Trials@uspto.gov
571-272-7822

Paper 55
Entered: June 14, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO. LTD.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

IPR2023-00442
Patent 10,130,681 B2

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

NEW, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Dismissing in Part and Denying in Part Patent Owner's Motion to Exclude Evidence
37 C.F.R. § 42.64(c)
Determining Challenged Claims 1, 3–11, 13, 14, 16–24, and 26 Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

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

A. Procedural History

On July 1, 2022, Petitioner filed its Petition (Paper 2, "Petition") seeking *inter partes* review of claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Patent Owner timely filed a Preliminary Response. Paper 7 ("Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-Reply. Paper 8 ("Prelim. Reply"); Paper 9 ("Prelim. Sur-Reply"). On July 19, 2023, and pursuant to 35 U.S.C. § 314, we instituted *inter partes* review of challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Paper 10 ("Institution Decision" or "Dec.").

After institution of trial, Patent Owner filed a Response (Paper 26, "PO Resp."), to which Petitioner filed a Reply (Paper 40, "Pet. Reply"), and Patent Owner, in turn, filed a Sur-Reply (Paper 45, "Sur-Reply").

Patent Owner filed a Motion to Exclude Evidence (Paper 46, "Mot. Exclude") and Petitioner filed an Opposition to the Motion to Exclude

(Paper 48, "Opp. Mot. Exclude"). Patent Owner then filed a Reply to Petitioner's Opposition to the Motion to Exclude (Paper, 49, "Reply Mot. Exclude").

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner identifies itself, Samsung Bioepis Co., Ltd., as the real party-in-interest. Pet. 6. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 43 at 2.

B. Related Matters

Petitioner identifies *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880 and IPR2021-00881, and IPR2022-01225 (PTAB). Paper 38, 6. Final Written Decisions in IPR2021-00880 and IPR2021-00881 were entered on November 9, 2022, and in IPR2022-01225 on January 9, 2024. Petitioner further identifies as related matters *Samsung Bioepis Co., Ltd. v. Regeneron Pharmaceuticals, Inc.*, IPR2023-00739, *Biocon v. Regeneron Pharmaceuticals, Inc.*, IPR2024-00566 (joined with IPR2023-00739), *Samsung Bioepis Co., Ltd. v. Regeneron Pharmaceuticals, Inc.*, IPR2023-00884, *Celltrion Inc. v. Regeneron Pharmaceuticals, Inc.*, IPR2024-00260 (joined with IPR2023-00884). Paper 38 at 2.

Petitioner also identifies the following district court litigations as related matters: *Regeneron Pharmaceuticals, Inc. v. Samsung Bioepis, Inc.*, No. 1:23-cv-00094 (N.D. W.Va.); *Regeneron Pharmaceuticals, Inc. v. Samsung Bioepis, Inc.*, No. 1:23-cv-00106 (N.D. W.Va.); *Regeneron Pharmaceuticals, Inc. v. Formycon*, No. 1:23-cv-00097 (N.D. W.Va.),

Regeneron Pharms., Inc. v. Mylan Pharms. Inc., 1:22-cv-00061-TSK (N.D. W.Va.) and *Regeneron Pharmaceuticals, Inc. v. Celltrion, Inc.*, No. 1:23-CV-0089 (N.D. W.Va) as related matters. Paper 38 at 2–3.

Patent Owner additionally identifies *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2022-01226 (PTAB) (Final Written Decision entered January 9, 2024). Paper 43 at 2. Patent Owner also identifies as a related matter *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated before institution). *Id.* at 4.

