patent Owner contends that non-secret use of an invention for experimental purpose is not anticipatory if the inventor retains control of the invention. *Id.* (citing *City of Elizabeth*, 97 U.S. at 134–35). Patent Owner notes that this doctrine has been applied to the initiation of clinical trials. *Id.* (citing, e.g., *Eli Lilly & Co. v. Zenith Goldline Pharms.*, 471 F.3d 1369, 1380–81 (Fed. Cir. 2006)).

Patent Owner contends that the disclosure in Dixon of the initiation and design of trials—studies for which Regeneron retained control—does not, therefore, anticipate the challenged claims because the trials were experiments to perfect the invention. PO Resp. 33 (citing *In re Omeprazole Pat. Litig.*, 536 F.3d 1361, 1372–75 (Fed. Cir. 2008)).

4. Analysis

a. Challenged independent claims 1 and 34

We conclude that Petitioner has demonstrated, by a preponderance of the evidence, that the challenged claims of the '601 patent are anticipated by Dixon.

In the -00881 Decision, we determined that independent claims 1 and 14 of the '338 patent were unpatentable under 35 U.S.C. § 102 as anticipated

by Dixon. For the convenience of the reader, we present a claim chart comparing independent claims 1 and 34 of the present challenged claims and claim 1 of the '338 patent in the -00881 Decision. Differences between the challenged claims and claim 1 of the '338 patent are indicated in italics:

| **IPR2022-01226 US 10,888,601 B2 Claim 1** | **IPR2022-01226 US 10,888,601 B2 Claim 34** | **IPR2021-00881 US 9,254,338 B2 Claim 1 (unpatentable)** |
|---|---|---|
| 1. A method for treating *age related macular degeneration* in a patient *in need thereof* | 34. A method for treating an angiogenic eye disorder in a patient *in need thereof*, | 1. A method for treating an angiogenic eye disorder in a patient, |
| Comprising *intravitreally* administering, to *said* patient, *an effective amount of aflibercept* | said method comprising administering to the patient *an effective sequential dosing regimen*<br>of a single initial dose of a VEGF antagonist,<br>followed by one or more secondary doses of the VEGF antagonist,<br>followed by one or more tertiary doses of the VEGF antagonist | said method comprising sequentially administering to the patient<br>a single initial dose of a VEGF antagonist,<br>followed by one or more secondary doses of the VEGF antagonist,<br>followed by one or more tertiary doses of the VEGF antagonist; |
| *which is 2 mg approximately* every 4 weeks for *the first 3 months*,<br>*followed by 2 mg approximately* once every 8 weeks or once every 2 months | wherein each secondary dose is administered 4 weeks after the immediately preceding dose; and<br>wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose | wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and<br>wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose; |

| | | |
|---|---|---|
| . | wherein the VEGF antagonist is a receptor-based chimeric molecule comprising *an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component.* | wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2. |

As should be readily apparent to the reader, challenged claims 1 and 34 of the present Petition and claims 1 of the '338 patent are substantially the same. The independent claims of the '601 patent require treating a patient "in need thereof," whereas the preamble of claim 1 of the '338 patent merely requires treating a patient. However, the slight difference in this preambular language does not functionally alter the claimed method of treatment in any of the claims.[16]

[16] Claim 1 of the '601 patent more narrowly describes treating patients with age-related macular degeneration rather than an "angiogenic eye disorder." However, it was well-known in the art that age-related macular degeneration is a species of angiogenic eye disorder, and Dixon expressly discloses the use of aflibercept in the treatment if age-related macular degeneration. *See* Ex. 1001, col. 1, ll. 31–60; Ex. 1006, generally.

Similarly, the challenged independent claims of the '601 patent require "an effective amount" or "an effective sequential dosing regimen." We have explained, in Section IV.A.3.f above, that we construe the terms "an effective amount" and "an effective sequential dosing regimen" to mean, respectively, "the amount (2 mg) recited in claim 1 administered at the recited dosage intervals" and "administration of a VEGF receptor inhibitor at the recited dosage intervals and in the amount disclosed by the Specification (i.e., 0.5–5.0 mg) as being therapeutically effective" and not as requiring a "high degree of efficacy," as argued by Patent Owner. Claim 1 of the '601 patent additionally recites a 2 mg dose of aflibercept administered at the intervals common to all of the claims. Dixon expressly teaches administration of 2 mg of aflibercept at these intervals. *See* Ex. 1006, 1576 (e.g., "This non-inferiority study will evaluate the safety and efficacy of intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses)).

Finally, claim 34 of the '601 patent recites a genus of VEGF antagonist which includes the species of VEGF antagonist recited in claim 1 of the '388 patent and disclosed by Dixon. *See* Ex. 1006, 1575, 1576 (Fig. 1).

Because we concluded, in the -00881 Decision, that claim 1 of the '338 patent is anticipated by Dixon, we incorporate here by reference our reasoning in the -00881 Decision with respect to the corresponding limitations of independent challenged claims 1 and 14 of the '601 patent. *See* -00881 Decision, 26–46.

Briefly, in the -00881 Decision, we concluded that the preponderance of the evidence, including Dixon's express teaching that aflibercept and VEGF Trap-Eye have the "same molecular structure" demonstrated that Dixon inherently disclosed the claimed amino acid sequence of VEGF Trap-Eye (aflibercept). *See* Ex. 3001, 32–40. The Board found that the disclosures of Dixon, the prosecution history, and Patent Owner's own documents, demonstrated that aflibercept and VEGF Trap-Eye were the same well-characterized single drug, rather than, as Patent Owner suggested, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye." *Id.* at 39.

With respect to Patent Owner's arguments in the present *inter partes* review, as an initial matter, we have explained, in Sections IV.A.2–3 above, why we conclude that the exclusion criteria and the BCVA limitations are not limiting upon the claims and are entitled to no patentable weight. Consequently, we do not reach Patent Owner's arguments with respect to the exclusion criteria of claims 9 and 36 or the BCVA limitations of challenged claims 5 and 6.

Similarly, we have explained why we reject Patent Owner's arguments that the language of the claims requires a "high degree of efficacy" that is noninferior to the "standard of care," which was Lucentis or off-label Avastin, and we consequently are not persuaded by Patent Owner's arguments attempting to import any such requirement into the challenged claims. *See supra* Section IV.A.1.f.

We fail to see the relevance of Patent Owner's arguments that knowing how to make VEGF Trap-Eye would not necessarily result in treatment or that even if VEGF Trap-Eye were successfully synthesized, the

disclosed dosing regimen will not necessarily result in treating angiogenic eye disorders in some patients. *See* PO Resp. 29–32. The challenged claims of the '601 patent are not directed to a method of synthesizing VEGF Trap-Eye, or claim the compound itself. Rather, the challenged claims recite of administering the compound to a patient. As such, the method is directed to the dosage regimen. Dixon expressly discloses the claimed method of administration of VEGF Trap-Eye to a patient. Furthermore, and as we explain in Section IV.A.1.f above, we reject Patent Owner's contention that the claims require a high degree of efficacy in *any* patient. Rather the claims are directed to the method of administration of the drug.

Finally, with respect to Patent Owner's arguments that Dixon does not anticipate the challenged claims because it describes an experimental use, we considered this argument in the -0881 Decision and rejected it. *See* Ex. 3001, 44–45. Briefly, in considering this question, the Board emphasized that Dixon is a printed publication that discloses each element of the claimed invention. *Id.* at 44. In particular, the reference discloses treating an angiogenic eye disorder by administering VEGF-Trap Eye according to the dosing regimen recited by the challenged claims to the patient, concluding that "[a]nti-VEGF therapy has vastly improved the treatment of neovascular AMD in terms of both safety and efficacy." *Id.* at 44–45 (citing Ex. 1006, 1576) (alteration in original). Based on those disclosures, the Board found that the intended purpose of the claimed methods is to treat an angiogenic eye disorder and that such treatment only requires administering the recited dosing regimen to a patient for that purpose, without any requirement that such treatment achieves any particular level of efficacy. *Id.* at 45.

We adopt the same reasoning here, and conclude that Patent Owner has not established that Dixon is unavailable as anticipatory prior art because Dixon did not disclose an unclaimed feature for the method of treating, i.e., a particular level of effectiveness. Patent Owner's argument is, consequently, not persuasive.

b. Challenged dependent claims 2–9, 35–39, 41–43, and 45

As an initial matter, and for the reasons we have explained in Sections IV.A.2.f respectively, challenged dependent claims 9 and 36 recite the exclusion criteria as their sole limitation. Because we conclude that this limitation cannot be accorded patentable weight, these claims share the fate of dependent claims 8 and 35, from which they depend and which we address below.

i. Challenged claims 2, 8, 42, and 43

These claims all require that the angiogenic eye disorder to be treated is age-related macular degeneration. Claims 2 and 8 further require that the age-related macular degeneration be neovascular (wet), and claim 43 lists age-related macular degeneration as one of a number of angiogenic eye disorders. *See* Ex. 1001, claims 2, 8, 42, 43.

Dixon expressly discloses treating patients with neovascular (i.e., "wet") age-related macular degeneration. Ex. 1006, 1573, 1576 ("The first part, VIEW 1 (VEGF Trap: Investigation of Efficacy and safety in wet age-related macular degeneration) will enroll ~1200 patients with neovascular AMD"). Patent Owner does not dispute this disclosure of Dixon, and we

conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 2, 8, 42, and 43.

ii. Challenged claims 3 and 4

Challenged claims 3 and 4 recite, respectively, "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score." Ex. 1001, claims 3, 4.

Dixon discloses that in phase 2, "[p]atients initially treated with 2.0 . . . mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) … ETDRS [BCVA] letters with 29[%] … gaining … ≥ ~15 ETDRS letters at 52 weeks." (Ex. 1006, 1576). Petitioner contends, and Patent Owner does credibly not dispute, that a gain of ≥ ~15 ETDRS BCVA letters necessarily encompasses a loss of less than 15 letters. Pet. 47 (citing Ex. 1002 ¶ 162). Dixon also discloses that for phase 3 (VIEW) "the primary outcome will be the proportion of patients who maintain vision at week 52 (defined as a loss of < 15 ETDRS letters)." *Id.* (citing Ex. 1006, 1576; Ex. 1002 ¶ 162).

We therefore conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 3 and 4.

iii. Challenged claims 5 and 6

Dixon also inherently discloses the BCVA limitations. A reference may anticipate inherently if a claim limitation that is not expressly disclosed "is necessarily present, or inherent, in the single anticipating reference."

*Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1337 (Fed. Cir. 2010). As we have explained Dixon discloses the claimed 2Q8 dosing regimen. Example 6 of the '601 Specification discloses that "at Week 52, 55.3% of VEGFT-treated patients gained ≥15 letters vs 30.1 % of sham-treated patients (P <0.01). At Week 52, VEGFT-treated patients gained a mean of 16.2 letters vs 3.8 letters for sham-treated patients (P <0.001)." Ex. 1001, col. 15, ll. 14–18; *see Arbutus Biopharma Corp. v. ModernaTX, Inc.*, 65 F.4th 656, 664 (Fed. Cir. 2023) ("To anticipate, the prior art need only meet the inherently disclosed limitation to the same extent as the patented invention"); *see also King Pharms.*, 616 F.3d at 1275. Consequently, a person of ordinary skill in the art, following the method disclosed by Dixon, would have necessarily achieved the results recited in claims 5 and 6, and challenged claims 5 and 6 are thus inherently disclosed by Dixon.

iv. Challenged claim 7

Challenged claim 7 recites "wherein approximately every 4 weeks comprises approximately every 28 days or approximately monthly." Ex. 1001, claim 7.

Dixon discloses "[Phase 3] will evaluate the safety and efficacy of…2.0 mg at an 8 week dosing interval (following three monthly doses)." Ex. 1006, 1576. Patent Owner does not dispute this disclosure of Dixon, and we conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claim 7.

v. Challenged claim 35

Challenged claim 35 recites "the VEGF antagonist is aflibercept." Ex. 1001, claim 7.

Dixon discloses that "[o]ne promising new drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." Ex. 1006. Abstr. Dixon further discloses that VEGF Trap-Eye, the active agent in its disclosed AMD studies, and aflibercept, "have the same molecular structure," although there are variations in the formulation (i.e., further purification and differences in buffers) of VEGF Trap-Eye employed in the vision studies, to make it compatible with intravitreal injection. *Id.* at 1575.

We conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claim 35.

vi. Challenged claims 37 and 38

Challenged claims 37 and 38 recite "wherein all doses of the VEGF antagonist are administered to the patient by intraocular administration" (claim 37) or by "intravitreal administration," (claim 38) which is a type of intraocular administration. Ex. 1001, claims 37 and 38; *see also* Ex. 1002 ¶¶ 69, 179; Ex. 1001, col. 2, ll. 47–50 (describing intravitreal administration as a species of intraocular administration).

Dixon discloses that that "all anti-VEGF agents for neovascular AMD are administered only by intravitreal injection." Ex. 1006, 1574. Dixon also discloses that "the low intravitreal dose of 2 mg allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity." *Id.* at 1575. Dixon further discloses that the VIEW

study, which embodies the claimed method of the '601 patent, will evaluate "the safety and efficacy of intravitreal VEGF Trap-Eye." *Id.* at 1576. Patent Owner does not dispute these disclosures of Dixon.

We therefore conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 37 and 38.

vii. Challenged claims 39, 41, and 45

Challenged claims 39, 41, and 45 all recite administered doses of "about 2 mg" (claim 39) or "2 mg" (claims 41, 45) VEGF antagonist. Ex. 1001, claims 39, 41, 45.

Dixon discloses that a 2 mg intravitreal dose "allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity as it will be rapidly bound to VEGF and inactivated." Ex. 1006, 1575. Dixon further discloses that, in the VIEW study, "intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses)" are administered. *Id.* at 1576. Patent Owner does not dispute these disclosures.

We consequently conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 39, 41, and 45.

## V. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has demonstrated, by a preponderance of the evidence, that challenged claims 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable as being anticipated by Dixon (Ground 1). Because we conclude that all of the

challenged claims are thus anticipated, we do not reach the additional Grounds 2–7 proposed in the Petition. Furthermore, Petitioner's Motion to Exclude Evidence is granted-in-part, denied-in-part and dismissed-in-part. Patent Owner's Motion to Exclude Evidence is denied-in-part and dismissed-in-part.

## VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, based on a preponderance of the evidence, claims 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is granted in part, denied in part and dismissed in part;

FURTHER ORDERED that Patent Owner's Motion to Exclude is denied-in-part and dismissed-in-part

FURTHER ORDERED that because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

| Ground | Claims | 35 U.S.C. § | Reference(s)/ Basis | Claims Shown Unpatentable [17] | Claims Not shown Unpatentable |
|---|---|---|---|---|---|
| 1 | 1–9, 34–39, 41–43, 45 | 102 | Dixon | 1–9, 34–39, 41–43, 45 | |
| 2 | 1–9, 34–39, 41–43, 45 | 102 | Adis | | |
| 3 | 1–9, 34–39, 41–43, 45 | 102 | Regeneron 2008 | | |
| 4 | 1–9, 34–39, 41–43, 45 | 102 | NCT-795 | | |
| 5 | 1–9, 34–39, 41–43, 45 | 103 | Dixon, Papadopoulos ,Wiegand | | |
| 6 | 1–9, 34–39, 41–43, 45 | 103 | Dixon, Rosenfeld-2006, Papadopoulos , Wiegand | | |
| 7 | 1–9, 34–39, 41–43, 45 | 103 | Dixon, Heimann-2007 Papadopoulos , Wiegand | | |
| | **Overall Outcome** | | | 1–9, 34–39, 41–43, 45 | |

[17] As noted in Section III.A.1, we do not reach Petitioners' anticipation grounds based on Adis, Regeneron 2008, NCT-795, and NCT-377, or Petitioners' obviousness grounds as we have determined that those claims are unpatentable based on the Dixon anticipation ground, as noted in the table.

IPR2022-01226
Patent 10,888,601 B2

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# EXHIBIT 5

*Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*,
No. 22-61, Dkt. 665 (N.D. W. Va. Dec. 27, 2023)

# UNITED STATES DISTRICT COURT

for the

Northern District of West Virginia

Regeneron Pharmaceuticals, Inc.

*Plaintiff(s)*

v.

Civil Action No. 1:22-cv-61

Mylan Pharmaceuticals, Inc., et al.

*Defendant(s)*

## JUDGMENT IN A CIVIL ACTION

The court has ordered that:

☐ Judgment award ☐ Judgment costs ☒ Other

other: The Court concludes that Regeneron has demonstrated by a preponderance of the evidence that the Defendants have infringed claims 4, 7, 9, 11, 14, 15, 16, and 17 of the ’865 Patent; Regeneron has demonstrated by a preponderance of the evidence that the Defendants will induce infringement of claims 6 and 25 of the ’572 Patent and claims 11 and 19 of the ’601 Patent; (continued below)

This action was:

☐ tried by jury ☐ tried by judge ☒ decided by judge

decided by Judge Thomas S. Kleeh

Mylan has not demonstrated by clear and convincing evidence that claims 4, 7, 9, 11, 14, 15, 16, and 17 of the ’865 Patent are anticipated or obvious in light of the prior art or invalid under 35 U.S.C. § 112 for lack of written description, lack of enablement, or indefiniteness. Mylan has not demonstrated by clear and convincing evidence that claim 6 of the ’572 Patent is invalid as anticipated; Mylan has demonstrated by clear and convincing evidence that claim 6 of the ’572 Patent is invalid as obvious; Mylan has not demonstrated by clear and convincing evidence that claim 25 of the ‘572 patent is invalid as anticipated; Mylan has demonstrated by clear and convincing evidence that claim 25 of the ‘572 patent is invalid as obvious; Mylan has not demonstrated by clear and convincing evidence that Claim 11 of the ‘601 Patent is invalid as anticipated; Mylan has demonstrated by clear and convincing evidence that Claim 11 of the ‘601 patent is invalid as obvious; Mylan has demonstrated by clear and convincing evidence that Claim 19 of the ‘601 Patent is invalid as obvious.

Date: December 27, 2023

*CLERK OF COURT*

Cheryl Dean Riley

/s/ D. Kinsey

*Signature of Clerk or Deputy Clerk*

# EXHIBIT 6

Disclaimer of U.S. Patent No. 10,464,992, filed Jan. 17, 2024

PTO/SB/43 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE


## DISCLAIMER IN PATENT UNDER 37 CFR 1.321(a)

| Name of Patentee | Docket Number (Optional) |
|---|---|
| Regeneron Pharmaceuticals, Inc. | |
| **Patent Number** | **Date Patent Issued** |
| 10,464,992 | November 5, 2019 |

Title of Invention
VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

I hereby disclaim the following complete claims in the above identified patent: 1-18

Regeneron Pharmaceuticals, Inc. is disclaiming claims 1-18 in the '992 Patent for the sake of efficiency, as the patent is no longer needed.

The extent of my interest in said patent is (if assignee of record, state liber and page, or reel and frame, where assignment is recorded): Assignee of record (reel/frame: 047899/0360)

The fee for this disclaimer is set forth in 37 CFR 1.20(d).

- ☐ Patentee claims small entity status. See 37 CFR 1.27.
- ☐ Small entity status has already been established in this case, and is still proper.
- ☐ A check in the amount of the fee is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The Director is hereby authorized to charge any fees which may be required or credit any overpayment to Deposit Account No. 50-2387 .

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

Signed at TARRYTOWN, State of NEW YORK, this 17TH day of JANUARY 2024.

Frank R. Cottingham — Signature

50,437 — Registration Number, if applicable

Frank Cottingham
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UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

# ELECTRONIC ACKNOWLEDGEMENT RECEIPT

| APPLICATION # | RECEIPT DATE / TIME | ATTORNEY DOCKET # |
|---|---|---|
| **16/159,269** | **01/17/2024 02:45:18 PM Z ET** | **P35063US10/1106854.00082** |

## Title of Invention

VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

## Application Information

| | | | |
|---|---|---|---|
| APPLICATION TYPE | Utility - Nonprovisional Application under 35 USC 111(a) | PATENT # | 10464992 |
| CONFIRMATION # | 5813 | FILED BY | Natherine Ordanza |
| PATENT CENTER # | 63982808 | FILING DATE | 10/12/2018 |
| CUSTOMER # | 191459 | FIRST NAMED INVENTOR | Eric FURFINE |
| CORRESPONDENCE ADDRESS | - | AUTHORIZED BY | Michael Lewis |

## Documents

**TOTAL DOCUMENTS: 1**

| DOCUMENT | PAGES | DESCRIPTION | SIZE (KB) |
|---|---|---|---|
| P35063US10_SD.pdf | 1 | Statutory disclaimers per Manual of Patent Examining Procedure(MPEP) 1490. | 355 KB |

## Digest

| DOCUMENT | MESSAGE DIGEST(SHA-512) |
|---|---|
| P35063US10_SD.pdf | 2E1BE737D31AE0FE1FCE23EA62B8A076041225E1B091332DF48E0171830BBED9EF7696BF86EFF0F35B8491CE4693C2C7A1FCE993E1DEAADD280C13EEF14FCA29 |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

# ELECTRONIC PAYMENT RECEIPT

| APPLICATION # | RECEIPT DATE / TIME | ATTORNEY DOCKET # |
|---|---|---|
| 16/159,269 | 01/17/2024 02:45:18 PM Z ET | P35063US10/1106854.00082 |

## Title of Invention

VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

## Application Information

| | | | |
|---|---|---|---|
| APPLICATION TYPE | Utility - Nonprovisional Application under 35 USC 111(a) | PATENT # | 10464992 |
| CONFIRMATION # | 5813 | FILED BY | Natherine Ordanza |
| PATENT CENTER # | 63982808 | AUTHORIZED BY | Michael Lewis |
| CUSTOMER # | 191459 | FILING DATE | 10/12/2018 |
| CORRESPONDENCE ADDRESS | - | FIRST NAMED INVENTOR | Eric FURFINE |

## Payment Information

| PAYMENT METHOD | PAYMENT TRANSACTION ID | PAYMENT AUTHORIZED BY |
|---|---|---|
| CARD / 0128 | E20241GE45467749 | Michael Lewis |

| FEE CODE | DESCRIPTION | ITEM PRICE($) | QUANTITY | ITEM TOTAL($) |
|---|---|---|---|---|
| 1814 | STATUTORY DISCLAIMER, INCLUDING TERMINAL DISCLAIMER | 170.00 | 1 | 170.00 |
| | | | TOTAL AMOUNT: | $170.00 |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

# EXHIBIT 7

Excerpts of *Regeneron Pharms., Inc. v. Amgen Inc.*, No. 24-264, Amgen Inc.'s Answer to Complaint and Counterclaims (C.D. Cal. Feb. 2, 2024)

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UNITED STATES DISTRICT COURT

FOR THE CENTRAL DISTRICT OF CALIFORNIA

REDACTED VERSION OF DOCUMENT
PROPOSED TO BE FILED UNDER SEAL

REGENERON PHARMACEUTICALS, INC., a New York Corporation,

Plaintiff,

v.

