Trials@uspto.gov
571-272-7822

Paper 94
Date: November 9, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

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

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:

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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

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[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.

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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

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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;

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> 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

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(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

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> 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.

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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

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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).

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[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.

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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

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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

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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).

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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,

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> 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

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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),

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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

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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.

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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).

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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.*,

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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,

Petitioner Fresenius Ex. 1015, 0039

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

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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.

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[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.

Petitioner Fresenius Ex. 1015, 0063

PETITIONER:

Paul Molino
William Rakoczy
Neil McLaughlin
Heinz Salmen
RAKOCZY MOLINO MAZZOCHI SIWIK LLP
paul@rmmslegal.com
wrakoczy@rmmslegal.com
nmclaughlin@rmmslegal.com
hsalmen@rmmslegal.com

Teresa Rea
Deborah Yellin S
hannon Lentz
CROWELL & MORING LLP
trea@crowell.com
dyellin@crowell.com
slentz@crowell.com

Lora Green
Yahn-Lin Chu
WILSON SONSINI GOODRICH & ROSATI
lgreen@wsgr.com
ychu@wsgr.com

PATENT OWNER:

Deborah Fishman
Amanda Antons
Alice Sin Yu Ho
ARNOLD & PORTER KAYE SCHOLER LLP
deborah.fishman@kayescholer.com
amanda.antons@arnoldporter.com
alice.ho@arnoldporter.com