Of particular relevance to our decision in this proceeding is the Final Written Decision entered in *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-01225 (the "-01225 IPR"), in which Mylan challenged the same claims of the '681 patent that Petitioner now challenges in the present *inter partes* review. *See* IPR2022-01225, Paper 96. In the -01225 IPR Final Written Decision, entered on January 9. 2024, the Board found that all of the challenged claims were unpatentable. *Id.*

Also of relevance to our present decision is the Final Written Decision entered in IPR2021-0881 (the "-00881 IPR") on November 9, 2022, and which challenged claims 1, 3–11, 13, 14, 16–24 and 26 of U.S. Patent No. 9,254,338 B2 ("the '338 patent"). *See* IPR2021-00881, Paper 94 (the "-00881 Decision"). Both the '681 patent and the '338 patent at issue in IPR2021-00881 share a common Specification. *See generally*, Ex. 1001; IPR2021-00881, Ex. 1001. Moreover, and as we explain in Section IV.D.3 below, independent claims 1 and 14 of the '338 patent are identical to claim 1 of the '681 patent, with the exception that the '681 patent claims recite certain exclusion criteria as an additional limitation. In the -00881 Decision,

the panel found that the challenged claims were unpatentable as anticipated by the Dixon reference asserted by Petitioner in the present *inter partes* review. *See generally* -00881 IPR, Paper 94.

C. The Asserted Ground of Unpatentability

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

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1, 3–11, 13, 14, 16–24, 26	103[1]	Dixon[2], CATT[3], MACTEL[4], PIER[5]

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

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

[3] NCT00593450, *CATT Patient Eligibility Criteria*, *available at*: www.clinicaltrials.gov/ct2/show/NCT00593450 (last visited July 5, 2023) ("CATT") Ex. 1031.

[4] NCT00685854, *Pilot Study of Intravitreal Injection of Ranibizumab for Macular Telangiectasia With Neovascularization (MACTEL 2)*, *available at*: https://clinicaltrials.gov/ct2/history/NCT00685854?V_1=View#StudyPageTop (last visited July 5, 2023 ("MACTEL") Ex. 1032.

[5] C.D. Regillo et al., *Randomized, Double-Masked, Sham-Controlled Trial of Ranibizumab for Neovascular Age-related Macular Degeneration: PIER Study Year 1*, 145(2) AM. J. OPHTHALMOL. 239–48 (2008) ("PIER") Ex. 1034.

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

D. The '681 Patent

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

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

E. Representative Claim

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

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

Ex. 1001, col. 21, ll. 40–63.[6]

---

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

F. Priority History of the '681 Patent

The '681 patent issued from U.S. Application Ser. No. 15/471,506 (the "'506 application") filed on March 28, 2017, and claims the priority benefit of, *inter alia*, US Provisional Application Ser. No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

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

III. PATENT OWNER'S MOTION TO EXCLUDE EVIDENCE

Patent Owner moves to exclude Petitioner's: (1) Exhibit 1031 and those portions of Petitioner's Petition, Reply, and the Chaum Declaration relying on that exhibit; (2) Exhibits 1071 and 1072, and portions of Petitioner's Reply relying on those exhibits; and (3) Exhibit 1029. Mot. Exclude, 1. We address each of Patent Owner's arguments in turn.

A. Exhibit 1031

Exhibit 1031 ("CATT") is a document entitled "CATT Patient Eligibility Criteria" that Petitioner relies upon as disclosing some or all of the exclusion criteria recited in independent claims 1 and 14 of the '681 patent. Exhibit 1031 is prefaced by an affidavit by Mr. Nathaniel E. Frank-White, a Records Request Processor at the Internet Archive. Ex. 1031, 1–2. In his affidavit, Mr. Frank-White attests that CATT is "true and accurate copies of the Internet Archive's records of the archived files for the URLs and the dates specified in the attached coversheet." *Id.* at 1.

Patent Owner argues that neither the Petition nor the accompanying papers provide any evidence or explanation establishing that Exhibit 1031 is a disclosure of exclusion criteria from the CATT clinical trial. Mot. Exclude 2. According to Patent Owner, Exhibit 1031 is not a study protocol, ClinicalTrials.gov entry, or scientific publication. *Id.* Rather, Patent Owner asserts, it appears to be an excerpt from a larger document of unknown origin and authorship, and that it contains no indication that its listed "eligibility criteria," were in fact included in the CATT study protocol, or in any other document upon which a person of ordinary skill in the art would have relied. *Id.* Patent Owner notes that it timely objected to Petitioner's introduction of Exhibit 1031 in its Preliminary Response. *Id.* at 1–2 (citing Prelim. Resp. 26).