AMGEN INC., a Delaware Corporation,

Defendant.

Case No. 2:24-cv-264-JWH-E
Hon. John W. Holcomb

**AMGEN INC.'S ANSWER TO COMPLAINT AND COUNTERCLAIMS**

Amgen Inc. ("Amgen"), Defendant in the above-captioned action, hereby answers the Complaint (the "Complaint") of Plaintiff Regeneron Pharmaceuticals, Inc. ("Regeneron") and counterclaims against Regeneron. Each paragraph below corresponds to the same-numbered paragraph in the Complaint. Headings are included as a matter of organization/formatting consistent with the Complaint, and do not require admitting or denying.

Amgen denies all allegations in the Complaint, whether express or implied, that are not specifically admitted below. Any factual allegation below is admitted only as to the specific admitted facts, not as to any purported conclusions, characterizations, implications, or speculations that may arguably follow from the admitted facts. Amgen denies that Regeneron is entitled to the relief requested or to any other relief.

## INTRODUCTION

1. Amgen admits that Regeneron markets EYLEA® (aflibercept), which is FDA-approved to treat patients with certain eye diseases. Amgen admits that it is seeking FDA approval under the Biologics Price Competition and Innovation Act ("BPCIA"), 42 U.S.C. §§ 262(k)-(*l*), to commercialize "ABP 938," Amgen's proposed biosimilar of Regeneron's EYLEA® (aflibercept) product. Amgen admits that Regeneron brings its Complaint under 42 U.S.C. § 262(*l*)(6)(A) and 35 U.S.C. § 271(e). Amgen denies that Regeneron brings its Complaint under 42 U.S.C. § 262(*l*)(9)(A). Amgen lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations of Paragraph 1, and on that basis, Amgen denies them.

2. Amgen admits that Regeneron markets EYLEA® (aflibercept) and that FDA first approved EYLEA® (aflibercept) in 2011. Amgen lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations of Paragraph 2, and on that basis, Amgen denies them.

3. Amgen admits that the active ingredient in EYLEA® (aflibercept) is a genetically engineered fusion protein called aflibercept. Amgen admits that the FDA first approved EYLEA® (aflibercept) in 2011 to treat neovascular (wet) age-related macular degeneration. Amgen admits that the FDA has also approved EYLEA® (aflibercept) for the treatment of diabetic macular edema, macular edema following retinal vein occlusion, diabetic retinopathy, and retinopathy of prematurity. Amgen lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations of Paragraph 3, and on that basis, Amgen denies them.

4. Amgen admits that on October 31, 2023, Amgen publicly announced that the "FDA accepted the Biologics License Application for ABP 938, an investigational biosimilar to EYLEA® (aflibercept)." Amgen admits that it submitted its BLA under 42 U.S.C. § 262(k). Amgen admits that the BPCIA was enacted in 2010 as part of the Affordable Care Act and that the BPCIA created a new, abbreviated pathway for the approval of biosimilar products. Amgen denies the remaining allegations of Paragraph 4.

5. Amgen denies the allegations of Paragraph 5.

**PLAINTIFF**

6. Amgen lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 6, and on that basis, Amgen denies them.

**DEFENDANT**

7. Amgen admits that Amgen is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business located at One Amgen Center Drive, Thousand Oaks, California 91320. Amgen admits that its business is focused on the development of biologic medicines, which includes development of biosimilar medicines, including ABP 938, a proposed

112, 115, 116, 119, 132, 251, 256, and/or 282, or under other judicially created bases for invalidation.

**FOURTH ADDITIONAL DEFENSE**
**(Equitable Doctrines)**

417. Regeneron's claims of patent infringement are barred in whole or in part by the equitable doctrines of waiver, estoppel, and/or unclean hands.

**FIFTH ADDITIONAL DEFENSE**
**(Prosecution History Estoppel)**

418. Regeneron's claims of patent infringement under the doctrine of equivalents, if any, are barred in whole or in part by the doctrine of prosecution history estoppel and/or prosecution disclaimer.

**SIXTH ADDITIONAL DEFENSE**
**(No Injunction)**

419. Regeneron is not entitled to an injunction with respect to the Asserted Patents under any theory because Regeneron has not suffered and will not suffer irreparable harm, Regeneron is not without an adequate remedy at law, and public policy concerns weigh against injunctive relief.

**SEVENTH ADDITIONAL DEFENSE**
**(Not an Exceptional Case)**

420. If Regeneron is entitled to any remedy, it is not entitled to a finding that this case is exceptional warranting attorney's fees under 35 U.S.C. § 285, or pursuant to the Court's inherent power.

**EIGHTH ADDITIONAL DEFENSE**
**(Prior User Defense of 35 U.S.C. § 273)**

421. Amgen is not liable for infringement of one or more of the Asserted Patents under 35 U.S.C. § 273 because even assuming Amgen has ever used any of the subject matter claimed in one or more of the Asserted Patents, Amgen, acting in good faith, commercially used the subject matter of one or more of the Asserted

Patents in the United States in connection with an internal commercial use at least one year before the effective filing date of one or more of the Asserted Patents.

**NINTH ADDITIONAL DEFENSE**
**(Safe Harbor Defense of 35 U.S.C. § 271(e)(1))**

422. Amgen is not liable for infringement of one or more of the Asserted Patents because Amgen is exempt from liability under the safe harbor of 35 U.S.C. § 271(e)(1), which provides: "It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products."

**TENTH ADDITIONAL DEFENSE**
**(Limitation on Damages Under 35 U.S.C. § 287)**

423. On information and belief, Regeneron has failed to mark articles in accordance with the requirements of 35 U.S.C. § 287. Regeneron's claims are barred or limited under 35 U.S.C. § 287.

**ELEVENTH ADDITIONAL DEFENSE**
**(Costs Barred Under 35 U.S.C. § 288)**

424. Regeneron's demand for costs is barred or limited under 35 U.S.C. § 288.

**TWELFTH ADDITIONAL DEFENSE**
**(Patent Misuse)**

425. Regeneron's claims of patent infringement are barred in whole or in part by the doctrine of patent misuse, including in view of at least the reasons relating to Regeneron's inequitable conduct.

**THIRTEENTH ADDITIONAL DEFENSE**
**(Lack of Standing)**

426. Regeneron lacks standing to assert the Asserted Patents.

specific intent to deceive the U.S. Patent and Trademark Office into issuing the claims.

106. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether the '338 Patent is unenforceable due to inequitable conduct.

107. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

108. Amgen is entitled to a judicial declaration that the '338 Patent is unenforceable due to inequitable conduct.

**SIXTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NO. 9,315,281**

109. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

110. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '281 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '281 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

111. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '281 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

112. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '281 Patent, Amgen would not be liable for infringement of the '281 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith,

commercially used the subject matter" of the '281 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '281 Patent.

113. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '281 Patent.

114. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

115. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '281 Patent.

**SEVENTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 9,315,281**

116. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

117. One or more of the claims of the '281 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

118. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '281 Patent are invalid.

119. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

120. Amgen is entitled to a judicial declaration that one or more of the claims of the '281 Patent are invalid.

280. One or more of the claims of the '865 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

281. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '865 Patent are invalid.

282. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

283. Amgen is entitled to a judicial declaration that one or more of the claims of the '865 Patent are invalid.

**THIRTY-FIRST COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NO. 11,104,715**

284. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

285. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '715 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '715 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

286. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '715 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

287. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '715 Patent, Amgen would not be liable for infringement of the '715 Patent under 35 U.S.C. § 273

because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '715 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '715 Patent.

288. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '715 Patent.

289. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

290. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '715 Patent.

**THIRTY-SECOND COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,104,715**

291. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

292. One or more of the claims of the '715 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

293. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '715 Patent are invalid.

294. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

295. Amgen is entitled to a judicial declaration that one or more of the claims of the '715 Patent are invalid.

327. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

328. Amgen is entitled to a judicial declaration that the '572 Patent is unenforceable due to inequitable conduct.

**THIRTY-EIGHTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NO. 11,306,135**

329. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

330. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '135 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '135 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

331. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '572 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

332. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '135 Patent, Amgen would not be liable for infringement of the '135 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '135 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '135 Patent.

333. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether

Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '135 Patent.

334. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

335. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '135 Patent.

**THIRTY-NINTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY OF U.S. PATENT NO. 11,306,135**

336. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

337. One or more of the claims of the '135 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

338. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '135 Patent are invalid.

339. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

340. Amgen is entitled to a judicial declaration that one or more of the claims of the '135 Patent are invalid.

**FORTIETH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF UNENFORCEABILITY OF U.S. PATENT NO. 11,306,135 DUE TO INEQUITABLE CONDUCT**

341. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

362. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether the '135 Patent is unenforceable due to inequitable conduct.

363. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

364. Amgen is entitled to a judicial declaration that the '135 Patent is unenforceable.

**FORTY-FIRST COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,459,374**

365. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

366. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '374 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '374 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

367. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '374 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

368. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '374 Patent, Amgen would not be liable for infringement of the '374 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '374 Patent in the United States "in

connection with an internal commercial use" at least one year before the effective filing date of the '374 Patent.

369. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '374 Patent.

370. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

371. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '374 Patent.

**FORTY-SECOND COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,459,374**

372. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

373. One or more of the claims of the '374 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

374. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '374 Patent are invalid.

375. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

376. Amgen is entitled to a judicial declaration that one or more of the claims of the '374 Patent are invalid.

399. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether the '374 Patent is unenforceable due to inequitable conduct.

400. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

401. Amgen is entitled to a judicial declaration that the '374 Patent is unenforceable.

**FORTY-FOURTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NO. 11,472,861**

402. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

403. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '861 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '861 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

404. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '861 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

405. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '861 Patent, Amgen would not be liable for infringement of the '861 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '861 Patent in the United States "in

connection with an internal commercial use" at least one year before the effective filing date of the '861 Patent.

406. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '861 Patent.

407. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

408. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '861 Patent.

**FORTY-FIFTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,472,861**

409. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

410. One or more of the claims of the '861 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

411. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '861 Patent are invalid.

412. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

413. Amgen is entitled to a judicial declaration that one or more of the claims of the '861 Patent are invalid.

**FORTY-SIXTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,505,593**

414. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

415. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '593 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '593 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

416. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '593 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

417. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '593 Patent, Amgen would not be liable for infringement of the '593 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '593 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '593 Patent.

418. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '593 Patent.

419. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

420. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '593 Patent.

**FORTY-SEVENTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,505,593**

421. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

422. One or more of the claims of the '593 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

423. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '593 Patent are invalid.

424. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

425. Amgen is entitled to a judicial declaration that one or more of the claims of the '593 Patent are invalid.

**FORTY-EIGHTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF UNENFORCEABILITY**
**OF U.S. PATENT NO. 11,505,593 DUE TO INEQUITABLE CONDUCT**

426. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

427. The '593 Patent is unenforceable due to inequitable conduct before the U.S. Patent and Trademark Office for at least the reasons set forth in Amgen's (3)(B) Statement.

428. The following individuals are subject to a duty to disclose information material to the patentability of claims under examination: (1) each inventor named in the application; (2) each attorney or agent who prepares or

448. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

449. Amgen is entitled to a judicial declaration that the '593 Patent is unenforceable.

**FORTY-NINTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,535,663**

450. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

451. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '663 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '663 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

452. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '663 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

453. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '663 Patent, Amgen would not be liable for infringement of the '663 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '663 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '663 Patent.

454. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether

Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '663 Patent.

455. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

456. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '663 Patent.

**FIFTIETH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,535,663**

457. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

458. One or more of the claims of the '663 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

459. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '663 Patent are invalid.

460. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

461. Amgen is entitled to a judicial declaration that one or more of the claims of the '663 Patent are invalid.

**FIFTY-FIRST COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,542,317**

462. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

463. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '317 Patent at least because Amgen will not directly or

indirectly infringe one or more claims of the '317 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

464. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '317 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

465. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '317 Patent, Amgen would not be liable for infringement of the '317 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '317 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '317 Patent.

466. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '317 Patent.

467. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

468. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '317 Patent.

496. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

497. Amgen is entitled to a judicial declaration that the '317 Patent is unenforceable.

**FIFTY-FOURTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NO. 11,548,932**

498. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

499. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '932 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '932 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

500. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '932 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

501. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '932 Patent, Amgen would not be liable for infringement of the '932 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '932 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '932 Patent.

502. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether

Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '932 Patent.

503. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

504. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '932 Patent.

**FIFTY-FIFTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,548,932**

505. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

506. One or more of the claims of the '932 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

507. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '932 Patent are invalid.

508. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

509. Amgen is entitled to a judicial declaration that one or more of the claims of the '932 Patent are invalid.

**FIFTY-SIXTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,555,176**

510. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

511. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '176 Patent at least because Amgen will not directly or

indirectly infringe one or more claims of the '176 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

512. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '176 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

513. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '176 Patent, Amgen would not be liable for infringement of the '176 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '176 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '176 Patent.

514. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '176 Patent.

515. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

516. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '176 Patent.

**SIXTY-FIRST COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,680,930**

543. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

544. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '930 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '930 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

545. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '930 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

546. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '930 Patent, Amgen would not be liable for infringement of the '930 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '930 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '930 Patent.

547. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '930 Patent.

548. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

549. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '930 Patent.

**SIXTY-SECOND COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,680,930**

550. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

551. One or more of the claims of the '930 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

552. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '930 Patent are invalid.

553. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

554. Amgen is entitled to a judicial declaration that one or more of the claims of the '930 Patent are invalid.

**SIXTY-THIRD COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,707,506**

555. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

556. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '506 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '506 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

557. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '506 Patent

**SIXTY-SIXTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF NON-INFRINGEMENT**
**OF U.S. PATENT NO. 11,753,459**

576. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

577. Amgen has not infringed, and will not infringe, any valid and enforceable claim of the '459 Patent at least because Amgen will not directly or indirectly infringe one or more claims of the '459 Patent for at least the reasons set forth in Amgen's (3)(B) Statement.

578. Under 35 U.S.C. § 271(e)(1), Amgen has not directly or indirectly infringed, and will not directly or indirectly infringe, the '459 Patent because particular activities related to ABP 938, such as the manufacture or testing of ABP 938 related to submission of the BLA, were and will be solely for uses related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs.

579. In the alternative, to the extent Amgen has ever used any of the subject matter claimed in any valid, enforceable claim of the '459 Patent, Amgen would not be liable for infringement of the '459 Patent under 35 U.S.C. § 273 because Amgen, or an entity controlled by Amgen, "acting in good faith, commercially used the subject matter" of the '459 Patent in the United States "in connection with an internal commercial use" at least one year before the effective filing date of the '459 Patent.

580. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether Amgen has infringed, and whether Amgen will infringe by its commercial marketing of ABP 938, any valid and enforceable claim of the '459 Patent.

581. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

582. Amgen is entitled to a judicial declaration that Amgen has not and will not infringe, directly or indirectly, one or more of the claims of the '459 Patent.

**SIXTY-SEVENTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF INVALIDITY**
**OF U.S. PATENT NO. 11,753,459**

583. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

584. One or more of the claims of the '459 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

585. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '459 Patent are invalid.

586. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

587. Amgen is entitled to a judicial declaration that one or more of the claims of the '459 Patent are invalid.

**SIXTY-EIGHTH COUNTERCLAIM**
**DECLARATORY JUDGMENT OF UNENFORCEABILITY**
**OF U.S. PATENT NO. 11,753,459 DUE TO INEQUITABLE CONDUCT**

588. Amgen incorporates by reference the foregoing paragraphs as if fully set forth herein.

589. The '459 Patent is unenforceable due to inequitable conduct before the U.S. Patent and Trademark Office for at least the reasons set forth in Amgen's (3)(B) Statement.

590. The following individuals are subject to a duty to disclose information material to the patentability of claims under examination: (1) each inventor named in the application; (2) each attorney or agent who prepares or

641. One or more of the claims of the '926 Patent are invalid under 35 U.S.C. § 101, 102, 103, and/or 112 for at least the reasons set forth in Amgen's (3)(B) Statement.

642. An actual, substantial, and justiciable controversy exists between Amgen and Regeneron about whether one or more of the claims of the '926 Patent are invalid.

643. The controversy between the parties is amenable to specific relief through a decree of a conclusive character.

644. Amgen is entitled to a judicial declaration that one or more of the claims of the '926 Patent are invalid.

**PRAYER FOR RELIEF**

WHEREFORE, Amgen respectfully requests that this Court enter judgment on its Counterclaims in its favor against Regeneron and grant the following relief:

A. Declare that Amgen has not, does not, and will not infringe one or more of the claims of the Asserted Patents;

B. Declare that one or more of the claims of the Asserted Patents are invalid;

C. Declare that one or more of the Asserted Patents are unenforceable;

D. Declare that this is an exceptional case and award to Amgen its attorneys' fees and costs pursuant to 35 U.S.C. § 285;

E. Award attorneys' fees and costs to Amgen; and

F. Award such other relief as this Court may deem just and proper, including under 28 U.S.C. § 2202.

Dated: February 2, 2024

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# EXHIBIT 8

*Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, No. 22-61,
Dkt. 427 (N.D. W. Va. Apr. 19, 2023)

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

**REGENERON PHARMACEUTICALS, INC.,**

**Plaintiff/Counter-Defendant,**

**v.** **CIVIL NO. 1:22-CV-61 (KLEEH)**

**MYLAN PHARMACEUTICALS INC.,**

**Defendant/Counter-Claimant.**

**ORDER ON CLAIM CONSTRUCTION**

## INTRODUCTION

The patents now before the Court with terms requiring construction are: U.S. Patent No. 11,084,865 ("the '865 patent" or the "Formulation Patent") (Dkt. 146, '865 patent); U.S. Patent Nos. 10,888,601 ("the '601 patent") and 11,253,572 ("the '572 patent") (collectively, the "Dosing Patents") (Dkt. 146, '601 patent; Dkt. 146, '572 patent); and U.S. Patent No. 11,104,715 ("the '715 patent" or "the Manufacturing Patent") (Dkt. 146, '715 patent).[1]

[1] Regeneron initially asserted U.S. Patent Nos. 11,053,280, and 11,299,532, (Dkt. 146, MOB at 3, n.3), but has since withdrawn these from the first stage of the litigation.

**ORDER ON CLAIM CONSTRUCTION**

This Court has examined the disputes over the construction of these claim terms and, on January 24, 2023, held a hearing pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).

**GENERAL CONCLUSIONS OF LAW**

Claim construction is the process by which the Court gives legal effect to the meaning of the claims of the asserted patents. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 321-22 (2015). "It is not an obligatory exercise in redundancy" and is not required where a term's meaning is apparent from the claim language itself or its scope is not disputed. *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). "[S]ome line-drawing problems . . . [are] properly left to the trier of fact." *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007).

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 (quotation marks 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.").[2]

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. 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 (quotation marks 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

[2] An "independent" claim is a standalone claim that contains all the limitations that define an invention, whereas a "dependent" claim refers back to, and incorporates by dependency, a previous independent claim and further limits the claim. *See generally* 37 C.F.R. § 1.75.

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.*, 2022 WL 17178691, at *5-6 (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.").

"[A] court 'should also consider the patent's prosecution history.'" *Phillips*, 415 F.3d at 1317. "Yet because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* To find disavowal of the ordinary meaning of a claim term in view of the specification based on statements in the prosecution history, the Federal Circuit requires that the alleged disavowing actions or statements made during prosecution be "both clear and unmistakable." *CUPP Comput. AS v. Trend Micro Inc.*, 53 F.4th 1376, 1382 (Fed. Cir. 2022).

Where the court "reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history), the judge's determination will amount solely to a determination of law." *Teva*, 574 U.S. at 331. However, in

situations where the patent does not provide the meaning for a claim term, a "court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Id.* In those circumstances, the court may "make subsidiary factual findings about that extrinsic evidence." *Id.* at 332. But extrinsic evidence cannot be used to "contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Phillips*, 415 F.3d at 1324. "[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." *Genuine Enabling Tech. LLC v. Nintendo Co.*, 29 F.4th 1365, 1373 (Fed. Cir. 2022) (quoting *Phillips*, 415 F.3d at 1318); *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996) ("[E]xpert testimony ... may not be used to vary or contradict the claim language. Nor may it contradict the import of other parts of the specification." (citation omitted)); *Omega Eng'g, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1332 (Fed. Cir. 2003) ("Yet, Omega submits its expert declarations not to shed light on this field of art, but to rewrite the patent's specification and explicitly provide for the laser splitting

device, lenses, and prisms to strike the center of the energy zone. That we cannot accept."). Accordingly, "where the patent documents are unambiguous, expert testimony regarding the meaning of a claim is entitled to no weight." *Vitronics*, 90 F.3d at 1584.

## DISPUTED TERMS

### A. The Formulation Patent (The '865 Patent)

#### a. "Organic Co-Solvent"

The parties agree that a plain and ordinary meaning applies to the term "organic co-solvent." (*See, e.g.*, Dkt. 124, ROB at 3; Dkt. 146, MOB at 9). The specification of the '865 patent is clear that "all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs." (Dkt. 146, '865 patent at 8:23-26).

The scientific literature explains why there is a need for co-solvents:

> Frequently a solute is more soluble in mixtures of solvents than in one solvent alone. This phenomenon is known as *cosolvency*, and the solvents that, in combination, increase the solubility of the solute are called *cosolvents.*

(Dkt. 146, Ex. 50 at 225 (emphasis in original)).