Patent Owner further argues that Exhibit 1031 should be excluded under Federal Rules of Evidence ("FRE") 702 and 703. Mot. Exclude 6. Patent Owner contends that Petitioner is attempting to use the testimony of its expert, Dr. Chaum, to introduce hearsay evidence that would be otherwise inadmissible. *Id.* at 7.

Petitioner relies, in part, on Exhibit 1031 as demonstrating that the exclusion criteria recited in the independent claims of the '681 patent would have been obvious. *See, e.g.*, Pet. 42–47. However, as we explain below (*see* Section IV.A.3), and as we previously concluded in our Final Written Decision in the -01225 IPR (*see* -01225 IPR, Paper 96 at 45–52)[7], the

[7] We also noted that, although not in any way binding upon our Decision, the court in the parallel district court litigation of the '681 patent reached the same conclusion subsequent to a *Markman* hearing upon the matter. *See* -01225 IPR, Paper 96 at 50 (citing -01225 IPR, Ex. 1112, 34–35).

exclusion criteria are not limiting upon the claims of the '681 patent under the printed matter doctrine.

Because we again conclude that the exclusion criteria do not limit the challenged claims of the '681 patent, the parties' arguments concerning whether those limitations would have been obvious over the cited prior art, including Exhibit 1031, are moot. Patent Owner's motion to exclude Exhibit 1031 is consequently dismissed.

B. Exhibits 1071 and 1072

Exhibit 1071 is a Supplementary Appendix to a published journal article, D.M. Brown et al., *Ranibizumab versus Verteporfin for Neovascular Age-Related Macular Degeneration*. 355 NEW ENGL. J. MED. 1432–44 (2006) ("Brown"). *See* Ex. 1071, 1. Exhibit 1071 discloses "methods and supplementary tables" relating to the clinical study described in Brown (the "ANCHOR study"). *Id.* at 2–3. Relevantly, Ex. 1071 discloses eligibility and exclusion criteria for the ANCHOR study. *Id.* at 2.

Exhibit 1072 is also a Supplementary Appendix to a published journal article, P.J. Rosenfeld et al., *Ranibizumab for Neovascular Age-Related Macular Degeneration*, 355 NEW ENGL. J. MED. 1419–31 (2006) ("Rosenfeld"). *See* Ex. 1072, 1. Exhibit 1072 discloses "Eligibility Criteria for [the] MARINA Study" described in Rosenfeld and, relevantly, discloses exclusion criteria for that study. *Id.* at 2–4.

Patent Owner contends that Exhibits 1071 and 1072 are unauthenticated hearsay and therefore should be excluded under FRE 401-03, 802, and 901-02. Mot. Exclude 7. Specifically, Patent Owner argues that Petitioner has not established that either Exhibit 1071 or 1072 was

published in the prior art, and are unauthenticated hearsay. *Id.* Patent Owner notes that it timely objected to these exhibits as irrelevant under FRE 401–403, and as hearsay and unauthenticated under FRE 802 and 902. *Id.* (citing Paper 41 at 1–2).

As with Exhibit 1031 above, Petitioner relies upon Exhibits 1071 and 1072 as evidence supporting its allegations that the exclusion criteria limitations of the challenged claims would have been obvious over the prior art. However, we previously concluded in the -01225 IPR, and conclude again below, that the exclusion criteria are not limiting upon the challenged claims of the '681 patent. *See* -01225 IPR, Paper 96 at 45–52; Section IV.A.3, *infra*. The arguments concerning whether Exhibits 1071 and 1072 support the obviousness of the exclusion criteria limitations over the prior art are therefore moot. We consequently dismiss Patent Owner's motion to exclude Exhibits 1071 and 1072 as moot.

C. Exhibits not cited in the pleadings

Finally, Patent Owner moves to exclude any Exhibits that are not cited in the pleadings, and which "ha[ve] no bearing on any fact that is of consequence in determining the outcome of the proceeding." Mot. Exclude 7–8 (quoting *One World Techs., Inc. v. Chamberlain Grp., Inc.*, IPR2017-00126, Paper 56, at 16–17 (PTAB Oct. 24, 2018)). Patent Owner specifically moves to exclude Exhibit 1029, which Patent Owner asserts was not cited in Petitioner's pleadings, and to which Patent Owner timely objected with sufficient particularity. *Id.* at 8.

Exhibit 1029 is U.S. Patent No. 9,669,069 B2 (the "'069 patent). The '069 patent is closely related to the '338 and '681 patents, and its claims

were canceled as unpatentable as a result of the Final Written Decision entered in the related IPR2021-00880 (the "-00880 IPR"). *See* IPR2021-00880, Paper 89. The Petition in the present *inter partes* review lists the '069 patent as Exhibit 1029 in its Table of Exhibits (*see* Pet. v), and discusses the '069 patent a number of times, both as the subject matter of a trial related to this *inter partes* review, and in its context relating to the common subject matter of the '069, '338 and '681 patents. *See* Pet. 6, 9, 24 n.2, 57. Although Petitioner does not cite to the '069 patent as "Exhibit 1029" in the text of its pleadings, it nevertheless expressly identifies the '069 patent in its Petition as Exhibit 1029, and discusses the patent therein. *Id.*

Patent Owner's argument that Exhibit 1029 was not cited by Petitioner, or that it "has no bearing on any fact that is of consequence in determining the outcome of the proceeding," is thus baseless, and we deny Patent Owner's motion to exclude the Exhibit. As for other, unnamed, "Exhibits not cited in the pleadings," although we do not customarily rely extensively on Exhibits *not* cited by the parties in support of their arguments, Patent Owner's Motion to Exclude does not specify any other Exhibits to which it has timely objected, nor does it cite any legal basis under the Federal Rules of Evidence for excluding such unspecified Exhibits. *See* PTAB, *Consolidated Trial Practice Guide* (November 2019) ("CTPG") at 79; *available at*: https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf?MURL=TrialPracticeGuideConsolidated (requiring that a motion to exclude should: (a) identify where in the record the objection originally was made; (b) identify where in the record the evidence sought to be excluded was relied upon by an opponent; (c) address objections to

exhibits in numerical order; and (d) explain the basis and grounds for each objection). We consequently deny Patent Owner's motion to exclude such Exhibits.

D. Summary

For the reasons we have explained above, we dismiss as moot Patent Owner's Motion to Exclude Exhibits 1031, 1071, and 1072. We deny Patent Owner's motion to exclude Exhibit 1029 and any unnamed "Exhibits not cited in the pleadings."

IV. ANALYSIS

A. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Samsung Bioepis Exhibit 1118
Page 13

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

Petitioner accepts that the preamble of claim 1 is limiting, and agrees with the Board's previous rejection, in the related -00881 *inter partes* review, of Patent Owner's position that the preamble requires a particular level of efficacy. Pet. 19 (citing Ex. 1004, 18). According to Petitioner, the plain and ordinary meaning of the term "treating" does not require a specific level of efficacy, but only that the method be administered for the purpose of treatment of an angiogenic eye disease. *Id.* (citing Ex. 1002 ¶ 84).