Mylan's expert, who undisputedly is one of ordinary skill in the art, provided the meaning of organic co-solvent to those of ordinary skill: the term "solvent" is well-known in the art (and

commonly defined) as a pharmaceutical excipient (*i.e.*, an ingredient) "[u]sed to dissolve another substance in preparation of a solution." (Dkt. 146, MacMichael Decl. ¶ 52) (internal citations omitted). Dr. MacMichael cites to multiple literature sources from the pharmaceutical formulation art to support this common understanding of a person of ordinary skill in the art. (*Id.* ¶¶ 40-44; *see* Dkt. 269-1, MYL PPP at slides 9-14).[3]

Dr. MacMichael explains that a person of ordinary skill in the art also knows that a co-solvent is a pharmaceutical excipient used in conjunction with a primary solvent to increase the solubility of the substance in question. (Dkt. 146, MacMichael Decl. ¶¶ 52-53; Dkt. 269-1, MYL PPP at slide 15 ("A co-solvent, by definition, changes the overall behavior of the -- of the combined mixtures of the two solvents.")). More specifically, the co-solvent works in conjunction with a primary solvent (*e.g.*, water) to better dissolve the drug substance. (Dkt. 146, MacMichael Decl. ¶ 19). In the '865 patent, the drug substance is the specific

[3] (*See also* Dkt. 146, Ex. 44 at 125 (to prepare solutions, "…one or more solvents are used to dissolve the drug substance"); Dkt. 146, Ex. 49 at 211 (solvent is "the dispersing medium" that dissolves the solute); *id.* at 229 ("A common way to increase drug solubility is through the use of a water miscible organic solvent…. Addition of a cosolvent … thereby improv[es] solubility"); Dkt. 146, Ex. 52 at 1014 ("injectable formulations currently on the market… utilize one or more cosolvents to solubilize the active constituents…. The use of water-miscible cosolvents is by far the most versatile means of increasing the solubility of drugs"); Dkt. 146, Ex. 53 at 912 ("Cosolvents are used to increase the solubility of the poorly soluble drug in water… Water-miscible cosolvents operate on the principle of lowering the dielectric constant property of water, thereby increasing the aqueous solubility of poorly water-soluble drugs.")).

VEGF antagonist fusion protein required by the claims. (*Id.* ¶ 54; *see also* Dkt. 269-1, MYL PPP at slide 8). Dr. MacMichael thus concludes that a person of ordinary skill in the art would understand the phrase "organic co-solvent" in claim 1 to have its plain and ordinary meaning: *an organic substance added to a primary solvent to increase the solubility of [another substance]*. (*See, e.g.*, Dkt. 146, MacMichael Decl. ¶¶ 55, 57).

Regeneron argues that "organic co-solvent" should be given its plain and ordinary meaning, but does not give the Court a different plain and ordinary meaning construction for the term "organic co-solvent." (Dkt. 146, MOB at 11; Dkt. 173, MRB at 3).

This Court "rejects[] at the outset[] the notion that the disputed claim terms … can be construed simply by reference, without explanation, to the 'plain and ordinary meaning.'" *Baxter Healthcare Corp. v. Mylan Lab'ys Ltd.*, 346 F. Supp. 3d 643, 653 (D.N.J. 2016). Regeneron "cannot avoid defining its own claim terms by asserting that its claims have a plain meaning," and effectively appoint itself "arbiter of whether its [own] claims are clear and unambiguous." *Liebel-Flarsheim Co. v. Medrad Inc.*, No. 1:04-CV-607, 2006 WL 335846, at *6 (S.D. Ohio Feb. 14, 2006) (quoting *Moore U.S.A., Inc. v. Standard Register Co.*, 2000 WL 876884, at *3 (W.D.N.Y. 2000)) (internal quotations omitted).

Regeneron proposes that the Court just "acknowledge[e]" that "polysorbate is an organic co-solvent," and need not "consider what additional substances this [organic co-solvent] claim term encompasses." (Dkt. No. 124, ROB at 6). That is not the proper course of action.

First, it has long-been established that "claims are not construed 'to cover' or 'not to cover' the accused device." *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985); *see also NeoMagic Corp. v. Trident Microsys., Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002) (same). Second, it will not "resol[ve the] disputed meanings and technical scope [of the claims]" or "clarify… what the patentee covered by the claims." *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). Mylan challenges the '865 patent claims on both non-infringement and invalidity. (*See, e.g.*, Dkt. 47, Answer at Counterclaim ¶¶ 156-57; *see also* Dkt. 269-1, MYL PPP at slides 22-23 (illustrating the inapplicability of Regeneron's proposal to the prior art)). Claims must be construed similarly for infringement and invalidity. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001); *W.L. Gore Assocs., Inc. v. Garlock, Inc.*, 842 F.2d 1275, 1279 (Fed. Cir. 1988). The term "organic co-solvent" needs a single clear

construction that will apply for both analyses. Only Mylan's claim construction proposal serves that purpose.

Since Dr. MacMichael's description of an "organic co-solvent" is unrebutted, it is adopted as the plain and ordinary meaning of "organic co-solvent."

The intrinsic record, and the role of polysorbates

Regeneron did not provide an actual construction to assist the Court to clarify the meaning of "organic co-solvent" to one of ordinary skill, but Regeneron does ask the Court to confirm that various ingredients ***must always*** qualify as the claimed "organic co-solvent," namely "polysorbate 20, polysorbate 80, polyethylene glycol, or propylene glycol, or a combination thereof." (Dkt. 124, ROB at 5). Regeneron accuses Mylan of wanting to preclude them from being categorized as organic co-solvents. (Dkt. 124, ROB at 5; Dkt. 174, RRB at 6).

Mylan does not dispute that there are ***some formulations*** where a polysorbate ingredient may act as a co-solvent. The specification does label some formulations' polysorbate as a "co-solvent." (*See, e.g.*, Dkt, 146, MacMichael Decl. ¶ 59 (acknowledging that polysorbate may be used as a co-solvent in certain embodiments of the '865 patent)). But deciding whether a particular ingredient in a particular formulation qualifies as an "organic co-solvent" under the claims is premature—that analysis

occurs after claim construction, and during the infringement and invalidity part of the case. (Dkt. 173, MRB at 2-3; Hearing Tr. at 38:19-40:7). Mylan objects to permanently pre-judging ***all*** polysorbates as ***always*** organic co-solvents, irrespective of formulation purpose or amounts, during claim construction. (Dkt. 146, MOB at 9-10; Dkt. 124, MRB at 4; Hearing Tr. at 57:22-60:2).

Regeneron responds that the meaning of co-solvent cannot consider whether a given ingredient is serving a function, role or purpose within the formulation, citing *Ecolab, Inc. v. Environchem, Inc.*, 264 F.3d 1358, 1367 (Fed. Cir. 2001) and *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 731 (Fed. Cir. 2014). (Dkt. 174, RRB at 8-11; Hearing Tr. at 21:8-22:16; Dkt. 268, REG PPP at slide 21).

In *Ecolab*, the district court construed the term "substantially uniform" to require that the claimed alkaline detergent produce a "homogenous cleaning solution … over the life of the cast." *Ecolab*, 264 F.3d at 1364-65. The Federal Circuit disagreed that this latter requirement—staying homogenous over the life of the cast—was required by the "substantially uniform" claim language. *Id.* at 1367. The Federal Circuit *did* agree though that while "there is no claimed functional requirement as to forming a homogeneous wash solution throughout the cast life," the detergent solution *did* have to "contain components capable of 'ware and hard

surface washing.'" *Id.* at 1366. Thus, *Ecolab* does not preclude ensuring that the meaning of "co-solvent" describes what a solvent is supposed to do, *e.g.*, help dissolve something.

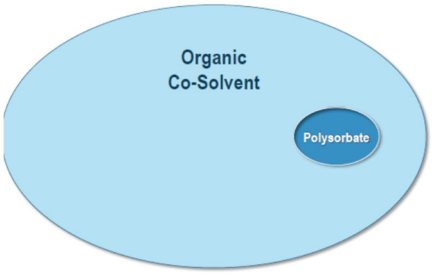
The parties vigorously contested the significance of *GlaxoSmithKline* at the hearing. (Hearing Tr. at 22:4-23:18, 54:11-55:11). *GlaxoSmithKline* involved a Section 112 written description challenge; the Federal Circuit considered this question "***without*** resolving the claim-construction dispute." 744 F.3d at 726 (emphasis added). GlaxoSmithKline's claims were to the drug dutasteride, and "any 'pharmaceutically acceptable *solvate thereof*,'" with solvate referring to a "crystalline" structural arrangement of the atoms of the drug compound. *Id.* at 726-27 (emphasis in original). When the Federal Circuit explained that "solvate" lacked a functional component, it was in the context of differentiating prior *written description* cases where patentees claimed a functional result without a sufficiently supportive specification. *Id.* at 730-31 (reciting cases involving claims to plasmids with a DNA coding sequence broadly defined by its function; claims to all genetic material capable of encoding insulin; claims to an antibody's ability to bind to an antigen, etc.). Even so, when the Federal Circuit discussed the GlaxoSmithKline patent's written description, it noted that a solvate must "originate[] in a 'solution,' which is a mixture of

two substances: a 'solute' dissolved in a 'solvent.'" *Id.* at 727. *GlaxoSmithKline*'s description of a solvent as something that *dissolves* something else is what Dr. MacMichael explained "[p]ersons of skill in the art widely understand": co-solvents are "***used to dissolve*** another substance." (Dkt, 146, MacMichael Decl. ¶ 20) (emphasis added); *see also id.* at ¶ 41 (citing Dkt. 146, Ex. 44; Dkt. 146, Ex. 49; Dkt. 146, Ex. 50; Dkt. 146, Ex. 51; Dkt. 146, Ex. 52).

The function that an ingredient plays in a formulation is not an idle issue. Water is a universally recognized solvent, but in some contexts, does not work as a solvent (*e.g.*, it cannot dissolve sand). (Hearing Tr. at 58:4-14; Dkt 146, Ex. 49 at 211 (noting mixing sand and water only produces a suspension, not a solution)). Polysorbates may in some circumstances—including for some of Regeneron's specification examples or dependent claims—qualify as a co-solvent. But the scientific literature recognizes polysorbate's role in a pharmaceutical formulation as a "surfactant." (Dkt. 173, MRB at 4-6; Hearing Tr. at 45:2-46:15; Dkt. 269-1, MYL PPP at slides 10, 14; MOB Ex. 53 at 11 ("*Surface active agents:* polysorbate 80…")). The terms surfactants and "co-solvents" also are not used interchangeably. *AstraZeneca*, 384 F.3d at 1338-41 (specification recognized that surfactants and co-solvents were different categories of solubilizers); *see also* Dkt.

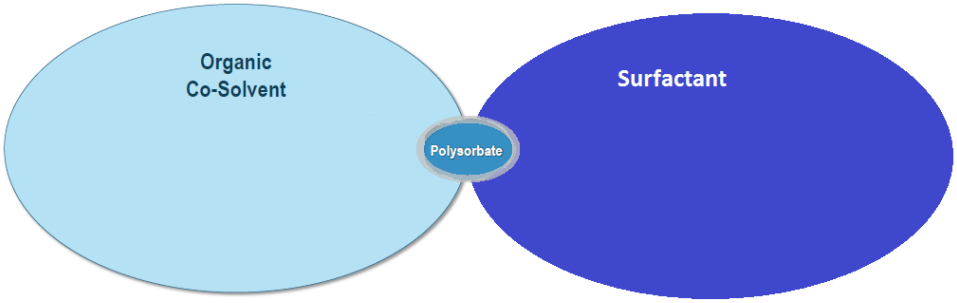
146, Ex. 53 at 917 (three different categories of solubilizers: cosolvents, surface active agents, and complexing agents). Even in this litigation, for other claims, Regeneron calls polysorbate a surfactant.[4]

At oral argument, Regeneron presented a Venn Diagram proposing that the relationship between organic co-solvent and polysorbate looked like this:




(Dkt. 268, RGN PPP at slide 17). The evidence of record suggests this is more accurate:

[4] Regeneron continues to assert, *e.g.*, claim 7 of the '572 Dosing Patent, which requires a regimen that uses aflibercept "formulated with a nonionic surfactant." (Dkt. 146, '572 patent at claim 7). In its pleadings, Regeneron alleges that Mylan infringes the '572 patent claims. (Dkt. 1, Compl. at 32-34, ¶¶ 223-232). Regeneron and its expert assert that the same polysorbate Regeneron wants to call a "co-solvent" for the purpose of the '865 patent *also* meets the "formulated with a nonionic surfactant" element of the '572 Dosing Patent's formulation claims. Regeneron's infringement contentions and expert report regarding infringement are not currently part of the claim construction record, since Regeneron submitted them after the Markman briefing and/or hearing; Mylan is willing to file the relevant evidence if needed by the Court.




(Hearing Tr. at 58:15-60:2). The parties plainly dispute whether, for any given formulation, polysorbate always qualifies as an organic co-solvent; a surfactant; or both. Since Regeneron's contentions accuse polysorbate of being a co-solvent for this patent, and a surfactant for another patent, it is hardly surprising that Mylan's invalidity contentions likewise identify prior art formulations with polysorbates could satisfy the '865 patent's co-solvent element. (Hearing Tr. at 16:16-17:18, 52:8-53:11; Dkt. 268, RGN PPP at slides 19-20). This also indicates that the parties' dispute is more of an infringement/invalidity dispute, not a claim construction dispute, the latter of which must stay focused on what "organic co-solvent" means to one of ordinary skill, having reviewed the intrinsic evidence.

Regeneron's other specification-related arguments also do not justify changing the plain and ordinary meaning of "organic co-solvent" to mandate including all polysorbates.

Regeneron could have used lexicography in the specification to change the plain and ordinary meaning to mandate that organic

co-solvents means polysorbate. *Phillips*, 415 F.3d at 1312–17. But the standard for lexicography is "exacting." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014). Regeneron admits it did not use lexicography here. (*See, e.g.*, Dkt. 174, RRB at 1; Hearing Tr. at 73:18-23, 9:23-10:15). Patentees can disavow claim scope if the specification "describes a feature of the invention" and "criticizes other products" that "lack the same feature." *AstraZeneca*, 384 F.3d at 1340. But there must be a clear "demonstrat[ion of] an intent to deviate from the ordinary and accustomed meaning of a claim term through expressions of manifest exclusion or restriction." *Intellectual Ventures I LLC v. T-Mobile USA, Inc.*, 902 F.3d 1372, 1378-79 (Fed. Cir. 2018) (cleaned up)). Regeneron does not contend disavowal applies. (*See e.g.*, Dkt. 174, RRB at 13-14).

Regeneron suggested that its specification defined "co-solvents" by implication to require polysorbate. (Hearing Tr. at 9:17-10:20). Regeneron insists that "the specification repeatedly confirms that substances like polysorbate ***are*** organic co-solvents," in a "repeated and unequivocal" way. (Dkt. 124, ROB at 5 (emphasis added), 6; *see also* Dkt. 174, RRB at 6).

The specification carefully avoids being so absolute. The specification repeatedly qualifies its polysorbate and polyethylene glycol descriptions. For example, in column 2, the

specification states that "the organic co-solvent ***may be*** polysorbate… polyethylene glycol … or a combination thereof," not 'is" or "must include" one or more of these ingredients. (Dkt. 146, '865 patent at 2:39-42) (emphasis added). Similarly, when column 2 states that the "organic co-solvent is polysorbate and/or PEG," and gives examples of preferred formulations, the immediately preceding text qualifies all of them as reflective of "various ***embodiments***." (*Id.* at 2:49-50) (emphasis added). The same holds true for the formulations with polysorbate in column 3 onwards, which are specific formulation recipes described as "specific preferred embodiment[s]" or "examples." (*Id.* at 3:1-10; *id.* at 3:28-29 ("In another ***embodiment***, the organic co-solvent is selected from one or more of polysorbate…) (emphasis added); *id.* at 7:2-5 ("An ***example*** of a pharmaceutically acceptable liquid formulation comprises … an organic co-solvent ***such as*** polysorbate…"); *see generally* cols. 3-4 (describing formulations with polysorbate as embodiments)). The '865 patent claims also avoid such absolutes, such as by stating "wherein said organic co-solvent ***comprises*** polysorbate." (*Id.* at claims 2-5; Dkt. 269-1, MYL PPP at slide 5); *CIAS, Inc. v. All. Gaming Corp.*, 504 F.3d 1356, 1360-61 (Fed. Cir. 2007) (noting that "comprising" just means "including").

But even assuming the desirability of defining "organic co-solvent" by implication, the '865 patent's specification forecloses that option, reiterating that "the terminology used herein is for the purpose of ***describing particular embodiments only***; [it] ***is not intended to be limiting***." (Dkt. 146, '865 patent at 8:8-13) (emphasis added). The specification emphasizes that the "scope of the present invention ***will be limited only to the appended claims***." (*Id.* at 8:13-14 (emphasis added); *id.* at 5:32-38 (stating that examples and embodiments were non-limiting, and that "the scope of the present invention will be limited only by the appended claims")). Regeneron thus asks the Court for a claim construction to change its claims' parameters based on its particular embodiments, despite its specification reiterating not once, but twice, to ***not*** do that. Regeneron's approach thus conflicts with the specification.

Regeneron alternatively speculates that if proof of an ingredient's "functional" behavior is needed to qualify as a co-solvent, this causes all of the claims to exclude preferred embodiments. (Dkt. 124, ROB at 7; Dkt. 174, RRB at 8-9). The briefing citations and excerpt of Dr. MacMichael's testimony that Regeneron provided at oral argument on claims 2-5 does not support the premise. (Hearing Tr. at 55:12-56:13; Dkt. 268, RGN PPP at slide 27).

The '865 patent has 64 claims. While claim 1 requires a co-solvent, claim 51 does not, even though claim 51 does expressly require using polysorbate in the formulation. (Dkt. 146, '865 patent at claim 51 ("ophthalmic formulation comprising: (a) 40 mg/ml of a glycosylated VEGF antagonist fusion protein" from "SEQ ID NO:4; (b) ***0.03% to 0.1% polysorbate***" and other excipients) (emphasis added)). Claim 51 corresponds to embodiments, *e.g.*, those in column. 2, lines 53 through 57; in Example 3 (40 mg/mL formulation, fusion protein, 0.03% polysorbate 20, and other excipients); and in Example 4 (40 mg/mL formulation, fusion protein, 0.03% polysorbate 20, and other excipients). Example 2 of the '865 patent also is an embodiment of claim 1. (Hearing Tr. at 42:25-43:6). Regeneron thus does have claims that cover its polysorbate embodiments; and its non-polysorbate embodiments. While courts should consider whether a claim construction would exclude all embodiments, "where the patent describes multiple embodiments, every claim does not need to cover every embodiment." *Pacing Techs., LLC v. Garmin Int'l, Inc.*, 778 F.3d 1021, 1026 (Fed. Cir. 2015).

Thus, in view of the intrinsic record, "organic co-solvent" cannot be construed to require covering all polysorbates in all circumstances. *See Conoco, Inc. v. Energy & Env't Int'l., L.C.*, 460 F.3d 1349, 1358 (Fed. Cir. 2006) (finding a specification that

stated an amount of alcohol "may vary widely but it usually forms between about 0 and 70 weight percent of the suspending material" did not limit the claims to between 0 and 70 percent).

Given the above, the Court adopts Mylan's definition of "co-solvent" to have its plain and ordinary meaning to a person of ordinary skill in the art: it is an organic substance added to the primary solvent to increase the solubility of the solute, here a VEGF antagonist. The Court will decide the question of whether a specific formulation with polysorbate 20, polysorbate 80, polyethylene glycol, or propylene glycol satisfies the "organic co-solvent" claim language during the infringement and invalidity part of this case.

**b. "Present in Native Conformation"**

The parties generally agree that the "native" protein for purposes of the claims here is the original, intact, aflibercept fusion protein, standing alone as a single molecule. (Hearing Tr. at 29:15-17 (Regeneron stating "you have something present in the native conformation. That's the aflibercept by itself."); *id.* at 61:22-24 (Mylan stating "native conformation, Your Honor, is a reference to the protein in its original form and structure, without any degradation.")).

Proteins are complex biologic molecules. The specification recognizes that the nature of proteins' structures present

pharmaceutical formulators with unique issues. Proteins can degrade chemically, through "deamination" reactions, "aggregation," by "clipping of the peptide backbone," and by "oxidation of methionine residues." (Dkt. 146, '865 patent at 5:56-58). Proteins can degrade physically, through "many phenomena, including, for example, aggregation and/or precipitation." (*Id.* at 5:58:60). If aflibercept is chemically changed, it is no longer aflibercept; if it is aggregated or precipitated, it also will no longer be a "single aflibercept molecule by itself." (Hearing Tr. at 28:25 – 30:7).

Plain and ordinary meaning

Dr. MacMichael, consistent with the specification, explained that the "plain and ordinary meaning of the term '[present in] native conformation' requires the VEGF antagonist fusion protein to be present in a form that does not exhibit chemical or physical instability. A POSA would understand that aflibercept '[present in] native conformation' is present in a form that does not exhibit chemical or physical instability." (Dkt. 146, MacMichael Decl. ¶ 21).

Rather than rebut Dr. MacMichael's explanation of how a person of ordinary skill in the art would understand the term "native conformation," Regeneron suggests that the entire claim limitation in which the term appears—i.e., "wherein at least 98% of the VEGF

antagonist is present in native conformation…as measured by size exclusion chromatography"—has a plain and ordinary meaning. (*See, e.g.*, Dkt. 124, ROB at 8-9). That sidesteps the question of what "native conformation" ordinarily means. Regeneron did not give the Court an actual construction of the disputed claim term, "native conformation." Regeneron had to provide its different meaning, if any. *Liebel-Flarsheim*, 2006 WL 335846, at *6; *Baxter*, 346 F. Supp. 3d at 653. It didn't. Mylan's ordinary meaning applies.

The intrinsic record, and concepts of stability

Regeneron argues that "native conformation" cannot consider "all aspects of physical and chemical stability," but "only" the "aspects of stability that are described in the specification and that may be the measured by the specific technique required by the claims," (Dkt. 174, RRB at 11; Dkt. 268, RGN PPP at slide 31), which is just protein "size[], not different oxidation or deamination profiles." (Dkt. 174, RRB at 12). At oral argument, Regeneron's counsel characterized this as a measure of aggregation only. (Hearing Tr. at 30:19-31:7).