Patent Owner argues, as it argued previously in the -00881 and -01225 IPRs, that the language of the preamble reciting a "method for treating an angiogenic eye disorder" requires not only an intent to treat, but, additionally, efficacy on par with monthly Lucentis.[8] PO Resp. 9–10. Briefly, Patent Owner again contends that the claimed methods of the '681 Patent, which recite "initial" and "secondary" doses followed by less frequent "tertiary" doses, "allow[ed] for less frequent dosing" while maintaining comparable efficacy to monthly Lucentis. PO Resp. 12–13 (citing Ex. 1001, col. 1, ll. 52–62). Patent Owner contends that the'681 Patent was "groundbreaking" because it maintained initial gains with less frequent "tertiary doses." *Id.* at 14 (citing Ex. 1001, col. 2, ll. 7–24).

Patent Owner argues further that prior art cited in the Specification of the '681 patent, and the exemplary embodiments disclosed by the

---

[8] "Lucentis is an intravitreal injection formulation of ranibizumab, "a vascular endothelial growth factor (VEGF) inhibitor . . . indicated for the treatment of patients with: Neovascular (Wet) Age-Related Macular Degeneration (AMD) (1.1) Macular Edema Following Retinal Vein Occlusion (RVO) (1.2) or (3) Diabetic Macular Edema (DME) (1.3)." Ex. 2216.

Specification, support its contention that the claimed regimen recited in the challenged claims achieved and maintained efficacy in the treated population. PO Resp. 14–15. Patent Owner also argues that the prosecution history of the '681 patent supports its claim construction. *Id.* at 16. Patent Owner asserts that it overcame a double patenting rejection by explaining that the "treatment protocol" encompassed by the claimed invention resulted in surprising efficacy, i.e., noninferiority to ranibizumab, despite less frequent dosing. *Id.* (citing Ex. 1025, 463–468, 488–492). Patent Owner contends that, at the time of the '681 patent's filing, a person of ordinary skill in the art would not have considered a less frequent dosing regimen that was inferior to the standard-of-care to be "treating" an angiogenic eye disorder. *Id.* at 17 (citing Ex. 2056 ¶¶ 102–104; *Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1353–54 (Fed. Cir. 2000)).

We previously addressed this issue, and Patent Owner's arguments, in both the -00881 and -01225 IPRs, and we here incorporate by reference our reasoning from both of those *inter partes* reviews. *See* -00881 IPR, Paper 94 at 17–23; -01225 IPR, Paper 96 at 33–37. To summarize, in each of those prior *inter partes* reviews, we concluded that: (1) the preamble to challenged independent claims 1 and 14 are limiting to the extent that they require "treating an angiogenic eye disorder in a patient"; (2) the intrinsic evidence supported the conclusion that it is the administration of the VEGF antagonist to a 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; and (3) Patent Owner's proposed construction that the language of the preamble requires a "high level of efficacy that was noninferior to the standard of care by the time the patent was filed in 2011,"

was not supported by the evidence and required impermissibly importing limitations into the claims. *See, e.g.*, -01225 IPR, Paper 96 at 34-37.

Specifically, we concluded that:

> [W]hen the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount," and discloses that "a therapeutically effective amount can be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder," or it may not. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

-01225 IPR, Paper 96 at 35–36 (quoting -00881 IPR, Paper 94 at 21–22 (citation omitted)). Furthermore, the Board found that:

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

Id. at 36 (quoting -00881 IPR, Paper 94 at 22 (citations omitted)).

We adopt the same reasoning here, and conclude that the evidence of record and the Specification of the '681 patent support construing the preamble's recitation of a "method for treating a patient with an angiogenic eye disorder" as meaning administering a compound, i.e., the recited VEGF antagonist, to a patient for the purpose of improving or providing a beneficial effect in their angiogenic eye disorder. We find that, as in *Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, although the claims "encompass a clinical result, they do not *require* such a result." (emphasis added). 8 F.4th 1331, 1343 (Fed. Cir. 2021). We consequently reject Patent Owner's proposed construction that the language of the preamble reciting a "method for treating an angiogenic eye disorder" requires not only an intent to treat, but, additionally, a high degree of efficacy on par with monthly Lucentis. *See* PO Resp. 9–10.

2. <u>"Initial dose," "Secondary Dose," and "Tertiary Dose"</u>

Petitioner next contends that a person of ordinary skill in the art would understand each of these claim terms as expressly defined in the '681 patent's Specification. Pet. 22.

The Specification of the '681 patent defines the claim terms as follows:

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

> secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of dosing regimens, but will generally differ from one another in terms of frequency of administration.

Ex. 1001, col. 3 ll. 34–44. Petitioner also notes that the Specification further explains that "the immediately preceding dose" means "in a sequence of multiple administrations, the dose of VEGF antagonist which is administered to a patient prior to the administration of the very next dose in the sequence with no intervening doses." Pet. 22–23 (citing Ex. 1001, col. 3, ll. 31–38; Ex. 1002 ¶¶ 89–90).

We adopt Petitioner's proposed construction of the claim terms "initial dose," "secondary dose," and "tertiary dose." Petitioner proposes adoption of the definitions expressly set forth in the Specification of the '681 patent, *viz.*, that the initial dose is the dose "administered at the beginning of the treatment regimen," and is followed by the secondary doses that are "administered after the initial dose," and the tertiary doses are "administered after the secondary doses" and may be distinguished from the secondary doses "in terms of frequency of administration." Ex. 1001, col. 3, ll. 36–44.

Patent Owner does not expressly dispute Petitioner's construction, other than to argue that, by 2011, a person of ordinary skill in the art would have understood "initial" and "secondary" doses to correspond to loading doses and "tertiary" doses to correspond to maintenance doses. PO Resp. 13 (citing Ex. 2056 ¶ 66; Ex. 2349, 6–11. Patent Owner contends that the purpose (and expected effect) of loading doses was to achieve visual acuity gains and retina drying, and the goal of less frequent maintenance doses was

Samsung Bioepis Exhibit 1118
Page 18

to maintain the efficacy achieved with loading doses. *Id.* at 14 (citing Ex. 2056 ¶ 66).

As we have explained above, we do not find persuasive Patent Owner's argument that the definition of these terms requires a high, or otherwise defined, degree of efficacy. As we stated in the -00881 and -01225 Decisions:

> 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."*

-01225 IPR, Paper 96 at 38 (quoting -00881 IPR, Paper 94 at 25 (emphasis added). We see no need or reason to upend this construction now, and we adopt Petitioner's proposed definition of the claim terms "initial dose," "secondary doses," and "tertiary doses" as the express definition provided by the '681 Specification.

3. <u>The exclusion criteria</u>

The "exclusion criteria" limitation of independent challenged claims 1 and 14 recites:

> [W]herein exclusion criteria for the patient include all of:
>
> (1) active intraocular inflammation;
>
> (2) active ocular or periocular infection;
>
> (3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 58–62.

Both parties agree that the exclusion criteria recited in challenged independent claims 1 and 14 are limiting upon the claims.[9] Pet. 23, 59; PO Resp. 18 ("The parties agree that the Exclusion Criteria are entitled to patentable weight"). Such agreement notwithstanding, we previously concluded, in the -01225 IPR, that the exclusion criteria of the '681 patent are *not* limiting upon the claims under the printed matter doctrine. *See* -01225 IPR, Paper 96 at 45–52. We therefore concluded that the exclusion criteria should not be accorded patentable weight. *Id.* We adopt the same reasoning in the present *inter partes* review, which we summarize below.

As an initial matter, we note that, at oral argument, and subsequently, both Patent Owner and Petitioner each agreed to incorporate into the record of the present *inter partes* review all evidence and argument regarding whether the claimed exclusion criteria should be given patentable weight that were raised by the parties in IPR2022-01225. The parties further agreed that this agreement obviated the need for additional briefing on the patentable weight issue in the present *inter partes* review. Hearing Tr. 42–43; Ex. 3002.