Dr. MacMichael's testimony—which is unrebutted—confirms that a person of ordinary skill in the art knows that aflibercept may be able to comply with the claims' size exclusion chromatography (SEC) test, without independently satisfying the "native conformation" standard. (Dkt. 268, RGN PPP at slide 38 (citing

MacMichael Dep. Tr. at 203:8-19)). The '865 patent's specification knew how to discuss aggregation properties; for example, it described and defined "substantially free of aggregates," to mean that "at least 90% of the weight of fusion protein is not present in an aggregate" at the time of formulation. (Dkt. 146, '865 patent at 6:45-55 (also defining "substantially free of contaminants")). Had Regeneron wished to focus solely on the state of protein aggregation, as it proposes to do with its current construction, Regeneron should have used aggregation-specific terms, versus the more general "native conformation" term that those of ordinary skill in the art know is tied to multiple stability considerations.

Regeneron's approach also creates the same problem that Judge Bailey raised in *AstraZeneca AB v. Mylan Pharms., Inc.*, No. 22-35, 2022 WL 17178691, at *6-7 (N.D.W. Va. Nov. 23, 2022): it collapses and subsumes a separate "native conformation" claim term element into what Regeneron calls its aggregate test requirement, which would render the "native conformation" language directed to intact aflibercept superfluous. (Dkt. 174, RRB at 12; Hearing Tr. at 66:5-69:18). These multiple distinct elements can't be rolled into one.

Regeneron proposes that since it used "stable" and "native conformation" in other claims in related patents, "native

conformation" can't involve *any* general stability concepts. (Dkt. 174, RRB at 11-12). The patent it cites, U.S. Patent No. 8,092,803, does not support this premise. The '803 patent's claim 1 applies the term "stable" to the phrase, "liquid ophthalmic formulation," thereby referencing the formulation as a whole. (Dkt. 174, '803 patent at claim 1). The claim applied the term "native conformation" to its description of the VEGF-antagonist, which is the protein within the formulation. (*Id.*) This also differentiates the decision Regeneron relied on, *AstraZeneca*, 2022 WL 17178691, at *6-7: Judge Bailey concluded that the "pharmaceutical composition" could not be construed to be "stable" because other claims in the same family limited the pharmaceutical composition to a stable one. Here, there is nothing inconsistent with a claim requiring the *entire formulation*, which includes both the drug and its excipients, to be stable, while also ensuring that *the protein component* in that formulation independently remains chemically and physically intact in its native conformation.

Regeneron's "stability" argument also conflicts with the prosecution history. Regeneron had claims that lacked the "native conformation" term, which the PTO rejected. (*See* Dkt. 146, Ex. 16 at 2-6). To overcome the rejection, Regeneron added the language "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." (*Id.* at 2). Regeneron represented this element as "relating to the ***stability*** of the protein conformation in storage over a period of time" and represented that this element was "not contained within any of the claims" of the '261 patent that served as the basis for the double-patenting rejection. (*Id.* at 5). The PTO relied on this amendment to withdraw the rejection. (Dkt. 146, Ex. 15 at 2). During prosecution, Regeneron also characterized the "present in native conformation" clause as relating to the general stability of the required protein (*id.* at 2, 5); but now says the term does not involve general stability, rather only purity. (Dkt. 174, RRB at 11-14). Regeneron should be held to its statements to the PTO that "native conformation" relates to the more generalized stability concepts.

Given the above, and both the understanding of those of ordinary skill in the art, as well as the intrinsic record, the term "native conformation" itself is not limited to, and is not only evaluated by, one size exclusion chromatography test, as Regeneron proposes.

Thus, the claim language, "native conformation" is construed to be given its plain and ordinary meaning, which is the original intact form of the VEGF antagonist, which is a form that does not

exhibit chemical or physical instability. The question of whether a given VEGF antagonist in a particular embodiment or formulation meets other claim elements (*e.g.*, percentages following storage at 5°C for two months as measured by size exclusion chromatography), is properly considered during the infringement and invalidity part of the case.

**B. "The Treatment Patents" or "Dosing Method Patents" (The '572 and '601 patents)**

Independent of the claim constructions above, Mylan argues that neither claim term can be construed to have any patentable weight. The Federal Circuit has identified several reasons why, as a matter of law, language found in patent claims cannot be construed to have patentable weight. This question is properly decided during claim construction. *Praxair*, 890 F.3d at 1033 ("the Board properly addressed the printed matter doctrine during claim construction"); *In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018) (noting that the district court addressed the issue of whether purpose and results claim language was limiting during claim construction).

Claim language that conveys information cannot be construed to have patentable weight.

Claim language is construed to lack patentable weight when it involves subject matter that 35 U.S.C. § 101 treats as unpatentable—such as abstract ideas, information, or mental steps.

*Praxair*, 890 F.3d at 1032. One doctrine, called the "printed matter" doctrine, historically "referred to claim elements that literally encompassed 'printed' material," but "the doctrine has evolved over time to guard against attempts to monopolize the conveyance of information using any medium." *C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1381 (Fed. Cir. 2020). While the original "'printed matter' cases involved the addition of printed matter, such as written instructions, to a known product," the Federal Circuit has found "no principled reason for limiting their reasoning to that specific factual context ... [T]he rationale underlying these cases extends to the situation … wherein an instructional limitation is added to a method … known in the art." *King Pharms. Inc. v. Eon Labs Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010). Method claim language that describes "things to think about" as opposed to, "actions to take," is usually construed to lack patentable weight. *Praxair*, 890 F.3d at 1033-34 (limitation "merely requires a medical provider to *think* about the information claimed" and deserved no patentable weight).

Old methods cannot be made new or different by adding on statements of purpose or result.

In the context of method of treatment claims, an independent but related reason why claim language lacks patentable weight is when language within a claim just describes an old method, without transforming it into something new. This happens when, *e.g.*,

patent claims just add statements of purpose, or proposed results, to the existing old method.

For pharmaceutical treatment methods, the Federal Circuit has explained that when claim language "is only a statement of purpose and intended result," and the language "does not result in a manipulative difference in the steps of the claim," such claim language is non-limiting. *Bristol-Myers*, 246 F.3d at 1376. Even when a patentee argues that the method steps would impact the efficacy of the treatment method, if the claimed process "is not directed to a new use," but "the same use," the claim language lacks patentable weight, because "[n]ewly discovered results of known processes directed to the same purpose[s] are not patentable." *Id.*; *In re Copaxone*, 906 F.3d at 1023 (dependent claims that merely described results or outcomes of claimed method construed to be non-limiting statements of intended effect).

Thus, if claim language "does not change the express dosing amount or method already disclosed in the claims, or otherwise result in a manipulative difference in the steps of the claims," it is "non-limiting" and lacks patentable weight. *In re Copaxone*, 906 F.3d at 1023.

> The exclusion criteria and BCVA scores are information; and neither changes the manipulative steps of the method.

Following the legal analyses above, for method-of-use claims, the key issue is whether the claim language is 1) informational; and 2) functionally related to the substrate—that is, the language changes not mere thoughts or outcomes, but provides ***action steps*** that the method requires. *See C R Bard*, 979 F.3d at 1381 (noting the test for printed matter is whether it "merely informs people of the claimed information, or whether it instead interacts with the other elements of the claim to … ***cause a specific action*** in a claimed process.") (emphasis added); *Bristol-Myers*, 246 F.3d at 1376 (stating that language "is only a statement of purpose and intended result" where its "expression does not result in a ***manipulative difference in the steps of the claim***") (emphasis added); *King*, 616 F.3d at 1279 ("Informing a patient about the benefits of a drug in no way transforms the process of taking the drug …. Irrespective of whether the patient is informed about the benefits, ***the actual method … is the same.")*** (emphasis added).

The claim language, "wherein the exclusion criteria for the patent include…" lacks patentable weight.

Regeneron initially argued that its "exclusion criteria" were intended to "define the population that is to be treated." (Dkt. 124, ROB at 19). A list of exclusion criteria to help doctors identify the patients to treat is informational under *Praxair* claims 1 and 3. *Praxair* claim 1's claim language gave doctors information so that they could "elect to avoid treating one or

more … patients with inhaled nitric oxide" to "avoid putting the one or more patients at risk of pulmonary edema." *Praxair*, 890 F.3d at 1029. Claim 3 instructed doctors to weigh the comparative risks of treatment options "in order to arrive at a decision of whether or not to treat" the patient. *Id.* at 1033. The Federal Circuit characterized such steps as language that "merely requires a medical provider to *think about* the information" before making a treatment decision. *Id.* That is all that happens with exclusion criteria—the criteria list things to think about for the patient groups to potentially treat.

The PTAB agreed in its "exclusion criteria" claim analysis. It characterized the "exclusion criteria" as a "list" that "relays direct information to the practitioner" comparable to "the listing of contraindications included with the packaging of any other drug," and hence "analogous to claim 1 in *Praxair*." (Dkt. 254-2, '601 patent Inst. Decision at 13-14).

At oral argument, Regeneron disputed that its language could be "informational," because "patients don't come to the doctors prescreened," calling it a "gating decision that the physician has to make before continuing and treating those patients that do not have the infection or the inflammation." (Hearing Tr. at 92:4-13, 134:3-13). Mylan pointed out that under *Praxair* claims 1 and 3 this still is "informational" because it merely asks doctors to

think about the question; the information from the "decision" doesn't change the dosing method. (*Id.* at 108:12-18, 110:4-16). The "information" ***is*** the exclusion criteria, because, like a sheet of paper listing contraindications for a drug product, it suggests thinking about whether a patient is in the state of inflammation of infection. (*Id.* at 102:2-116:18, 140:13-141:17). The dose, drug, and schedule that the '572 and '601 patents claim, was known, old, and doesn't change based on the outcome of reading, knowing about, or thinking about any information pertaining to a patient's state of inflammation/infection. (*See, e.g.*, Hearing Tr. at 102:2-104:10; Dkt. 146, MOB at 1 ("Regeneron cannot now recapture claim scope long known")).

The Federal Circuit is clear that for claim instructions to be "informational" it does not require the "information" to be presented as an instruction sheet; "[t]here is no meaningful distinction between claim limitations directed to written information," or "verbal information," or "mentally processed information." *Praxair*, 890 F.3d at 1033-34. Since all that happens here with the exclusion criteria, even under Regeneron's non-clinical trial construction, is that a doctor mentally processes information about the condition of a patient, the "exclusion criteria" claim language is plainly directed to informational content.

Regeneron argued that its exclusion criteria can be salvaged for the same reasons as *Praxair* claim 9. The claims here are simply not structured the same way as *Praxair* claim 9. In *Praxair* claim 9, the doctor started treatment, did an assessment, and if the doctor got a certain result from that assessment, the claims then "***require[d]*** a medical provider to take a specific action, discontinuing treatment." *Praxair*, 890 F.3d at 1035. Thus, in Praxair claim 9, the patients were (a) actually undergoing a treatment regimen; and (b) their medical provider was obligated to *change* the existing treatment regimen's steps upon receiving the information.

Regeneron proposed that its "exclusion criteria" do "prescribe actions," namely "assessing and excluding" the patients. (Dkt. 174, RRB at 19-20; Hearing Tr. at 85:17-21; Dkt. 268, RGN PPP at slide 63). Mylan responds that the "exclusion criteria" language does not "require" a doctor or patient to take any action at all. (Dkt. 146, MOB at 14-17; Dkt. 173, MRB at 18-20; Hearing Tr. at 106:6-108:11). As discussed in Section IV(F)(1)(b)(iii) above, the "action" the doctor may take would preclude using claim 1's method in the first instance. (*See, e.g.*, Dkt. 269-1, MYL PPP at slide 72). This distinguishes the claims here from Praxair claim 9, where the method was required to start, ***then*** it could be modified based on the information. *Praxair*, 890

F.3d at 1035. All that will happen here under Regeneron's proposed construction is that the method will never begin upon prescreening and finding infection/inflammation. That won't change the method of dosing 2 mg aflibercept, on the regimen schedule set forth in the underlying independent claim 1.

The PTAB agreed with Mylan. Even assuming that an "assessment" gets made, as Regeneron suggests, the express language of the "claims do not expressly recite any positive step to be performed" or a "negative step *not* to be performed" once the assessment is made. (Dkt. No. 254-2, '601 patent Inst. Decision at 14). Regeneron's own witnesses also acknowledged that doctors can treat patients with aflibercept or not, even in the face of an ocular infection or inflammation. (Dkt. 269-1, MYL PPP at slide 61 (citing Chu Tr. at 120:21-121:20)). If this knowledge does not force a change in the treatment regimen, then the language is advisory, not mandatory. (Dkt. 254-2, '601 patent Inst. Decision at 13-14; Dkt. 269-1, MYL PPP at slide 60).

District courts are not bound by the PTAB. *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293-94 (Fed. Cir. 2017). This is because "the PTAB properly may reach a different conclusion based on the same evidence," for the PTAB and district courts function under different evidentiary standards and burdens of proof (preponderance of the evidence before the PTAB, clear and

convincing evidence before the district court). *Id.* at 1294.[5] The Federal Circuit has recognized though that "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

Thus, while the PTAB decision is useful persuasive evidence, and Regeneron has indicated it will attempt to develop the record further on this point before the PTAB, (Hearing Tr. at 87:6-88:5), the Court makes its own findings without deference to the PTAB.

The claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice. Even assuming that the doctor or patient secures the results of inflammation or infection screening, and learns the benefits of patients not taking aflibercept when their eyes are not inflamed or infected (which is *Praxair* claim 1); or pauses to weigh the risk of delaying treatment because of infection or inflammation versus the risks of delaying treatment because a patient risks blindness (which is Praxair claim 3)—what changes? The language does not ***require*** any action step to be taken as a consequence. Nothing has "transform[ed] the process of taking the drug" aflibercept in the claimed method—the "actual

[5] The PTAB is scheduled to issue a Final Decision for the '601 patent by January 11, 2024. Under current Federal Circuit precedent, even if this Court were to uphold the validity of the '572 and '601 patent claims being disputed here after trial, the PTAB can independently declare those same claims unpatentable; if the PTAB's judgment is affirmed, Regeneron cannot enforce such claims against Mylan.

method" found in the underlying independent claim, *e.g.*, 2 mg of aflibercept, on the stated dosing schedule, remains the same. *King*, 616 F.3d at 1279 (when claim language did not change the underlying treatment method, it deserved no patentable weight).

Even under Regeneron's "assess and exclude" approach, a patient either never starts the method (and hence the method doesn't change); or, if doctors screened for the information and found no infection or inflammation, the same method proceeds. (Hearing Tr. at 90:1-93:20). This confirms that the "exclusion criteria" are, at best, a non-binding informational "option" for doctors to consider. (*See, e.g.*, Dkt. 254-2, '601 patent Inst. Decision at 15).

Claims that had an actual active step based on the exclusion criteria to be analogous to the *Praxair* claim 9 situation would ***require*** that patients lacking ocular inflammation or infection participate in a modified method (such as a different drug, dose, or schedule); or ***require*** ongoing treatment to stop—but that would only happen if inflammation or infection arises while the method is underway, and Regeneron insists its exclusion criteria are directed to pre-screening *before the method even starts*. (Dkt. 124, ROB at 19-20; Hearing Tr. at 92:4-23, 107:5-109:15, 131:3-25; Dkt. 269-1, MYL PPP at slides 58-60).

As noted in Section IV(F)(1)(b)(iii), above, the specifications of the '601 and '572 patents did discuss action steps involving assessment and administration, or changing dosing regimens based on patient characteristics, but the action words associated with those steps in the specification are missing from the disputed claims, and courts cannot rewrite claims to add them. *See Arlington Indus.*, 632 F.3d at 1255 n.2; *see also Apple*, 757 F.3d at 1297-98 (how a patentee claims their invention is "the claim drafter's choice" and "any resulting risk that emanates from that choice is not a basis for the court to rewrite a claim").

Regeneron, as discussed above, also urges applying the exclusion criteria to patients on an individual basis, not within a clinical trial context. Mylan points out that the failure of the exclusion criteria to modify the underlying dosing method, should an individual patient meet them, also independently renders the claim language non-limiting under *Bristol-Myers*, 246 F.3d at 1376, and *In re Copaxone*, 906 F.3d at 1022-23. (Dkt. 173, MRB at 11-13, 16-18). This is because even assuming that an individual patient is diagnosed with the condition, satisfying the exclusion criteria does not mean doctors will change anything about the underlying method—not the drug, not the dose, not the schedule. (*See, e.g.*, Dkt. 173, MRB at 12-13, 18-19; Hearing Tr. at 103:2, 107:5-108:18; Dkt. 269-1, MYL PPP at slides 62-64, 68).

Consequently, since there is no ***requirement*** to take new action that flows from the "wherein the exclusion criteria for a patient include…" information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight.

The Best Corrected Visual Acuity claim language also lacks patentable weight.

Mylan reiterates that if Regeneron is given its proposed construction, such that Best Corrected Visual Acuity refers to an individual patient measurement that occurs outside the clinical trial context, then the claim language merely states a test result that a patient may or may not reach after the method is performed. (Dkt. 173, MRB at 11-18; Hearing Tr. at 110:11-113:4, 129:11-130:11). That independently gives the language no patentable weight.

Regeneron has not disputed that under its interpretation of Best Corrected Visual Acuity, all that happens is that a patient is tested to see if their Best Corrected Visual Acuity value meets the claims' test result threshold. There is no change or modification to the underlying dosing regimen if the test result is obtained, or not. Regeneron's witnesses confirmed that if a patient *is not* meeting a particular BCVA threshold, there in fact is no change that doctors can make to the regimen to ensure a given patient achieves a particular BCVA score. (*See, e.g.*, Hearing Tr.

at 112:7-18, 119:11-20, 129:1-10; Dkt. 269-1, MYL PPP at slide 68).

This renders the claims analogous to the claims in *Bristol-Myers*, where the additional claim elements involved tumor regression and reducing patient toxicity, yet the dosing schedule remained the same. *Bristol-Myers*, 246 F.3d at 1375-76. The Federal Circuit explained the added claim language reflected "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim," and thus the language was construed to be non-limiting. *Id.* at 1376.

The BCVA test score result also follows the claim structure of *In re Copaxone,* 906 F.3d at 1023, where the claim language stating that the dosing regimen would reduce a patient's frequency of relapses was "superfluous, [did] not change the claimed method," and thus was construed to be "non-limiting."

The Federal Circuit also explained that merely adding test score outcomes to a method, as was done in *King*, where patient blood AUC and other test measurements did not change the manipulative steps of the claim, also were non-limiting. 616 F.3d at 1277-79.

An old method of treating patients cannot be made new by describing the results that a patient can get from the treatment

method, whether those results involve reducing side effects; alleviating particular symptoms; or achieving certain test results. All that the Best Corrected Visual Acuity claim language does here under Regeneron's approach is measure a letter score result—it does not change the manipulative steps of the claim.

Thus, the Court finds that the phrase, "Best Corrected Visual Acuity (BCVA)" also is informational; does not change the manipulative steps of the claims; and also should be construed to have no patentable weight.

**C. Manufacturing Patent or Tustian Patents (The '715 Patent)**

**a. "Chemically Defined Medium"**

Intrinsic evidence – the specification definitional language

The parties agree that the specification uses definitional language for "chemically defined medium." (Dkt. 124, ROB at 24; Dkt. 146, MOB at 23). "When a patentee explicitly defines a claim term in the patent specification, the patentee's definition controls." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009). This definitional language includes the '715 patent at column 30 starting at line 44, and states:

> As used herein, the term "chemically defined medium" or "chemically defined media" (both abbreviated "CDM") refers to **a synthetic growth medium in which the identity and concentration of all the ingredients are defined.** Chemically defined media do not contain bacterial, yeast, animal, or plant

> extracts, animal serum, or plasma, *although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*. Chemically defined media may contain inorganic salts such as phosphates, sulfates, and the like needed to support growth. The carbon source is defined, and is usually a sugar such as glucose, lactose, galactose, and the like, or other compounds such as glycerol, lactate, acetate, and the like. … Methods of preparing chemically defined culture media are known in the art, for example, in U.S. Pat. Nos. 6,171,825 and 6,936,441, WO 2007/077217, and U.S. Patent Application Publication Nos. 2008/0009040 and 2007/0212770, the entire teachings of which are herein incorporated by reference.

(Dkt. 146, '715 patent at 30:44-31:5) (emphasis added). This CDM section specifically incorporates WO 217 by reference, (Dkt. 146, '715 patent at cover page, 30:67-31:5, 98:45-49), which makes its specification part of the 715 patent's specification "as if [it] were explicitly contained therein." *Finjan LLC v. ESET, LLC*, 51 F.4th 1377, 1382 (Fed. Cir. 2022) (citation and internal quotation marks omitted).

Both parties agree that the definition must include the bold text above. (Dkt. 124, ROB at 24; Dkt. 146, MOB at 23). Regeneron stops there, but would add the underlined language if the follow-on italicized language also is added. (Dkt. 124, ROB at 24). Mylan's construction included the underlined language, but Mylan would add the italicized text if it has its plain and ordinary

meaning, and *is not* interpreted to add undefined hydrolysates to a CDM. (Dkt. 146, MOB at 23-24).

The Court construes a chemically defined medium to first include the express definition in the specification, where a "chemically defined medium" or CDM means "a synthetic growth medium in which the identity and concentration of all the ingredients are defined. Chemically defined media do not contain bacterial, yeast, animal, or plant extracts, animal serum, or plasma…."

Given this definition, since chemically defined media 1) are defined; and 2) "do not include … yeast … or plant extracts," they cannot include hydrolysates. Hydrolysates are both chemically ***un***defined; and made from the expressly excluded yeast or plant extracts. (Dkt. 146, MOB at 23-24; Dkt. 173, MRB at 21-24). Mylan's expert confirms that those of ordinary skill in the art understand that hydrolysates are "***protein extracts*** derived from plants or yeast" that have been enzymatically digested, rendering them "***undefined*** mixtures of oligopeptides and other unknown components and contaminants." (Dkt. 146, Jungbauer Decl. ¶ 44, 74) (emphasis added). This is outside the scope of the specification's definition, which requires a CDM to be chemically defined. (Dkt. 146, '715 patent at 30:44-31:5; Dkt. 146, WO 217 at [009] (emphasis added); Dkt. 146, Jungbauer Decl. ¶ 74).

The WO 217 publication that column 30's definitional paragraph incorporates by reference highlights the distinction between a chemically defined medium and a hydrolysate one. It explains that cell culture media with "extracts" like "protein hydrolysates derived from plants or yeast" help cells grow efficiently, but come with a downside: "undefined mixtures of oligopeptides and other unknown components and contaminants," will cause "the quality of commercially available lots" to vary "extremely." (Dkt. 146, WO 217 at [003], [006], [009]). WO 217 states that a chemically defined cell culture media that "eliminate[d] … plant and/or yeast derived hydrolysates" and "which do not comprise any added supplementary proteins or oligopeptides," beneficially "increase[ed] the protein and/or virus expression per cell," gave consistent "cell growth" and "increased yield of desired products," and also "obviate[d] the addition of protein hydrolysate to the cell culture medium." (*Id.* at [013] – [016]).

The parties dispute the impact of the italicized text above from column 30 that follows: "…*although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*," and specifically, whether this text allows the CDM definition to reinstate hydrolysates. (Dkt. 146, '715 patent at 30:49-51).

Regeneron contends that the "… *although*" language expands CDM's definition to include hydrolysates. (Dkt. 124, ROB at 25). Mylan responds that Regeneron's approach eviscerates the immediately preceding definitional text as follows:

> a synthetic growth medium in which the ~~identity and concentration of all the ingredients are defined. Chemically defined~~ media do not contain bacterial~~, yeast~~, animal, ~~or plant~~ extracts, animal serum, or plasma…."

(*See* Dkt. 268, RGN PPP at slide 73). Specifically, allowing chemically undefined hydrolysates back into the chemically defined medium via the "…*although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*" clause would cause the medium to 1) fail the requirement that the identity and concentration of all ingredients be defined (and both parties agree this must be part of the CDM definition); and 2) fail the requirement of not containing "yeast … or plant extracts," because hydrolysates are "protein extracts derived from plants or yeast" that have been enzymatically digested. (Dkt. 146, MOB at 23-24; Dkt. 173, MRB at 21-24; Dkt. 146, WO 217 at [004] – [007]; Dkt. 146, Jungbauer Decl. ¶¶ 44, 72-73). If Regeneron intended to permit hydrolysates in the CDM, it could have simply eliminated the words in its definition rather than adding a new "…*although*" clause. Mylan thus proposes that the "…*although*" language must have a different meaning. Consistent with practice in the field

with supplements, it permits adding an ***individual*** protein or polypeptide (*e.g.*, insulin, a growth hormone), whose composition can be known and defined, and not run afoul of the other definitional requirements. (Dkt. 146, Jungbauer Decl. ¶¶ 74, 78; Dkt. 146, MOB at 26-27, Dkt. 176, MRB at 23-24; *see also* Dkt. 146, '715 patent; Dkt. 146, Ex. 45 at 108 ("A commonly used protein in CHO cell culture is insulin which functions as growth factor in CDM."); Dkt. 269-1, MYL PPP at slide 119).

Regarding the understanding of those of ordinary skill in the art, Regeneron offers no rebuttal testimony to Dr. Jungbauer. Regeneron calls Dr. Jungbauer's declaration improper extrinsic evidence under *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996). (Dkt. 174, RRB at 24). But "[e]xperts may be examined to explain terms of art," the "background science" and courts may "mak[e] a factual finding that, in general, a certain term of art had a particular meaning to a person of ordinary skill in the art at the time of the invention." *Teva*, 574 U.S. at 332 (citation and internal quotation marks omitted). Dr. Jungbauer's testimony is directed to that purpose, which is a proper claim construction role for his opinions and testimony. (*See* Dkt. 173, MRB at 26).

Regeneron's interpretation of the "…*although*" text, (Dkt. 174, RRB at 24-25), also conflicts with not just the rest of the

column 30 definition, including the incorporated WO 217 specification; but also several other sections of the '715 patent's specification which clearly distinguish between a chemically defined medium, CDM, and a soy hydrolysate medium.

For example, the '715 patent's specification discusses producing aflibercept:

> using a cell culture medium. ***In one embodiment***, the cell culture medium is a ***chemically defined medium*** ("CDM"). CDM is often used because ***it is*** a ***protein-free, chemically-defined*** formula using no animal-derived components and there is ***certainty as to the composition*** of the medium. ***In another embodiment***, the cell culture medium ***is*** a ***soy hydrolysate medium***.

(Dkt. 146, '715 patent at 2:22-28) (emphasis added). This language is clear that CDM ***is***, without exception chemically defined; has certainty as to the composition; and also is an embodiment that is different from the other embodiment—which ***is*** a soy hydrolysate medium.

Regeneron argues that because its current specification changed language in its original provisional application that read, "A CDM does not include hydrolysate such as, for example, soy hydrolysate," its CDMs can include hydrolysates under *MPHJ Tech. Invs., LLC v. Richo Ams. Corp.*, 847 F.3d 1363, 1368-69 (Fed. Cir. 2017). (*See, e.g.*, Dkt. 124, ROB at 25-26). But as Mylan points out, those skilled in the art know that soy hydrolysates

are undefined yeast or plant extracts, so this is a distinction without a difference. (Dkt. 173, MRB at 21-14; Dkt. 146, Jungbauer ¶¶ 73-74).[6] *MPHJ* also is distinguishable. In *MPHJ*, the provisional application discussed a one step operation; the later-filed application later converted it into a one step ***option***. *MPHJ*, 847 F.3d at 1368-69. The issued patent's specification "contain[ed] no statement or suggestion" that the scope of the invention might be limited to a one step operation, thus those skilled in the art "would reasonably conclude that the inventor intended that single-step operation would be optional, not obligatory." *Id.* at 1369. Here, as just noted above, the '715 patent ***retained*** its CDM specification definition and statements that expressly 1) exclude undefined components derived from plant extracts, 2) require the medium ingredients to be chemically defined; and 3) differentiate between a CDM and a soy hydrolysate medium.

More applicable is *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187 (Fed. Cir. 2013). SkinMedica's claims involved culturing

[6] Regeneron offers attorney argument via Exhibit 41 at page 19, that Sheff-CHO Plus PF ACF medium qualifies as defined because it lists specific amounts of the minerals calcium, iron and magnesium. (Dkt. 174, RRB at 25). Minerals are only a small subset of a hydrolysate composition, which contains thousands of unknown and undefined compounds. (Dkt. 146, WO 217 at [009]; Dkt. 269-1, MLY PPP at slides 100-101). Further, minerals are a different chemical class than proteins and peptides. Regardless, the legend on page 14 states "PF" refers to "protein free." (Dkt. 174, Ex. 41 at 14). Page 15 differentiates media that is "Defined" from media which is "non-animal hydrolysates," such as "UltraPrep Soy." (*Id.* at 15). Page 18 describes the Sheff-CHO Plus PF ACF medium as having a "various non-animal source," and made from enzymatic digestion. (*Id.* at 18; *id.* (describing ingredient ranges only as "typical")). Each fit the requirements for a non-chemically defined media.

cells in three dimensions in a cell culture medium. *SkinMedica*, 727 F.3d at 1190-91. SkinMedica's specification also disclosed growing cells "in two dimensions" on beads as a "convenient method for preparing, observing and studying cells in culture." *Id.* at 1191. SkinMedica urged its "three-dimensions" claims should cover these cell lines grown on beads. *Id.* at 1193-94. The Federal Circuit disagreed, because the intrinsic record confirmed that the "patentees clearly distinguish[ed] culturing with beads from culturing in three-dimensions." *Id.* at 1197. The specification did this by stating cell lines "grown as a monolayer or on beads, ***as opposed to*** cells grown in three-dimensions, lack the cell-cell and cell-matrix interactions characteristic of whole tissue in vivo"—using disjunctive language between the two terms, and describing their different effects. *Id.* (emphasis added). The '715 patent's specification, like *SkinMedica*'s, likewise uses disjunctive language to discuss chemically defined media ***or*** hydrolysate media; and emphasizes that the two different types of

media will yield significantly different effects.[7] (Dkt. 146, Jungbauer ¶ 79). By "directly contrast[ing] the term it is defining," CDM, with another listed alternative, soy hydrolysate medium, the '715 patent specification "plainly evinces an intent … to classify" the two cell culturing media as distinct. *SkinMedica*, 727 F.3d at 1202; *see also Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1270 (Fed. Cir. 2001) (construing "rate" and "mode" differently when "the patentees, throughout the specification, use the terms 'rate' and 'mode' to refer to separate and distinct concepts"); *Chi. Bd. Options Exch., Inc. v. Int'l Secs. Exch., LLC*, 677 F.3d 1361, 1371 (Fed. Cir. 2012) ("allocating" and "matching" construed to mean distinct processes based on specification).

[7] *See, e.g.*, Dkt. 146, '715 patent at 5:55-57 (protein "can be produced in cell culture medium including a chemically defined medium (CDM) ***or*** soy hydrolysate medium"); *id.* at 69:26-27 ("Anti-VEGF Protein Produced Using CDM"); *id.* at 70:15:34 ("In one embodiment, the anti-VEGF protein [made in CDM] can have a decreased level of fucosylated glycans … ***compared to*** the level of fucosylated glycans in an anti-VEGF protein produced using a soy hydrolysate"); *id.* at 70:35-54 ("the anti-VEGF protein [made in CDM] can have a decreased level of sialylated glycans . . . ***compared to*** the level of sialylated glycans in … protein produced using a soy hydrolysate"); *id.* at 70:55-71:7 (same medium comparison); *id.* at 71:8-27 (same medium comparison); *id.* at 98:56-65 (comparing examples "produced using CDM" 1, 2, or 3 to those "produced using soy hydrolysate"); *id.* at 106:11-16 ("The amount of 2-oxohistidines in MT1 (produced in a CDM) were higher than MT4 (produced in soy hydrolysate), ***suggesting that the media used to express aflibercept can have a significant effect***"); *id.* at 106:18-21 ("the … abundance of the peptide in MT1(CDM produced) was 0.015% ***compared to*** … the peptide in MT4 (soy hydrolysate produced"); *id.* at Table 6-1 (comparing results in a CDM versus soy hydrolysate); *id.* at Tables 6-2 through 6-5 (same); *id.* at 126:17-22 ("The total fucosylation, total sialylation, total galactosylation and mannose-5 observed …. ***These values*** for glycosylation ***differ*** from the glycosylation values obtained using soy hydrolysate") (all emphasis added).

Other claim terms, and the specification's definition of those terms, also support Mylan's proposed construction. Claims 1 and 16 (and the claims that depend upon them), use the term "cumulative concentration," requiring "cumulative concentration" ranges of particular components in the CDM. The specification expressly defines "cumulative concentration" as "the ***cumulative amount*** of a component divided by the volume of liquid in the bioreactor at the beginning of the production batch" and further defines "cumulative amount":

> As used herein, the term "cumulative amount" refers to the ***total amount*** of a particular component added to a bioreactor ***over the course of the cell culture to form the CDM*** …

(Dkt. 146, '715 patent at 31:6-9, 31:32-36). Adding hydrolysate, an undefined mixture of thousands of compounds of unknown identity and concentration, to a medium either before or during the time when the cell medium is in the bioreactor, precludes the bioreactor contents from qualifying as "chemically defined medium"—and render the cumulative concentration standards impossible to calculate, and thus meaningless. (Dkt. 146, MOB at 24, 26; Dkt. 173, MRB at 26-30; Dkt. 146, Jungbauer Decl. ¶¶ 75-79).

Regeneron responds that the cumulative concentration can be calculated at any point in time during the cell culture. (Dkt. 174, RRB at 27). But "any time" is not the same thing as what the specification's definition expressly requires measuring for the

claimed cumulative concentration—the "total amount … added to the bioreactor ***over the course of the cell culture*** to form the CDM." (Dkt. 146, 715 patent at 31:6-9 (emphasis added); Dkt. 146, Jungbauer ¶¶ 75-79).

Viewing the claims and specification as a whole, Regeneron's interpretation of the "…*although*" language to re-introduce hydrolysates invites legal error because it "contradicts the intrinsic record." *Profectus Tech. LLC v. Huawei Techs. Co., Ltd.*, 823 F.3d 1375, 1379 (Fed. Cir. 2016); *see also Phillips*, 415 F.3d at 1324 (noting that a court's construction may not "contradict claim meaning that is unambiguous in light of the intrinsic evidence"). It also conflicts with the specification's rationale for using CDM in the first place: to eliminate undefined media in cell culture, to avoid the "lot-to-lot variability" and "consistency" problems that hydrolysates caused for Regeneron. A more reasonable interpretation that does not conflict with the intrinsic record is that the "…*although*" clause lets an individual chemically defined protein or polypeptide supplement CDM. Whatever that component may be, it won't be the chemically undefined hydrolysates.

The prosecution history: Regeneron expressly differentiated between its claimed CDM and prior art hydrolysates

Regeneron finds it "hard to imagine a record that could more clearly demonstrate Regeneron's intent to define 'CDM' differently from how it is defined in the '635 provisional application," since there it defined CDM to expressly exclude hydrolysates. (Dkt. 174, RRB at 26). Mylan responds that hydrolysates are yeast or plant extracts, thus one of ordinary skill in the art knows that this a superficial and not substantive change—one of ordinary skill in the art knows that there is no *scientific* difference between stating, "CDM does not include hydrolysate" and "Chemically defined media do not contain … yeast … or plant extracts." (Dkt. 146, '715 patent at 30:47-51; Dkt. 174, MRB at 23-24; Dkt. 146, Jungbauer ¶ 74).

Critically, Regeneron relied on the difference between a CDM and an undefined medium with hydrolysates to differentiate the prior art during prosecution. Regeneron presented claims to the PTO that read as follows:

> 18. A method of producing aflibercept harvested from a host cell cultured in a chemically defined medium (CDM), comprising:
>
> (a) providing a host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept; and
>
> (c) harvesting aflibercept produced by said host cell …

(Dkt. 146, Ex. 27 at 5). The Examiner rejected that and other pending claims as anticipated by Regeneron's Johnson reference (U.S. Publication No. 2018/0223249), noting that Johnson taught carrying out the cell culture step "in a chemically defined medium." (Dkt. 146, Ex. 25 at 10-11).

Responding to the Examiner's rejection, Regeneron insisted that the Johnson publication's cell culture media could not anticipate the claimed CDM. While Regeneron acknowledged that Johnson discussed the "general use of cell culture media, including CDM," (Dkt. 146, Ex. 27 at 16), Regeneron argued that Johnson did not disclose the claimed CDM/antioxidant concentration elements, because Johnson used the antioxidants taurine and cysteine only "in serum free media ***which may contain hydrol[y]sates*** and not CDM." (*Id.*) (emphasis added). Regeneron argued this again regarding Johnson's use of cysteine: "the cysteine is not necessarily added to CDM and may instead be used with serum-free media ***containing hydrolysates***." (*Id.* at 17) (emphasis added).[8]

The prosecution history, viewed from the perspective of one of ordinary skill in the art, confirms that Regeneron distinguished between its chemically defined medium and one "which may contain"

[8] Johnson also distinguished between "chemically defined media, which is not only serum-free, but also hydrolysate free," and a cell culture medium which could be "serum free," but also contain "< 16 g/L of hydrolysates, such as soy hydrolysate…." (Dkt. 146, Johnson at [0059]).

or "containing" hydrolysates. (Dkt. 146, Jungbauer Decl. ¶¶ 87-89; Dkt. 146, Ex. 27 at 17). If hydrolysate-containing medium, in whole or in part, qualified as the chemically defined medium in the pending claims, then nothing distinguished Johnson's medium containing, *e.g.*, cysteine or taurine, from what the pending claims before the PTO required. *See Personalized Media Commc'ns, LLC v. Apple Inc.*, 952 F.3d 1336, 1340 (Fed. Cir. 2020) ("[A]n applicant's amendment accompanied by explanatory remarks can define a claim term by demonstrating what the applicant meant by the amendment."); *see also Tegal Corp. v. Tokyo Electron Am., Inc.*, 257 F.3d 1331, 1343 (Fed. Cir. 2001) ("In the prosecution history, [Plaintiff] also distinguished over the [prior art] reference by stating that 'the electrodes claimed in the present invention are not the same as those disclosed in [the reference],' which [Plaintiff] described as being spiked electrodes. Accordingly, the term 'electrode' must be construed so as not to cover a spiked electrode."). These clear prosecution history representations thus independently confirm that hydrolysates cannot be included within the scope of the claim term "chemically defined medium."

The Court adopts Mylan's construction. It more correctly adheres to the provided specification definition, as well as the remaining intrinsic evidence of record regarding the scope and

meaning of the claim language, which excludes hydrolysates from the CDM.

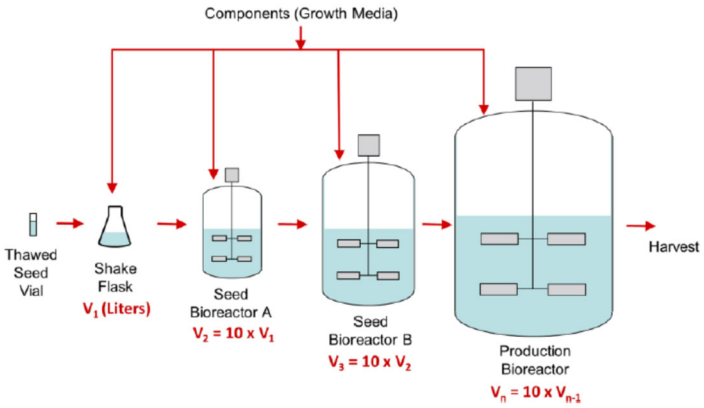
**b. "Harvested from a Host Cell Cultured in a Chemically Defined Media (CDM)"**

Plain and ordinary meaning

Both Regeneron and Mylan ask the Court to apply the plain and ordinary meaning to the "harvested from a host cell cultured in" CDM claim language.[9] The parties agree that for the phrase's use of the term "chemically defined medium (CDM)," the Court's construction for CDM above applies. Each party differs on what constitutes the ordinary meaning of "harvested from a host cell cultured in" CDM.

One of ordinary skill in the art knows that cell growth will start after "thawing a seed vial into a small container, along with a solution of sugars, amino acids, and other nutrients essential for the cells to survive, grow, and divide." (Dkt. 146, Jungbauer Decl. ¶ 45).

[9] Some now-dropped claims in the Manufacturing Patents also used the phrase, "a clarified harvest of a cell cultured in a chemically defined medium."




Regeneron seemingly agrees that a cell culturing process will involve culturing a cell with a cell culture medium under conditions suitable to the survival, growth, or proliferation of the cell. (Dkt. 268, RGN PPP at slide 77 (citing Jungbauer testimony)). Eventually, cells are transferred to the final bioreactor. After "growing for a period of time, typically a few days, in the largest container, the production bioreactor," the "cells are harvested and the protein they produced is purified, often by chromatography." (Dkt. 146, Jungbauer Decl. ¶ 48). As shown in the diagram above, *harvesting* is at the end of that bioreactor process. (*Id.* ¶¶ 46, 48; Dkt. 146, '715 patent at 2:29-35 (harvesting occurs after the cell culturing process)). Dr. Jungbauer's explanation is consistent with the '715 patent, which recognizes that proteins can be produced inside the cells, or "directly secreted" from the cell "into the [cell culture] medium." (Dkt. 146, '715 patent at 55:38-41). The proteins "may be

harvested" from that medium using various separation techniques, including chromatography. (*Id.* at 55:49-52; *see also id.* at 2:55-57 ("in one embodiment, a clarified harvest sample from a CDM culture comprising aflibercept is subjected to a capture chromatography procedure")).

A person of ordinary skill in the art also understands that to describe a protein as harvested from a host cell cultured in a particular medium, is to convey that the protein was harvested from a process made using only that particular medium. (Dkt. 146, Jungbauer Decl. ¶ 25). This is especially so when describing a protein harvested from a host cell cultured in a chemically defined medium—if the harvesting is not done from host cells cultured *throughout the process* in a chemically defined medium, then that cell culture process and product loses the whole point of being cultured in a way that is "chemically defined." (*Id.* ¶¶ 26, 75-79). The natural reading of the harvest-related claim language is that the harvest was made from a host cell cultured in CDM. (Dkt. 146, MOB at 26; Dkt. 173, MRB at 26-28; Dkt. 269-1, MLY PPP at slides 122, 138).

Regeneron did not put forth any rebuttal or contradictory testimony on the understanding of a person of ordinary skill in the art from anyone who qualifies as a person of ordinary skill in

the art. Mylan's expert testimony is consistent with the intrinsic record.

Thus, the plain and ordinary meaning of "harvested from a host cell cultured in a chemically defined medium (CDM)" generally means that the protein will be harvested from a host cell cultured in CDM throughout; and the cell culture at the time of harvesting will likewise be from cells being cultured in the CDM.

The context of the claims

Regeneron argues that the phrase, "harvested from a host cell cultured in chemically defined medium (CDM)" need not be treated as involving one start-to-finish process, but can be considered piecemeal, so that a host cell need only be "cultured in a chemically defined medium" at "*some point* during the cell culture process," while the "harvesting" step need not use a chemically defined medium at all, but can come from host cells cultured in a bioreactor using a non-chemically defined medium. (Dkt. 124, ROB 27; Dkt. 174, RRB at 26).

Mylan responds that Regeneron's approach improperly rewrites the claims to eliminate both the meaning of harvesting from host cells cultured in the medium, as well as the "chemically defined medium" requirement. Those of ordinary skill do not consider cells cultured in undefined media (even if put at one point in CDM), to

qualify as "harvested from a host cell cultured in a chemically defined medium." (Dkt. 146, Jungbauer Decl. ¶¶ 26, 75-79).

Regeneron admits that under its "for a period of time" construction, the only way to *avoid* its claims would be for a cell culture process to "occur entirely in non-CDM" from start to finish. (Dkt. 174, RRB at 27-28). Regeneron, in essence, seeks to cover *all* cell culture processes, so long as CDM medium is used at one moment in time. While Regeneron makes a purported fairness appeal with regard to Mylan's process to justify this, (*see* Dkt. ROB at 26-28; Dkt. 268, RGN PPP at slides 78-79), the Federal Circuit prohibits using the accused process to drive claim construction, which Regeneron's "at some point" theory transparently attempts to do. *NeoMagic*, 287 F.3d at 1074 (stating that "claims may not be construed by reference to the accused device"). It also conflicts with the ordinary meaning of CDM, harvesting, a natural reading of the claims, and is not supported by the intrinsic record. (Dkt. 173, MRB at 28-30; Dkt. 146, Jungbauer ¶¶ 84-89).

If the claims were to actually cover both CDM-based and non-CDM-based culturing, the claims could simply recite, "…aflibercept from cells cultured in a cell culture medium." But the claims purposefully joined "harvested from" *and* "a host cell" *and* "cultured in a chemically defined medium" together; that cannot be

disregarded just because the word "comprising" is later used in the claim. While "comprising" can permit "additional elements not required by a claim," the term "*does not remove the limitations that are present.*" *Power Mosfet Techs., LLC v. Siemens AG*, 378 F.3d 1396, 1409 (Fed. Cir. 2004) (emphasis added).

Since asserted independent claim 16 uses the relevant language identically to the other independent claims, it is representative for purposes of the "harvested from a host cell cultured in a chemically defined medium (CDM)" step, in bold italics below:

> 16. A method of producing aflibercept ***harvested from a host cell cultured in a chemically defined medium (CDM)***, comprising:
> …
> ***culturing said host cell in said CDM*** under conditions suitable in which said host cell expresses said aflibercept …
> and…
> harvesting aflibercept produced by said host cell.

(Dkt. 146, '715 patent at 262:52-263:4, 261:2-23).

Regeneron argues that the term "comprising" after the phrase, "harvested from a host cell cultured in a chemically defined medium (CDM)," justifies breaking the "harvesting" step apart from culturing the host cells in a CDM; and after this partition, they can apply their "at some point in time" meaning, citing *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364 (Fed. Cir. 2003). (Dkt. 124, ROB at 28-29; Hearing Tr. at 149:21-151:10). Mylan

responds that *Invitrogen* does not allow Regeneron to sever the harvesting step from cells cultured in CDM throughout the process range set forth in the claims. (Dkt. 173, MRB at 29).

The *Invitrogen* claim 1 stated as follows:

> 1. A process for producing transformable E. coli cells of *improved competence* by a process **comprising** the following steps in order:
> (a) *growing* E. coli cells in a growth-conducive medium at a temperature of *18° C. to 32° C.;*
> (b) rendering said E. coli cells competent; and
> (c) freezing the cells.

*Invitrogen*, 327 F.3d at 1366 (bold underline added; italics in original). The specification described the E. coli cell cultivation process as one that involved the claimed steps (a) and (b), but *also* other known growth steps, such as growing "master seeds," which were unclaimed steps. *Id.* at 1368-69. The specification taught that the master seeds had to be further processed "*before* becoming the primary seeds for use in the claimed method." *Id.* The claims also were limited to just one part of the cell growth phase: the "improved competence" process. *Id.* at 1369. The Federal Circuit thus found that the claims had not "addressed or limited" activities that "occurred before steps (a) and (b)." *Id.* at 1368. The description of the process as one for "improved competence" at certain temperatures, could "not preclude growth before the first step" at higher temperatures, such as a

cell growth phase that took place before the claimed improved competence process began. *Id.* at 1369.

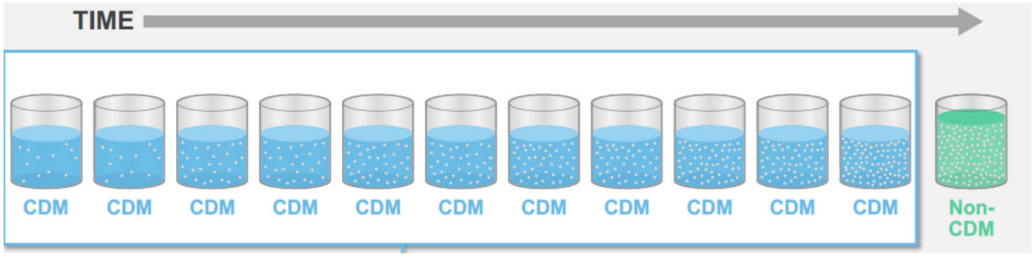
Regeneron argues that just as *Invitrogen* allowed cell culturing to occur at other temperatures, the same reasoning lets its cells use other culture media. (Dkt. 124, ROB at 28-29; Hearing Tr. at 150:23-151:10). Mylan responds that this is an oversimplification and a misapplication of the Invitrogen's reasoning. *Invitrogen*'s steps (a) and (b) expressly limited the claims to a limited "improved competence" cell culture step. The Federal Circuit just declined to expand the claimed "improved competence" temperature limits to different, unclaimed, process phases. *Invitrogen*, 327 F.3d at 1368-69. Here, by contrast, the '715 patent's claims do *not* use language carving up the cell culture process between start and harvest; and do *not* divide the cell culture process into subset steps. Aflibercept must be "harvested from a host cell cultured in a chemically defined medium (CDM)," without exception.

The correct way to apply *Invitrogen*'s analysis to the claims here is to start with *Invitrogen*'s claim 1 preamble, which used the term, "improved competence" and which preceded the term "comprising." *Invitrogen*, 327 F.3d at 1366. The Federal Circuit confirmed that this preamble limited the scope of the claimed process steps; and that all steps within the "comprising" part of

the method had to *also* fulfill the role of being "improved competence" steps. *Id.* at 1368-70. The '715 patent's claim 16 likewise places "harvested from a host cell cultured in a chemically defined medium (CDM)" in the preamble, and *before* the word "comprising":

> 16. A method of producing aflibercept **harvested from a host cell cultured in a chemically defined medium (CDM), comprising**: …

(Dkt. 146, '715 patent at 262:52-54) (emphasis added). Under *Invitrogen*, "harvested from a host cell cultured in a chemically defined medium" limits all of the steps in the claimed process; and likewise, all of the steps that are listed after "comprising" must be a part of the process of "harvested from a host cell cultured in a chemically defined medium (CDM)." *Invitrogen*, 327 F.3d at 1368-69. Thus, this scenario Regeneron presented at oral argument:




is not something that *Invitrogen* lets the '715 patent claims do, because this chops up one unified "host cell cultured in a" CDM preamble requirement into multiple sub-culture and media steps that fall outside it. (Dkt. 268, RGN PPP at slide 78).

Regeneron argues that requiring the full process from cell culturing to harvest to be in a chemically defined medium would either improperly add or remove claim limitations. (Dkt. 124, ROB at 28-29; Dkt. 174, RRB at 28). It does not. This approach applies and upholds the existing placement, scope, and order of the claim terms, and adheres to the intrinsic record.

Regeneron argued that re-using the host cell and chemically defined medium terms after "comprising" was good enough to convert the method steps into an open-ended process that creates multiple cell cultures to permit non-CDM culturing and harvesting. (Hearing Tr. at 149:4-20; Dkt. 268, RGN PPP at slides 80-81). The '715 patent's claim 16 does have steps after "comprising" involving aflibercept, host cells, and the medium; but they are not truly open-ended. The claim language states, "***said*** aflibercept," "***said*** host cell" and "***said*** CDM":

> 16. A method of producing ***aflibercept*** harvested from a ***host cell cultured in a chemically defined medium (CDM)***, comprising: …
> culturing ***said host cell*** in ***said CDM*** under conditions suitable in which ***said host cell*** expresses ***said aflibercept*** … and …
> harvesting aflibercept produced by ***said host cell***.

(Dkt. 146, '715 patent at 262:52-263:5) (emphasis added). As in *Invitrogen*, once claim 1 preceded the terms "aflibercept," "host cell" and "CDM" with the word "said," that language tied the terms'

scope to their limiting antecedent preamble phrase, "aflibercept harvested from a host cell cultured in a chemically defined medium (CDM)." *Invitrogen*, 327 F.3d at 1368 (Step (b) was limited to only those cells that "immediately result from Step (a) … Step (b) conveys this by stating 'rendering *said* E. coli cells competent' (emphasis added)."); *see also Traxcell Techs., LLC v. Nokia Sols. & Networks Oy*, 15 F.4th 1136, 1144 (Fed. Cir. 2021) ("it would defy the concept of antecedent basis" for claims that used "said first computer" to not be "tied to all those functions" the claims imposed on the first computer). The cell culture steps can't be further split into different media.

*Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337 (Fed. Cir. 2007), also rejects Regeneron's open-ended construction theory here. In *Dippin Dots*, the patentee argued that the term "comprising" at the beginning of the claim rendered its later steps open ended, so that a specified method step—freezing a composition into a bead shape—covered a process that made both bead-shaped spheres *and* irregular particles. *Dippin' Dots*, 476 F.3d at 1343. Regeneron similarly argues that its listed process step of aflibercept harvested from a host cell cultured in a CDM includes cell cultures produced in CDM *and* non-CDM. (Dkt. 124, ROB at 28-30; Dkt. 174, RRB at 28-30; Dkt. 268, RGN PPP at slides 78-79). The Federal Circuit reiterated that comprising is not a "weasel word" that

abrogates claim limits. *Dippin' Dots*, 476 F.3d at 1343. It does not "render every word and phrase" in the recited steps open-ended; *recited* steps must be practiced as-recited. *Id.* The district court in *Dippin Dots* thus correctly construed the step of freezing the composition into a bead shape to mean a beads-only process, not a step that permitted a combination of beads ***and*** other particles. *Id.* Similarly, here the recited step of "culturing said host cell in said CDM" cannot be opened up to mean multiple culture steps occurring in non-CDM; the cell culturing process can only allow CDM.

Thus, the term "comprising" cannot expand the claims to allow host cells to be cultured in CDM only "at some point in time," or have aflibercept be harvested from non-CDM.

The context of the specification

Regeneron's "at some point in time" approach via the word "comprising" also conflicts with the specification. The term "comprising" does not let patentees capture subject matter that is contrary to the written description. *Trading Techs. Int'l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1354-55 (Fed. Cir. 2010).

Mylan reiterates that Regeneron's interpretation is scientifically inconsistent, and conflicts with the specification. (Dkt. 146, MOB at 27-29; Dkt. 174, MRB at 25-26). The main focus of the '715 patent was to establish a cell culture process that

eliminated non-defined media entirely, to produce "certainty as to the composition" and to avoid the "reproducibility/consistency" and "lot-to-lot variability" issues that arose with Regeneron's use of hydrolysate in earlier processes. (Dkt. 146, '715 patent at 2:24-27; Dkt. 146, Ex. 12 at [0046], [00164]; Dkt. 269-1, MYL PPP at slide 102). Regeneron's "at some point" theory would include in the process the very undefined ingredients that the specification says to avoid; and reintroduces the reproducibility, consistency, and lot-to-lot variability problems that the specification and intrinsic record say using CDM is supposed to solve.

Regeneron also objects to the premise that the cells are in CDM at the time of harvesting, (Dkt. 124, ROB at 27-30; Dkt. 174, RRB at 26-30), and suggested at oral argument that just like its proposal that its one cell culturing step can be broken apart into multiple cell culturing steps, harvesting is an ongoing process, not an event that happens at the end, (Hearing Tr. at 148:5-151:10). Nothing in the specification supports that view.

The '715 patent confirms that proteins can be produced inside the cells, or "directly secreted" from the cell "into the [cell culture] medium." (Dkt. 146, '715 patent at 55:38-41). But when the proteins "may be harvested" from that medium, it requires using various separation techniques. (*Id.* at 55:49-52; *see also* at 2:55-

57 ("In one embodiment, a clarified harvest sample from a CDM culture comprising aflibercept is subjected to a capture chromatography procedure.")). No mention is made of splitting the culturing and harvesting steps, let alone into different media at different times, or switching media at harvesting time.

The specification is consistent with using CDM for the whole process. For example, Example 1 of the '715 patent discusses "Using a Chemically Defined Medium" for a "Cell Source and Harvest" process. (Dkt. '715 patent at 99:36-39). This process uses an "aflibercept producing cell line," which was "cultured ***and*** harvested using chemically defined media (CDM)." (Dkt, 146, '715 patent at 99:37-43); *see also id.* at 123:44-46 ("A clarified ***harvest using each of the CDM*** was prepared by centrifugation followed by 0.45 um filtration.") (all emphasis added).[10]

The specification also is clear that harvesting secreted proteins is an end-stage process where the proteins are separated from both the medium and cells by using *e.g.*, a concentration filter, or centrifugation followed by depth filtration and

[10] *See, e.g.*, Dkt. 146, '715 patent at 62:54-57 ("compositions can be obtained ***from*** the clarified ***harvest made using CDM***"); *id.* at 63:27-28 ("compositions can be obtained ***from*** a clarified harvest ***made using CDM***"); *id.* at 63:64-66 (same); *id.* at 64:14-17 (same); *id.* at 71:57-62 ("This invention includes culturing a host cell in a modified CDM under suitable conditions in which the cell expresses a recombinant protein of interest followed by harvesting a preparation of the recombinant protein of interest produced by the cell. Such a modified CDM can be used to produce the compositions as described above…."); *id.* at 71:63-72:13 (harvesting from the CDM once the CDM achieved particular cumulative concentrations) (all emphasis added).

affinity capture. (Dkt. 146, '715 patent at 55:45-52 (discussing harvesting process generally); *id.* at 76:53-60 (process with "a host cell in a CDM," where "protein is secreted from the host cell into the medium and a clarified harvest is obtained" has "biological sample obtained from the harvest" loaded onto chromatography column); *id.* at 123:44-46 ("A clarified harvest using each of the CDM was prepared by centrifugation….")).

The specification in *Invitrogen*, which Regeneron relies on, made clear distinctions between cell culture steps that were not part of the claimed method (*e.g.*, storing and processing master seeds); and culturing primary cells during the claimed "rendering competent" step. *Invitrogen*, 327 F.3d at 1368-69. *Invitrogen*'s Example 3 used different temperatures for unclaimed process steps, including for ancestral growth, before reducing the temperature to the claimed range for the full "rendering … competent" step (b) stage. *Id.* at 1369. This showed a deliberate intent to carve that earlier step out of the claims' more limited temperature range.

By contrast here, the '715 patent's specification nowhere describes either host cell culturing or aflibercept harvesting involving CDM to be an "at some point" or even in any mixed-media process. Rather, it uniformly states that "compositions can be obtained from the ***clarified harvest made using CDM***." (Dkt. 146,

'715 patent at 62:54-55) (emphasis added).[11] The specification, including all examples, describe cultures and harvests either from CDM from start to harvest finish; or from a different culture from start to harvest finish. (Dkt. 146, Jungbauer Decl. ¶¶ 84-86). The '715 patent has *no* examples or other written description of switching or mixing the media during culturing, or by the time of harvesting. *See* 35 U.S.C. § 112 (specification must disclose the manner and process of making and using the invention "in such full, clear, concise, and exact terms" to permit the person of ordinary skill to understand what was invented).

When the specification does refer to a harvest's cell culture in a manner that is not specific as to the type of medium being used, it used language such as, "harvested cell culture fluid." (Dkt. 146, '715 patent at 54:44-45). The claims do not use this more general non-media specific term; the claims call for harvesting aflibercept from a host cell cultured in CDM.

Thus, the specification conveys that the host cell culturing, and aflibercept harvesting, both occur in the chemically defined medium (CDM) throughout.

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[11] *See also id.* at 63:27-28 ("compositions can be obtained ***from a clarified harvest made using CDM…***"); *id.* at 63:50-51; *id.* at 63:64-65 ("clarified harvest made using CDM"); *id.* at 64:14-15 (same); *id.* at 71:57-62 ("This invention includes ***culturing a host cell in a modified CDM*** under suitable conditions in which the cell expresses a recombinant protein of interest ***followed by harvesting a preparation*** of the recombinant protein of interest produced by the cell. Such a modified ***CDM can be used to produce the compositions*** as described above….") (all emphasis added).

The prosecution history

During prosecution of the 715 patent, Regeneron sought claims as follows:

> 1. A method of producing aflibercept having a reduced amount of aflibercept variants expressed in a host cell cultured in a chemically defined medium (CDM), comprising:
> (a) providing said host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept to produce an aflibercept sample; and
> (c) harvesting protein produced by said host cell, …
>
> 18. A method of producing aflibercept harvested from a host cell cultured in a chemically defined medium (CDM), comprising:
> (a) providing a host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept; and
> (c) harvesting aflibercept produced by said host cell, …
>
> 23. A method of increasing production of aflibercept harvested from a host cell cultured in a chemically defined medium (CDM) and reducing aflibercept sample color, comprising:
> (a) providing said host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under suitable conditions in which said host cell expresses aflibercept;
> (c) harvesting aflibercept produced by said host cell forming a harvest comprising aflibercept wherein: …

(Dkt. 146, Ex. 27 at 3, 5, 7; *see also* Dkt. 146, Ex. 25 at 11).

The PTO rejected these and other claims "as being anticipated by Johnson et al. (US Publication No. 2018/0223249 published 8/9/2018)." (Dkt. 146, Ex. 25 at 11). The PTO explained that the claim 1 above was directed in part to "a method of producing aflibercept by culturing a CHO host cell that expresses aflibercept in a chemically defined medium (CDM)," claim 18 above was directed in part to "a method of producing aflibercept produced by a host cell that expresses aflibercept wherein said host cell is cultured in a CDM that comprises an anti-oxidant," while pending claim 23 above was directed in part to "a method of increasing the production of aflibercept harvested from culturing a host cell that expresses aflibercept, wherein the host cell is cultured in a CDM that comprises an anti-oxidant…." (*Id.*)

The PTO observed that "Johnson et al. teach a method" of producing proteins such as aflibercept in a CHO host cell, "wherein said culturing is carried out in a chemically defined medium," and where antioxidants are used. (Dkt. 146, Ex. 25 at 11).

In response, Regeneron argued that:

> *Johnson* does not disclose ***producing and harvesting aflibercept in CDM*** having a target value of aflibercept variants…. Likewise, *Johnson* does not disclose ***producing and harvesting aflibercept in CDM*** having a target value of aflibercept variants that can be obtained by adding anti-oxidants where the cumulative concentration for all anti-oxidant in the CDM does not exceed 30 mM, as recited in some of the pending claims.

(Dkt. 146, Ex. 27 at 17) (emphasis added).

Regeneron thus clearly described its claimed process, and argued that it was different from Johnson's, because the steps of both producing ***and*** harvesting aflibercept, *i.e.*, the entire process, occurred ***in CDM***. Likewise, as noted in ¶¶ 180-182 above, Regeneron differentiated Johnson because Johnson used "serum free media which may contain hydrol[y]sates and not CDM." (Dkt. 146, Ex. 27 at 16). Regeneron thus explicitly foreclosed even the option of its claims using a medium that "may contain" hydrolysates at some point.

This again differentiates the prosecution history in *Invitrogen*. There, during prosecution the patentee replaced the original step (a)'s claim language "less than 37°C" with the amended and issued 18° C to 32° C temperature range; this "did not disclaim all growth above 32° C" for all steps, but rather "emphasized the advantages of growth at 18° C to 32° C [in step (a)] immediately before rendering the E. coli competent [in step (b)]." *Invitrogen*, 327 F.3d at 1369. Here, Regeneron emphasized that it was both producing in ***and*** harvesting from ***only CDM***, and that this CDM production and harvesting differentiated its claims from Johnson.

Regeneron's arguments before the PTO are analogous to those the patentee made in *Amgen Inc. v. Coherus BioSciences Inc.* that

were construed as limiting. 931 F.3d 1154, 1159-61 (Fed. Cir. 2019). In *Amgen*, the PTO rejected Amgen's claims to a pharmaceutical formulation; and Amgen responded that the PTO's prior art Holtz reference did not disclose "the particular combinations of salts recited" in Amgen's claims. *Id.* at 1158 (internal quotation marks omitted). Likewise here, the PTO rejected Regeneron's claims over Johnson; and Regeneron responded that Johnson did not disclose the particular CDM-only culturing and harvesting step. The Federal Circuit confirmed in *Amgen* that this was a "clear and unmistakable surrender" of a broader meaning for salts, and held the claims limited. *Id.* at 1161. The same is true here: Regeneron cannot secure coverage to a "partial" CDM process once it represented and confirmed to the PTO that its process was different from the prior art processes because culturing ***and*** harvesting occurred ***only in CDM***.

Regeneron points to a different part of the prosecution history where the PTO rejected a claim that read, a "method of producing aflibercept, comprising: (a) binding aflibercept from a clarified harvest cultured in a chemically defined medium to a Protein A resin…" as indefinite. (*See* Dkt. 124, Ex. 21 at 3; Dkt. 124, Ex. 20 at 3). The PTO pointed out the phrase lacked a proper antecedent basis, "because the claim does not state what is cultured in the CDM." (Dkt. 174, Ex. 20 at 3). The PTO pointed

out that "a harvest is typically the product of a culturing step rather than the substance which is cultured." (*Id.*)

In response, Regeneron amended the claims. Regeneron argues that its amendment made clear "that it was the cells, not the harvest, that must be 'cultured in a chemically defined medium (CDM).'" (*See* Dkt. 124, ROB at 30; Dkt. 124, Ex. 21 at 3). First, that is not at all how Regeneron phrased it to the PTO—what Regeneron stated is that the purpose of the amendment was "to clarify the use of the chemically defined medium and address the antecedent basis rejection for claim 27." (Dkt. 124, Ex. 21 at 7). Second, that doesn't change the premise that the entire cell culturing process must occur only in CDM.

Moreover, in the final claims that issued, the antecedent basis for what is cultured in the CDM is the language that was preserved in the preamble: "aflibercept harvested from a host cell cultured in a chemically defined medium (CDM)." (Dkt. 146, '715 patent at 262:52-263:4). And, what Regeneron's cited text from the prosecution history did not change, modify, or repudiate, was its clear representation that its claims differed from Johnson because it was ***producing and harvesting aflibercept in CDM*** only.

Regeneron argues that "[n]othing in the prosecution history suggests that the word 'comprising' in the Manufacturing Patents should be read to exclude cell culture processes having an

unrecited, non-CDM culturing step." (Dkt. 174, RRB at 30). To the contrary, the PTO's repeated rejections under 35 U.S.C. § 112 evidences the PTO's concern that Regeneron had not properly linked its claimed steps to their proper antecedent basis. (*See, e.g.*, Dkt. 146, Ex. 25 at 4-10). Further, Regeneron's unequivocal representation to the PTO regarding what it considered the scope of its claims, and that of the prior art, confirms that it intended its claims to cover "***producing and harvesting aflibercept in CDM***." (*See, e.g.*, Dkt. 146, Ex. 27 at 17).

Nothing in the intrinsic record justifies Regeneron's request to have the term harvesting from a cell cultured in CDM lose its ordinary meaning, or the repeated discussion that that the entire process will occur in CDM through harvest. Regeneron's "at some point in time" construction conflicts with the ordinary meaning, conflicts with the intrinsic record (the claims; the specification; and its representations made to the PTO), and also conflicts with the *Invitrogen* decision upon which Regeneron's "comprising" analysis was based.

Thus, the Court adopts Mylan's construction of this claim element, and rejects that "harvested from a host cell cultured in a chemically defined media (CDM)" could mean harvested from a host cell that "at some point in time" was cultured in a CDM.

**c. "Anti-Oxidants"**

Mylan originally identified the term "anti-oxidants" as needing construction and proposed that term be limited to "taurine, hypotaurine, glycine, thioctic acid, glutathione, choline chloride, hydrocortisone, Vitamin C, Vitamin E and combinations thereof." Regn. Ex. 26 at 7. Regeneron contends that the term is not so limited, and Mylan has refused to stipulate to Regeneron's position. Dkt. 102 at 7-9; Regn. Ex. 15 (Nov. 16, 2022 Mylan Email).

Claim 1 of the '715 refers to "anti-oxidants," without further limitation. By contrast, claim 3 of the '715 patent, which ultimately depends from claim 1, limits the set of anti-oxidants for that dependent claim to the following: "taurine, hypotaurine, glycine, thioctic acid, glutathione, choline, hydrocortisone, Vitamin C, Vitamin E or combinations thereof."

The specification of the '715 patent discloses "[n]on-limiting examples of the antioxidant," which include chemicals such as "S-carboxymethyl-L-cysteine" and "chelating agents" like "aurintricarboxylic acid" and "citrate." '715 patent, 23:64-24:3. Those exemplary anti-oxidants are excluded from Mylan's proposed construction of "anti-oxidants." At his deposition, Mylan's expert agreed that "anti-oxidants" are not limited to Mylan's list. Jungbauer Dep. 157:4-14.

The parties have a dispute over claim scope that the Court "must resolve." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008); *see also Baxter Healthcare Corp. v. Mylan Labs. Ltd.*, 346 F. Supp. 3d 643, 653 (D.N.J. 2016). The doctrine of "claim differentiation" presumes that an independent claim has a different, broader scope than its dependent claim, *see Hill-Rom Servs.*, 755 F.3d at 1374, such that subject matter within the scope of a dependent claim necessarily is within the scope of an independent claim from which it depends, *see Littelfuse*, 29 F.4th at 1380 (Fed. Cir. 2022) ("By definition, 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."). The presence of Mylan's list of anti-oxidants in dependent claim 3 gives rise to the strong presumption that claim 1—and the term "anti-oxidant" itself—is not so limited. *See id.*; *see also Intamin Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1335 (Fed. Cir. 2007); *AstraZeneca*, 2022 WL 17178691, at *5.

Mylan's proposed construction would also render claim 3 superfluous. Such a construction is "highly disfavored." *See Intel*, 21 F.4th at 810. Mylan's proposed construction also violates the fundamental rule that a construction that "most naturally aligns with the patent's description of the invention

will be, in the end, the correct construction." *Phillips*, 415 F.3d at 1316 (quoting *Renishaw*, 158 F.3d at 1250). Mylan's construction would exclude, without any basis, exemplary antioxidants recited by the specification. Therefore, the Court rejects Mylan's proposed construction and adopts Regeneron's proposal instead.

The Clerk is directed to forward a copy of this Order to all counsel of record.

DATED: April 19, 2023

Tom S Kleeh

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

# EXHIBIT 9

*Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*,
No. 22-61, Dkt. 691 (N.D. W. Va. Jan. 30, 2024)

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE NORTHERN DISTRICT OF WEST VIRGINIA**
**AT CLARKSBURG**

| | |
|---|---|
| REGENERON PHARMACEUTICALS, INC.,<br><br>Plaintiff,<br>v.<br><br>MYLAN PHARMACEUTICALS INC., and BIOCON BIOLOGICS INC.,<br><br>Defendants. | Civil Action No. 1:22-cv-00061-TSK |

**DEFENDANTS' EXPEDITED MOTION FOR ENTRY OF A SCHEDULING ORDER**

On December 5, 2023, Defendants Mylan Pharmaceuticals Inc. ("Mylan") and Biocon Biologics Inc. ("Biocon") (collectively, the "Biocon Defendants") submitted a brief response to Plaintiff Regeneron Pharmaceuticals, Inc.'s ("Regeneron") Motion to Convene Status Conference. (Dkt. No. 652-1). On January 30, 2024, the Court denied Regeneron's motion, finding no need to convene. (Dkt. No. 685). However, there are critical developments arising after Regeneron filed its motion that necessitate expedited[1] entry of a scheduling order in the ongoing litigation against the Biocon Defendants. Those events include: (1) issuance of the Court's Memorandum Opinion and Order Following Bench Trial; and (2) Regeneron's motion before the Judicial Panel on Multidistrict Litigation ("JPML" or "MDL") requesting, among other things, coordinated pretrial

[1] The Biocon Defendants were originally planning to provide this request today as a supplement to their response to Regeneron's Motion to Convene Status Conference. However, with the Court's Order this morning denying Regeneron's motion, Biocon is presenting its request to the Court as a new motion. Given the timing considerations and risk of further prejudice described herein, the Biocon Defendants respectfully request expedited action on this motion. Biocon and its predecessors have undertaken significant investment in obtaining and maintaining its position in front of other aflibercept biosimilar applicants. Absent expedited consideration, Biocon will be deprived of the benefits of that position.

proceedings in this Court involving the litigations of four other defendant groups. The Biocon Defendants oppose any attempt by Regeneron to further delay adjudication of the patents asserted against them over 17 months ago, and for the reasons described herein, with this motion the Biocon Defendants respectfully request entry of an expedited schedule to address the remaining issues following the June 2023 trial in this matter.

An expedited schedule will allow the Biocon Defendants to achieve a level of certainty and finality with regard to the asserted patents that remain in the case. The Biocon Defendants were subjected to a rapid first wave litigation, where Regeneron chose a subset of its patent claims for the first wave trial. There remain 18 patents[2] asserted against the Biocon Defendants that were not litigated in the first wave trial in June 2023 (the "Remaining Patents"). With the first wave complete, and the Court having entered its decision, the Biocon Defendants now seek certainty on those Remaining Patents. Multiple developments make further delay inequitable and entitle Defendants to that certainty on an expedited basis. Several other aflibercept biosimilar applicants (who filed well after Biocon) have now been sued; Regeneron is seeking from the JPML some level of consolidation among the cases; and Regeneron has thus far refused to engage in discussions regarding the scope and timing of the subsequent phase of the litigation. But the Biocon Defendants are at least a year and a half ahead of the other (later-filed) applicants, have already completed the first wave trial, already completed *Markman* proceedings, and already taken substantial discovery on most of the Remaining Patents. Thus, the Biocon Defendants are uniquely

[2] Of the original 24 asserted patents, (*see* Dkt. No. 1, at 3), three were litigated at the June 2023 trial, and three others have been disclaimed in their entirety by Regeneron. Immediate judgment in the Biocon Defendants' favor on those disclaimed patents is proper on the undisputed facts for the reasons described in Defendants' Motion for Summary Judgment. (Dkt. No. 679).

situated compared to each of the other biosimilar applicants, have already been delayed by nearly 18 months from achieving patent certainty, and would be prejudiced by any further delay.

## I. BACKGROUND.

The Biocon Defendants' biosimilar aflibercept application was filed with the FDA in late 2021, precipitating suit in August 2022, almost a year and a half before any other aflibercept biosimilar applicant was sued. (*Compare* Dkt. No. 1 (filed August 2022), *with Regeneron Pharms., Inc. v. Celltrion, Inc.*, Case No. 23-cv-00089, Dkt. No. 1 (N.D.W. Va.) (filed November 2023)). Regeneron asserted 24 patents in the initial suit, consistent with the parties' engagement in the BPCIA patent dance. (*See* Dkt. No. 1, at 3). With the filing of the suit, Regeneron also submitted a Motion Requesting Expedited Status Conference, in which it sought an expedited schedule. (Dkt. No. 7). In its request, in exchange for an expedited schedule, Regeneron represented to the Court that it would narrow to three patent families, (Dkt. No. 90, at 22:8-15), and no more than 25 claims from six total patents, (*id.*, at 23:2-13); it later committed to narrowing to no more than 12 claims before trial, (Dkt. No. 174, at 4 n.1). The Court granted Regeneron's request, and trial was scheduled for June 2023. (Dkt. No. 87). Consequently, the parties immediately initiated discovery and document production; in parallel, the parties also commenced claim construction on six of Regeneron's patents from three different patent families, including subject matter spanning dosing regimens, formulations, and upstream and downstream manufacturing methods. (*See id.*; *see also* Dkt. No. 88 (stipulation identifying initial patents)). Discovery was taken on these six patents, until the case was narrowed to four, which proceeded through expert discovery, and eventually a two-week trial on three of those patents: two dosing regimen patents (U.S. Patent Nos. 10,888,601 and 11,253,572) and a formulation patent (U.S. Patent No. 11,084,865). Following post-trial briefing and closing arguments, the Court issued its decision on December 27, 2023. (Dkt. No. 664). Following that decision, the Biocon Defendants

have diligently sought Regeneron's position regarding the scope of any subsequent litigation on the Remaining Patents, but Regeneron has not responded to those requests.

Beginning in November of 2023, nearly 16 months after the Biocon Defendants' suit was filed, Regeneron initiated litigation against a second group of aflibercept biosimilar applicants. *See, e.g.*, *Regeneron Pharms., Inc. v. Celltrion, Inc.*, Case No. 23-cv-00089 (N.D.W. Va.) ("the Celltrion Action"); *Regeneron Pharms., Inc. v. Samsung Bioepis Co., Ltd.*, Case No. 23-cv-00094 (N.D.W. Va.) ("the First Samsung Action"); *Regeneron Pharms., Inc. v. Formycon AG*, Case No. 23-cv-00097 (N.D.W. Va.) ("the Formycon Action"); *Regeneron Pharms., Inc. v. Samsung Bioepis Co., Ltd.*, Case No. 23-cv-00106 (N.D.W. Va.) ("the Second Samsung Action"); *Regeneron Pharms., Inc. v. Amgen, Inc.*, Case No. 24-cv-00264 (C.D. Cal.) ("the Amgen Action"). Those parties have been and continue to be engaged in disputes over service, jurisdiction, and preliminary injunction proceedings. Each of the other aflibercept biosimilar applicants (other than Amgen) have filed motions to dismiss for personal jurisdiction, seeking removal to different U.S. District Courts. (*See, e.g.*, The Celltrion Action, Dkt. Nos. 68-69; The First Samsung Action, Dkt. No. 47; The Formycon Action, Dkt. No. 57; The Second Samsung Action, Dkt. No. 14). And those parties litigating before this Court are subject to an injunction briefing and hearing schedule that goes out to May 2024, with resolution of their various disputes possibly extending beyond May 2024, while Amgen will not even appear before the California Court to discuss injunction proceedings until April 2024. (*Compare* The Celltrion Action, Dkt. No. 61, *with* The Amgen Action, Dkt. No. 51).

## II. ARGUMENT.

### A. The Biocon Defendants Need Certainty on the Remaining Patents.

The Biocon Defendants have litigated a first wave to a final decision, with a focus on the three patents Regeneron felt were its strongest. The Defendants invalidated two of those three

patents (the two dosing regimen patents expiring in 2032), (Dkt. 664, at 312-13), and have obtained favorable unpatentability decisions on a host of Regeneron's other dosing regimen patents before the Patent Trial and Appeal Board ("PTAB").[3] But numerous patents remain. What remains may be the dregs of Regeneron's portfolio, consisting of a hodge-podge of patents that the Biocon Defendants do not infringe or that are invalid—which explains why they did not make Regeneron's cut for assertion in the first wave trial. The Biocon Defendants are nevertheless entitled to finality on those Remaining Patents.

In the first wave, the Biocon Defendants moved quickly, based on a schedule Regeneron demanded, in an effort to chase what it claimed to be a statutory automatic permanent injunction (which, it turns out, was not even feasible). The parties engaged in significant and wide-ranging discovery in an unprecedented amount of time. Now the shoe is on the other foot. After the nearly 18-month delay that the Biocon Defendants endured to allow Regeneron to take its hand-picked initial patents to trial, the Biocon Defendants are entitled to freedom-to-operate certainty; the Biocon Defendants are seeking to achieve this certainty via an October 2024 trial, following a schedule commensurate with what Regeneron was afforded in the initial phase.[4] The Biocon Defendants and Regeneron have been in discussions regarding an expedited Federal Circuit appeal

[3] *See, e.g.*, *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, 2022 WL 16841860 (P.T.A.B. Nov. 9, 2022) (Final Written Decision); *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, 2022 WL 16842073 (P.T.A.B. Nov. 9, 2022) (same); *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, 2024 WL 111108 (P.T.A.B. Jan. 9, 2024) (same); *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, 2024 WL 110383 (P.T.A.B. Jan. 9, 2024) (same); *see also Biocon Biologics Inc. v. Regeneron Pharms., Inc.*, IPR2024-00201, Paper 11 (P.T.A.B. Jan. 16, 2024) (Institution Decision).

[4] Biocon does not concede that each of the Remaining Patents are eligible and/or suitable for trial, but to the extent Regeneron is able to convince this Court otherwise and any patents survive fact and expert discovery, Biocon deserves a quick trial to litigate remaining issues.

of the first wave issues. The Biocon Defendants thus seek a subsequent trial on a schedule that would align with the anticipated timing of that Federal Circuit appeal decision.

Regeneron argued previously that the "the legislative history confirms that the BPCIA was designed to facilitate 'litigat[ing] patent disputes quickly and efficiently.'" (Dkt. No. 7, at 5 (quoting *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 110th Cong. 119 (2007))). That is even more applicable here, where the Biocon Defendants' certainty on the Remaining Patents already has been delayed almost a year and a half. Biocon and its predecessors invested significant amounts of time, revenue, and effort in preparing and submitting the first aflibercept biosimilar application. They have been at the forefront of the effort to get a lower cost anti-VEGF drug to market for treating angiogenic eye disorders, and they filed their application with the FDA well before any other biosimilar applicants. The Biocon Defendants deserve to maintain that lead—no further delay is warranted.

### B. The Biocon Defendants Sit in a Unique and Advanced Position Compared to the Other Biosimilar Applicants.

The Biocon Defendants have already completed trial and received a court decision on three of Regeneron's central patents, while other parties have not yet even begun, and will be mired in jurisdictional fights for months before even commencing litigation proper. *See* Section I, *supra*. In addition, the Biocon Defendants have already completed *Markman* proceedings pertaining to most of the Remaining Patents (dosing regimen (6 patents), formulation (4 patents), and CDM (4 patents)), (Dkt. No. 427); completed most fact discovery; and completed expert discovery on a number of claims of the core patents. In other words, the Biocon Defendants are uniquely situated. Recognizing this, the Court should place the Biocon Defendants on track to reach a final trial with

minimal and expedited discovery, without subjecting them to the ongoing procedural entanglements confronting the other aflibercept applicants.

Further, in its MDL transfer brief, Regeneron has identified 13 patents-in-common across the six biosimilar aflibercept cases.[5] (*In re Aflibercept Patent Litig.*, MDL No. 3103, Dkt. No. 1-1 at 4 n.1 (J.P.M.L. Jan. 11, 2024) ("MDL Brief")). The Biocon Defendants already have taken discovery on most of these in the first wave, many of the claims have been held invalid before the PTAB, and the remaining Biocon-specific issues can be addressed with limited discovery. For example, of the dosing regimen patents, the four claims asserted from U.S. Patent Nos. 10,888,601 and 11,253,572 at the June 2023 trial have been held invalid by this Court; all challenged claims of U.S. Patent Nos. 9,669,069; 9,254,338; 10,130,681; and 10,888,601 have been held unpatentable by the PTAB; and two additional *inter partes* reviews directed to claims of U.S Patent Nos. 10,888,601 and 11,253,572 have been instituted by the Board and Biocon has moved to join those proceedings.[6] Of the formulation patents, U.S. Patent No. 11,084,865 already has been litigated by the Biocon Defendants at the June 2023 trial, with an expedited appeal soon underway. Other claims in that family have been (recently) disclaimed after being challenged at the PTAB. (*See, e.g.*, *Celltrion, Inc. v. Regeneron Pharms., Inc.*, IPR2023-00462, Paper 35 (P.T.A.B. Jan. 22, 2024) (Regeneron's Unopposed Motion to Terminate); Dkt. No. 679-3 (U.S. Patent No. 10,464,992 Disclaimer)). The members of the CDM family already have been the subject of some

[5] U.S. Patent Nos. 9,222,106; 9,254,338; 9,816,110; 10,130,681; 10,415,055; 10,464,992; 10,669,594; 10,888,601; 11,084,865; 11,066,458; 11,104,715; 11,253,572; and 11,306,135.

[6] Biocon's joinder motion in the '601 patent IPR has been granted. *See Biocon Biologics Inc. v. Regeneron Pharms., Inc.*, IPR2024-00201, Paper 11 (P.T.A.B. Jan. 16, 2024). Biocon's '572 patent IPR joinder motion remains pending, but Regeneron has informed the Board that it does not oppose joinder in view of the grant of joinder in the '601 patent IPR. *See Biocon Biologics Inc. v. Regeneron Pharms., Inc.*, IPR2024-00298, Paper 8 at 2 (P.T.A.B. Jan. 26, 2024). Thus, joinder in the '572 patent IPR is expected, as well.

fact discovery. But further, Regeneron has conceded non-infringement of those patents in view of the Court's claim construction, (Dkt. No. 433), and further discovery on those patents by the Biocon Defendants is unnecessary, pending any appeal. Regeneron also has been provided with substantial discovery pertaining to the M710 manufacturing process. What remains are a smattering of patents for which the Biocon Defendants have advanced non-infringement positions, and such patents should require little-to-no additional discovery, to the extent they are even trial-eligible.

In contrast, for the later-filed biosimilar applicants, both sides will likely aggressively pursue discovery on multiple fronts, on multiple continents, on different manufacturing processes; they will likely further engage, *de novo*, in written discovery, fact depositions (Samsung, *e.g.*, has ***52 patents*** asserted against it, likely requiring ***dozens*** of fact depositions), full *Markman* briefing, and full expert discovery and trial preparation, which could be delayed by possible Hague procedures necessary for discovery in South Korea and Europe.

Lastly, the differences between the products and manufacturing processes of the different aflibercept biosimilar applicants further distinguishes those cases from the Biocon Defendants'. While certain details have not been publicly disclosed, one can surmise from the patents being asserted against Samsung, Celltrion, Formycon, and Amgen that unique formulations are at issue, with competitor formulations likely including different ingredients. In addition, the manufacturing processes are likely to be different given that each biologic manufacturer typically uses a proprietary process specific to that company. In fact, the other biosimilar applicants have been sued on at least a dozen additional patents that have not been asserted against, or identified in the

patent dance against, the Biocon Defendants.[7] This means that non-infringement defenses across multiple patent families are likely to be disparate and unique to each defendant, not to mention highly confidential, which will further complicate any possible consolidation of the Biocon Defendants with those of the other, later-filed biosimilar applicants.

In sum, the Biocon Defendants have already completed trial on the patents Regeneron felt were its key patents, and require only a limited amount of additional discovery to prepare for a second wave trial (to the extent one is required). The other defendants have not even begun, and it may be months before a decision is made on preliminary issues, including jurisdiction and venue.

### C. No Prejudice to Regeneron—There is Substantial Prejudice to the Biocon Defendants Without Expedited Certainty.

Regeneron has argued to this Court for an expedited schedule of its own once before. (*See* Dkt. No. 7). Thus, it is clearly not prejudiced by such a scenario. By contrast, the Biocon Defendants will stand to lose a substantial amount of their investment in being ahead of other aflibercept biosimilar applicants if not granted expedited adjudication and/or dismissal of the Remaining Patents.

Not only that, but the public interest is harmed by allowing the Remaining Patents to delay entry of competition to the EYLEA market. *See, e.g.*, *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 100 (1993) ("[O]ur prior cases have identified a strong public interest in the finality of judgments in patent litigation … [and] emphasized the importance to the public at large of resolving questions of patent validity…" (citing, *e.g.*, *Blonder-Tongue Labs., Inc. v. Univ. of Ill. Found.*, 402 U.S. 313 (1971))); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1354

[7] These patents include, *e.g.*, U.S. Patent Nos. 7,771,997; 9,315,281; 9,562,238; 9,932,605; 10,905,786; 10,918,754; 11,268,109; 11,312,936; 11,525,833; 11,549,154; 11,680,930; 11,732,024. (*See* Dkt. No. 1, at 3 (listing the asserted patents)).

(Fed. Cir. 2005) ("[T]here is a significant public policy interest in removing invalid patents from the public arena.") (Gajarsa, J., concurring). Biosimilars have the potential to lower costs for consumers, which expands access to a wider patient population that would benefit from those lower costs in battling their (potentially sight-threatening) ophthalmic disorders. *See, e.g.*, Rebecca Taylor, *Biosimilars in Ophthalmology*, EYENET MAG., Jan. 2021, at 39 ("With biosimilar product development, pharmaceutical companies are able to create drugs similar enough to proven biotherapeutics in safety and efficacy—and they can do so more quickly and at a lower cost.").

In late 2022, Regeneron stood before this Court and explained that the parties already had participated in the "patent dance," thus "facilitating adjudication of remaining disputes," which "advanced the parties' understanding of what will be at issue in this case far beyond what would be achieved through the ordinary filing of a complaint." (Dkt. No. 7, at 2). Indeed, at that point Regeneron proclaimed the parties to be "much of the way down the runway" in terms of discovery. (Dkt. No. 90, at 5:1-12). The Biocon Defendants' request is ripe for expediting for much the same reason, in addition to the fact of having already litigated to judgment on a number of Regeneron's core patent claims. The Biocon Defendants' request also is consistent with the Defendants' prior stated desire to litigate to certainty all 24 asserted patents and be in a position to have that certainty as soon as practicable. (*See* Dkt. No. 26, at 5-6). The Biocon Defendants were forced to wait 18 months to accommodate Regeneron's first wave schedule to allow it to chase its statutory injunction on just a subset of the asserted patents. Given that precedent, Regeneron will not be prejudiced if litigation on the Remaining Patents is expedited, whereas significant prejudice accrues to the Biocon Defendants and the public with each passing day where certainty is lacking.

### D. The Pendency of the Motion for Transfer Does not Preclude Setting a Schedule for the Biocon Defendants Now.

The pending motion for transfer and coordinated pre-trial proceedings is not a basis to delay scheduling as to the remaining claims against the Biocon Defendants. It will be some months before there is a resolution of the issue by the JPML, which will not even be heard until March 28, 2024. *In re Aflibercept Patent Litig.*, MDL No. 3103, Dkt. No. 7 (J.P.M.L. Jan. 12, 2024). Even if the JPML elects to order transfer of the additional cases to this Court or another court, that will not make the scheduling, and any progress in this case, moot. A transferee court is not required to place all civil actions on the same "track" in a multi-district litigation. *See In re Bear Creek Techs., Inc., ('722) Patent Litig.*, 858 F. Supp. 2d 1375, 1377 (J.P.M.L. May 2, 2012) ("We refrain from dictating the structure of an MDL's pretrial proceedings…"). In the event that the transfer motion is granted, the Biocon Defendants would seek to have this matter proceed on a track separate from the others, given the proceedings to date and the harm to the Biocon Defendants in being forced to endure delays for the sake of later-filing defendants.

## III. CONCLUSION.

Accordingly, the Biocon Defendants respectfully request expedited entry of a schedule for a trial on the Remaining Patents by October 2024. A proposed Scheduling Order for the expedient adjudication of the Remaining Patents, consistent with that afforded Regeneron in the initial phase, is filed with this motion. The Biocon Defendants thank the Court for its attention to this matter.

Date: January 30, 2024

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**CERTIFICATE OF SERVICE**

I hereby certify that on January 30, 2024, I electronically filed the foregoing with the Clerk of the Court by using the Court's CM/ECF system. Counsel of record for all parties will be served by the Court's CM/ECF system.

Date: January 30, 2024

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# EXHIBIT 10

*Regeneron Pharms., Inc. v. Amgen Inc.*,
No. 24-264, Dkt. 39 (C.D. Cal. Jan. 20, 2024)

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**IN THE UNITED STATES DISTRICT COURT**
**FOR THE CENTRAL DISTRICT OF CALIFORNIA**

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|---|---|
| REGENERON PHARMACEUTICALS, INC.<br><br>Plaintiff,<br><br>v.<br><br>AMGEN INC.<br><br>Defendant. | Case No. 2:24-cv-264-JWH-Ex<br>Hon. John W. Holcomb<br><br>AMGEN'S OPPOSITION TO REGENERON'S *EX PARTE* APPLICATION FOR SCHEDULING ORDER |

Regeneron's *Ex Parte* Application for Scheduling Order should be denied because it does not satisfy any of the requirements for *ex parte* relief. *See Mission Power Eng'g Co. v. Cont'l Cas. Co.*, 883 F. Supp. 488 (C.D. Cal. 1995). There is no emergency or irreparable prejudice, Regeneron is not without fault in creating this situation, and it does not meet the procedural requirements discussed in *Mission Power*.

Amgen apologizes for burdening the Court with this filing on a Saturday evening. Amgen understands that a response to an *ex parte* application is typically due within 24 hours, so it responds today to ensure compliance with the Court's procedures.

There is no reason this Court must immediately decide Regeneron's request to have its *preferred schedule* for preliminary injunction proceedings. When filing an *ex parte* motion, courts in this District have said: "There had better be a fire." *Mission Power*, 883 F. Supp. at 492. Here, there is no imminent harm set to befall Regeneron. As Regeneron knew before filing this *ex parte* application, Amgen cannot begin commercial marketing of its biosimilar aflibercept product until the date identified by Regeneron in its application. (Application at 9:6-7; Trask Decl. Ex. 2 at 1 (1/16/24 email from J. Labbe to D. Berl).). The parties' scheduling disputes can be briefed and resolved through normal procedure.

Tellingly, Regeneron does not even reference *Mission Power* let alone attempt to satisfy its stringent requirements, including the requirements that Regeneron must establish and substantiate "irreparable prejudice" and that Regeneron was "without fault in creating the crisis." *Mission*, 883 F. Supp. at 492. Neither factor is met here. Nor does Regeneron's application comply with the *Mission Power* requirement to file a separate, stand-alone motion seeking substantive relief and limiting the *ex parte* issue to the dates on which the merits of that motion will be briefed and heard. *Id.*

Regeneron served its summons on Friday January 12. (Dkt. 36.) That same day, Regeneron provided Amgen with a proposed preliminary injunction schedule. (Trask Decl. Ex. 2 at 2-4.) One business day later, on Tuesday January 16, Amgen responded to Regeneron with an alternative schedule. (Trask Decl. Ex. 2 at 1; Ex. 3.) On Thursday January 18, Regeneron declared the parties to be at an impasse but waited until Saturday January 20 at 2:00 A.M. to file its *ex parte* application, demanding immediate entry of its desired schedule, serving the application on Amgen later that morning. Such tactics are expressly discouraged in *Mission Power* and this Court's Standing Order (at 15).

Making matters worse, Regeneron did not even properly protect Amgen's highly confidential competitively sensitive information, which was designated as confidential under 42 U.S.C. § 262(*l*)(1). This information remained available to the public as of the filing of this paper. Amgen has asked Regeneron to immediately remedy this situation, but because Regeneron chose to file its papers on a weekend, it has not yet been able to remove the filing from the public record. Regeneron's actions violate 42 U.S.C. § 262(*l*)(1)(H), which provides that "[t]he disclosure of any confidential information in violation of this paragraph shall be deemed to cause [Amgen] to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph." Amgen respectfully requests that, in addition to denying Regeneron's application, the Court order the immediate withdrawal of documents containing Amgen's confidential information from the public docket.

Even though Regeneron has yet to file a motion for a preliminary injunction against Amgen, Amgen is and has been willing to discuss a reasonable schedule and is prepared to present its position to the Court. But Regeneron's attempt to resolve the dispute using the *ex parte* procedure is improper. Far from any real-world crisis that requires this Court's emergency intervention, Regeneron's submission makes

clear that it seeks entry of its preferred schedule for strategic reasons: to bolster Regeneron's pending motion to transfer this case for pretrial purposes to West Virginia. But the Judicial Panel on Multidistrict Litigation is not due to hear Regeneron's motion until March 28, 2024. (Trask Decl. Ex. 7 at 2, JPML Dkt. entry 7.) And while the JPML has yet to rule on the merits of the transfer motion, Regeneron similarly tried to manufacture an emergency there, requesting expedited consideration of its motion to transfer, which the JPML promptly denied. (*Id.*)

Having lost its bid to expedite in front of the JPML, Regeneron now urges this Court to bypass the normal noticed motions procedure to grant it urgent *ex parte* relief, which relief is centered on Regeneron's *assumption* that it will succeed in its attempt to transfer this case to West Virginia. Amgen will fully brief the reasons why Regeneron's transfer motion should be denied in its opposition to the transfer motion, due to be filed before the JPML on February 2, 2024. (Trask Decl. Ex. 7 at 1, JPML Dkt. entry 6 (setting JPML briefing schedule).) To the extent the Court believes these issues are relevant to the scheduling of preliminary injunction proceedings in this case, Amgen would welcome the opportunity to present these issues in full to the Court.

* * *

Amgen respectfully requests that the Court either deny Regeneron's *Ex Parte* Application or issue a schedule for Amgen to file an opposition addressing the reasons Regeneron's proposed schedule is not right for this case. Amgen requests that, in addition to denying this application, the Court order Regeneron to take any and all steps necessary to remove the documents that contain Amgen's confidential information from the public docket immediately and that Regeneron certify that it has instituted more stringent precautionary measures to ensure that no further disclosure of Amgen confidential information occurs.

Dated: January 20, 2024

PROSKAUER ROSE LLP
Siegmund Y. Gutman
Scott P. Cooper
Shawn S. Ledingham, Jr.
Jennifer L. Roche

By: */s/ Shawn S. Ledingham, Jr.*
Shawn S. Ledingham Jr.

MARSHALL, GERSTEIN & BORUN LLP
John R. Labbe
Kevin M. Flowers
Thomas Burns

ROTHWELL, FIGG, ERNST, & MANBECK, P.C.
E. Anthony Figg
Joseph A. Hynds
Jennifer Nock
Brett A. Postal

Attorneys for Defendant AMGEN INC.

# EXHIBIT 11

*Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*,
No. 22-61, Dkt. 658 (N.D. W. Va. Dec. 11, 2023)

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE NORTHERN DISTRICT OF WEST VIRGINIA**
**CLARKSBURG DIVISION**

| | |
|---|---|
| REGENERON PHARMACEUTICALS, INC.,<br><br>Plaintiff,<br>v.<br><br>MYLAN PHARMACEUTICALS INC. and BIOCON BIOLOGICS INC.,<br><br>Defendants. | Case No. 1:22-cv-00061-TSK |

**DEFENDANTS' MOTION TO ENFORCE THE PROTECTIVE ORDER AND FOR SANCTIONS RELATED TO PLAINTIFF'S PROTECTIVE ORDER VIOLATIONS**

Defendants Biocon Biologics Inc. and Mylan Pharmaceuticals Inc. ("Defendants") hereby move the Court to order Plaintiff Regeneron Pharmaceuticals, Inc. ("Regeneron") to comply with the Stipulated Protective Order (Dkt. 91) and assure that Defendants' confidential information disclosed to unauthorized parties is properly accounted for. As set forth in the accompanying memorandum filed under seal, Regeneron has improperly disclosed information designated as "CONFIDENTIAL" or "OUTSIDE COUNSEL'S EYES ONLY" at least six times to in-house and outside counsel, domestic and foreign, not cleared under the Stipulated Protective Order in the months following trial. Defendants hereby move the Court to enforce the Stipulated Protective Order and to enter sanctions against Regeneron for the same, as well as enter any other relief it finds appropriate in light of Defendants' memorandum of law filed under seal. The basis for this motion, as set forth in the accompanying sealed memorandum of law, is that Regeneron has violated the Stipulated Protective Order and Defendants will suffer serious harm if not granted.

Date: December 11, 2023

STEPTOE & JOHNSON PLLC

***/s/ William J. O'Brien***
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*Attorneys for Defendants Biocon Biologics, Inc. and Mylan Pharmaceuticals Inc.*

**CERTIFICATE OF SERVICE**

I hereby certify that on December 11, 2023, I electronically filed the foregoing with the Clerk of the Court by using the Court's CM/ECF system, which will send notification of the same to all counsel of record.

***/s/ William J. O'Brien***

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*Counsel for Defendants*

# EXHIBIT 12

Redacted Email Correspondence Between Parties, dated Jan. 25, 2024 – Feb. 2, 2024

## John R. Labbe

**From:** John R. Labbe
**Sent:** Friday, February 2, 2024 8:41 PM
**To:** Kayali, Kathryn; Berl, David; Trask, Andrew; Eylea; Eylea Biosimilars
**Cc:** MGB-Amgen-ABP938; abp938@rothwellfigg.com; Gutman, Siegmund Y.; Ledingham, Jr., Shawn S.
**Subject:** RE: Regeneron v. Amgen - Case No. 2:24-cv-264-JWH-E

Kat,

I write in response to your email below from yesterday. Amgen is proposing that the parties work together to agree on an appropriate preliminary injunction schedule in view of the circumstances unique to Amgen's action. Although Amgen opposed, and the Court rejected, Regeneron's proposed schedule, Amgen expressed an interest to negotiate a reasonable schedule from the onset of the case. Specifically, Amgen proposed a schedule tailored to the circumstances of this case before Regeneron's ex parte application, which Regeneron rejected without making any counterproposals. As the Court's Order noted, "[t]he Court appreciates Amgen's willingness 'to discuss a reasonable schedule.'" Dkt. 51 at 3. Although the Court set a scheduling conference for April 5, 2024, the Court will no doubt expect the parties to appear that day with a proposed schedule. Yet your message below, questioning "what, if anything" the parties should do before April 5, suggests that Regeneron is unwilling to discuss a reasonable schedule or provide any information necessary to discuss the terms of a reasonable schedule.

Before the parties can exchange and respond to targeted discovery requests, Regeneron must identify the patents and claims for preliminary injunction proceedings. Regeneron's own proposed schedule acknowledged that the first step in the preliminary injunction process was for Regeneron to identify a narrow set of patents. This is the same first step that Regeneron included in each of its proposed schedules in the West Virginia actions as well. And on November 9, 2023, Regeneron proposed beginning preliminary injunction proceedings with Amgen by first identifying 4 patents. Regeneron provides no explanation for why it will no longer agree to identify the patents for the preliminary injunction proceeding as the first step in the process.

Our proposal of three patents and fifteen claims is reasonable for a preliminary injunction motion especially considering that Regeneron agreed to limit its case for trial against Biocon to three patents, and Regeneron previously proposed limiting preliminary injunction proceedings to four patents. If you have a reasonable counterproposal, please provide it and Amgen will consider it.

Moreover, we appreciate that discovery is a two-way street. The parties' are not in the same position, however. Amgen produced over 145,000 pages of documents to Regeneron in September 2023. You are now demanding that Amgen spend significant resources collecting, reviewing, and producing additional documents in response to requests that appear to relate to 29 patents covering many different technologies. It would be an inefficient use of the parties' and Court's resources to begin discovery on 29 patents, when both parties acknowledge that a small subset of these patents will be involved in any preliminary injunction proceeding. In contrast, Regeneron has yet to produce any documents to Amgen even though it has a "substantial production" at its fingertips that it has already produced to the other defendants.

Rather than condition negotiation of a preliminary injunction schedule on Amgen's production of documents on a wide range of topics, Regeneron should first identify the patents for preliminary injunction proceedings, and the parties should work together on a schedule, including for document production, in view of the asserted patents and other unique circumstances of this case. Accordingly, Amgen remains willing, as we always have been, to discuss a reasonable schedule.

Best,
John

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**From:** Kayali, Kathryn <KKayali@wc.com>
**Sent:** Thursday, February 1, 2024 10:52 AM
**To:** John R. Labbe <jlabbe@marshallip.com>; Berl, David <DBerl@wc.com>; Trask, Andrew <atrask@wc.com>; Eylea <Eylea@wc.com>; Eylea Biosimilars <Eylea.Biosimilars@weil.com>
**Cc:** MGB-Amgen-ABP938 <MGB-Amgen-ABP938@marshallip.com>; abp938@rothwellfigg.com; Gutman, Siegmund Y. <sgutman@proskauer.com>; Ledingham, Jr., Shawn S. <sledingham@proskauer.com>
**Subject:** RE: Regeneron v. Amgen - Case No. 2:24-cv-264-JWH-E

**External - This email is from an external email address outside the firm.**

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**Contains Amgen Confidential Information**

John:

Thank you for your email.

We do not understand the basis for your requests, nor the arbitrary deadline you selected for a response. The Court denied Regeneron's proposed schedule at Amgen's request, and Amgen did not request the Court enter a different schedule. The Court set a status conference for April 5, 2024--it is unclear what, if anything, Amgen is proposing should take place before that time, and Amgen's conduct is not conducive to the parties advancing preparations for preliminary injunction proceedings.

Regeneron offered to begin discovery in connection with preliminary injunction proceedings weeks ago, transmitting to Amgen on January 12 categories of documents relevant to those proceedings (see my email of January 23, 2024). The three defendants against whom Regeneron is pursuing preliminary injunction proceedings in West Virginia agreed to produce such documents. Amgen apparently refuses. Your January 25th response indicated that Amgen did not intend to produce any documents in response to Regeneron's January 12, 2024 requests, on the basis that the requests were sent too soon. In particular, you stated that Regeneron's "RFPs were sent to Amgen before the time that Regeneron is permitted to serve discovery requests under the Federal Rules of Civil Procedure." Since that time, we requested that you confirm that Amgen will collect in-process samples [redacted] To date, we have received no response to that request.

While Amgen has refused to participate in discovery, your email of January 25 requests that Regeneron produce documents to Amgen. Discovery must be a two-way street—either Amgen believes discovery is premature or Amgen believes discovery is now appropriate and will participate accordingly. Please let us know which is Amgen's position.

Likewise, we do not understand the basis for Amgen's demand that Regeneron identify no more than three patents and 15 claims that it will assert in a preliminary injunction proceeding. No Court has ordered Regeneron to limit the number of patents or claims it asserts against Amgen. Moreover, and as discussed above, Amgen has refused to provide discovery relevant to Regeneron's decision regarding which patents and/or claims it will assert. To the extent that Amgen wants Regeneron to narrow the number of patents it may assert in a motion for preliminary injunction, it should produce the documents we requested on January 12. Its failure to do so is delaying the parties' ability to advance preliminary injunction proceedings.

We are also surprised by your requests for information concerning the cases pending in West Virginia against Celltrion, Formycon, Bioepis, and Biocon. Regeneron sought to coordinate Amgen's case with the West Virginia cases, which would have permitted and/or facilitated Amgen's access to information concerning those cases. Amgen refused. Regeneron is not, therefore, in a position to provide Amgen information concerning the West Virginia cases that is not publicly available. We note for your convenience, however, that Judge Kleeh issued a redacted version of his December 27, 2023 opinion in the Biocon case on January 31, 2024.

We are even more surprised by your suggestion that Amgen's case should be coordinated with the West Virginia actions *after* preliminary injunction proceedings are complete. This proposal only underscores the substantial overlap between Amgen's case and those in West Virginia, and the fact that transfer of this case to West Virginia for pretrial proceedings would be both efficient and appropriate. As to your particular request that we consult you when discussing scheduling of future proceedings against Celltrion, Formycon, Bioepis, and Biocon, we cannot agree to do so. In view of Amgen's refusal to participate in the existing West Virginia schedule, we do not understand what consultation could be appropriate at this time. Further, your request for coordination—across cases pending in multiple jurisdictions with different governing protective orders—appears unworkable. To the extent that Amgen seeks to enhance efficiency by coordinating pre-trial discovery proceedings with those cases pending in West Virginia, it should accede to Regeneron's request for multi-district litigation transfer.

Regarding your request that the parties negotiate a preliminary injunction schedule, Regeneron remains willing to do so. However, the initiation of proceedings is predicated on Amgen producing the documents we requested on January 12. Please advise when we will receive those documents, so we may consider and negotiate a schedule accordingly.

Best,

Kat

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**From:** John R. Labbe <jlabbe@marshallip.com>
**Sent:** Wednesday, January 31, 2024 5:38 PM
**To:** Berl, David <DBerl@wc.com>; Trask, Andrew <atrask@wc.com>; Kayali, Kathryn <KKayali@wc.com>; Tony Bisconti <tbisconti@bklwlaw.com>; Eylea <Eylea@wc.com>; Eylea Biosimilars <Eylea.Biosimilars@weil.com>
**Cc:** MGB-Amgen-ABP938 <MGB-Amgen-ABP938@marshallip.com>; abp938@rothwellfigg.com; Gutman, Siegmund Y. <sgutman@proskauer.com>; Ledingham, Jr., Shawn S. <sledingham@proskauer.com>
**Subject:** RE: Regeneron v. Amgen - Case No. 2:24-cv-264-JWH-E

Counsel:

We write to follow up on our email from last week about a potential preliminary injunction schedule for this case.

We have not received any of the information we requested below that we believe is necessary to consider a preliminary injunction schedule. Please let us know when Regeneron will provide the requested information. If we do not hear from you by noon ET this Friday, we will assume that Regeneron is unwilling to provide the requested information to facilitate setting a preliminary injunction schedule at this time.

With respect to the remainder of the case following any preliminary injunction proceedings, Amgen is willing to discuss the possibility of coordination with the West Virginia cases once a schedule is entered for discovery in the West Virginia

actions and the California case against Amgen. For example, Amgen is willing to discuss coordination with respect to any patents that overlap in one or more of the ongoing aflibercept actions once a schedule for discovery is entered. To that end, please keep us informed when Regeneron begins discussing a potential case schedule for the post-preliminary injunction proceedings in the West Virginia cases. Please also let us know whether Regeneron and Biocon expect any discovery or other district court proceedings pending appeal of the Biocon trial decision. If so, please inform us of the proposed schedule and scope of proceedings.

Best,
John

MARSHALL GERSTEIN

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**From:** John R. Labbe <jlabbe@marshallip.com>
**Sent:** Thursday, January 25, 2024 3:02 PM
**To:** Berl, David <DBerl@wc.com>; Trask, Andrew <atrask@wc.com>; Kayali, Kathryn <KKayali@wc.com>; Tony Bisconti <tbisconti@bklwlaw.com>; Eylea <Eylea@wc.com>; Eylea Biosimilars <Eylea.Biosimilars@weil.com>
**Cc:** MGB-Amgen-ABP938 <MGB-Amgen-ABP938@marshallip.com>; abp938@rothwellfigg.com; Gutman, Siegmund Y. <sgutman@proskauer.com>; Ledingham, Jr., Shawn S. <sledingham@proskauer.com>
**Subject:** Regeneron v. Amgen - Case No. 2:24-cv-264-JWH-E

Counsel:

We write regarding a potential preliminary injunction schedule for this case. As stated in Amgen's opposition to Regeneron's *ex parte* application, Amgen is willing to discuss a reasonable schedule for any preliminary injunction motion that Regeneron may file. To do that effectively, however, Amgen requests that Regeneron provide the following information no later than January 30, 2024:

1) The no more than three patents and 15 claims that Regeneron will assert against Amgen for any preliminary injunction proceeding in this case;

2) The patents and claims that Regeneron has identified for preliminary injunction proceedings against each of Celltrion, Samsung Bioepis, and Formycon;

3) A redacted copy of the trial opinion issued on December 27, 2023, by Judge Kleeh in the Biocon case, Case No. 1:22-cv-61-TSK-JPM; and

4) The schedule for further proceedings in the Biocon case.

Best,
John


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