In *Praxair Distrib., Inc. v. Mallinckrodt Hosp. Prods. IP Ltd.*, our reviewing court held that the printed matter doctrine is not limited to literal printed matter, but is also applicable when a claim limitation "claims the content of information" absent an adequate functional relationship. 890 F.3d 1024, 1032 (Fed. Cor. 2018 (quoting *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015)). "Claim limitations directed to the content of information

---

[9] At oral argument, counsel for Petitioner stated that it was "agnostic" on the subject of whether the exclusion criteria are limiting upon the claims. Hearing Tr. 6.

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

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

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

There can be little question that the exclusion criteria are directed to informational content. Specifically, the limitation in question expressly states that the "exclusion criteria for the patient include all of: (1) active

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

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

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

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

practicing the method of the challenged claims of the '681 patent would be similarly free to ignore the conditions of the exclusionary criteria and still be practicing the claimed method.

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

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

In the parallel district court proceedings, the district court, acknowledging our Institution Decision in the -01225 IPR, arrived at the same conclusion with respect to essentially identical exclusion criteria limitations in Patent Owner's related '601 and '572 patents. *See* -01225 IPR, Ex. 1112. Noting that the claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice," the district court found that:

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

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

The district court noted that, even under Patent Owner's "assess and exclude" approach, a patient either never starts the method (and hence the method doesn't change) or, if doctors screened for the information and found no infection or inflammation, the method proceeds as claimed. -01225 IPR, Ex. 1112, 35. The district court concluded that this confirms that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.*

In the district court proceedings, the court continued:

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

-01225 IPR, Ex. 1112, 35 (emphases in original). The court concluded that because "there is no requirement to take new action [or to take no action] that flows from the 'wherein the exclusion criteria for a patient include ….' information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight." *Id.* at 37. We agree.

As the district court recognized, we are not bound by its decision (nor it by ours) because "the PTAB properly may reach a different conclusion based on the same evidence," for the Board and the district courts function under different evidentiary standards and burdens of proof. *See* -01225 IPR, Ex. 1112, 34 (quoting *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293–94 (Fed. Cir. 2017); *see also Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 282–83 (2016)). However, as the Federal Circuit recognized, "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

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

B. A Person of Ordinary Skill in the Art

Petitioner notes that the Petitioner in the '00881 IPR proposed that a person of ordinary skill in the art would have: (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field. Pet. 17–18 (quoting -00881 IPR, Paper 94 at 9–10). Furthermore, it was asserted that such a person would typically have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable

professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders, including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists. *Id.* at 18 (citing -00881 IPR Paper 94 at 10).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Response.

In the -01225 IPR, we adopted the same definition of a person of ordinary skill in the art for the challenged claims of the '681 patent, concluding that that definition was consistent with the level of skill in the art. *See* -01225 IPR, Paper 96 at 52–53. Having previously adopted this definition of the level of skill in the art for the claims of the '681 patent, we do so again in the present proceeding.

C. Principles of Law

1. Burden of Proof

"In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable." *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016 (citing 35 U.S.C. § 312(a)(3) (requiring *inter partes* review petitions to identify "with particularity … the evidence that supports the grounds for the challenge to each claim")). Therefore, in an *inter partes* review, the burden of proof is on the Petitioner to show that the challenged claims are unpatentable; that burden never shifts to the patentee. *See* 35 U.S.C. § 316(e); *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1375

(Fed. Cir. 2016) (citing *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015)).

2. Obviousness

To ultimately prevail in its challenge to Patent Owner's claims, Petitioner 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). A patent claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In determining obviousness when all elements of a claim are found in various pieces of prior art, "the factfinder must further consider the factual questions of whether a person of ordinary skill in the art would be motivated to combine those references, and whether in making that combination, a person of ordinary skill would have had a reasonable expectation of success." *Dome Patent L.P. v. Lee*, 799 F.3d 1372, 1380 (Fed. Cir. 2015); *see also WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1355 (Fed. Cir. 1999) ("When an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to

combine the references."). "Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988); *see also In re Magnum Oil Tools*, 829 F.3d at 1381 (finding a party that petitions the Board for a determination of unpatentability based on obviousness must show that "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.") (internal quotations and citations omitted).

An obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; *see In re Translogic Tech, Inc.*, 504 F.3d 1249, 1259 (Fed. Cir. 2007). In *KSR*, the Supreme Court also stated that an invention may be found obvious if trying a course of conduct would have been obvious to a person of ordinary skill in the art:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

550 U.S. at 421. "*KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless 'the improvement is more than the predictable use of prior art elements according to their established functions.'" *In re Kubin*, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009) (citing *KSR*, 550 U.S. at 417).

We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

D. Ground 1: Obviousness under 35 U.S.C. § 103 of claims 1, 3–11, 13, 14, 16–24, and 26 over Dixon (Ex. 1006), CATT (Ex. 1031), MACTEL (Ex. 1032), and PIER (Ex. 1034) (individually and collectively)

Claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are challenged as unpatentable under 35 U.S.C. § 103 as being obvious over Dixon, CATT, MACTEL, and PIER. Pet. 48–52.

1. Overview of Dixon

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

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

improving efficacy and extending duration of action," Ex. 1006, 1574, 1577; Ex. 1002 ¶ 78.

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

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

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

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

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

Id. (internal citations omitted).

2. CATT, MACTEL, and PIER

Petitioner relies upon CATT, MACTEL, and PIER, jointly and severally, as describing the exclusion criteria for clinical trials of the leading prior art anti-VEGF treatments, *viz.*, bevacizumab (Avastin®) and ranibizumab (Lucentis®). Pet. 42 (citing Ex. 1002 ¶¶ 99–110, 130–149). Because we have concluded, both in the Final Written Decision of the -01225 IPR, and in the present *inter partes* review (*see* Section IV.A.3, *supra*), that the exclusion criteria should not be accorded patentable weight, we need not characterize these references in this Decision.

3. Challenged independent claims 1 and 14

In the Final Written Decision in the -00881 IPR, we determined that independent claims 1 and 14 of the ’338 patent were unpatentable under 35 U.S.C. § 102 as anticipated by Dixon. For the convenience of the reader, we present below a claim chart comparing independent claim 1 of the present challenged claims of the ’681 patent, and claim 1 of the ’338 patent in the -00881 Decision:

Samsung Bioepis Exhibit 1118
Page 31

IPR2022-01225/ IPR2023-00442 US 10,130,681 B2 Claim 1	IPR2021-00881 US 9,254,338 B2 Claim 1 (unpatentable)
1. A method for treating an angiogenic eye disorder in a patient,	1. A method for treating an angiogenic eye disorder in a patient,
said method comprising sequentially administering to the patient 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;	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 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;	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

and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2;	multimerization component comprising amino acids 232–457 of SEQ ID NO:2.
wherein exclusion criteria for the patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks.	

As is evident from the chart above, challenged claim 1 of the present Petition and claim 1 of the ’338 patent are identical, with the sole exception, in the ’681 patent, of the additional limitation reciting the exclusion criteria. Similarly, challenged claim 14 of the present Petition and claim 14 of the ’338 patent are identical, with the exception of the same exclusion criteria limitation added in the ’681 patent. *See* Ex. 1028, col. 24, ll. 3–19; Ex. 1001, col. 23, ll. 5–23.

Because, in the -00881 and -01225 Decisions, we concluded that claim 1 of the ’338 patent and claim 1 of the ’681 patent are anticipated by Dixon, we incorporate here by reference our reasoning in the -00881 Decision with respect to the corresponding limitations of claim 1 of the ’681 patent. *See, e.g.,* -00881 Decision, 26–46.

Briefly, in the Final Written Decision in the -00881 IPR, we concluded that the preponderance of the evidence, including Dixon’s express teaching that aflibercept and VEGF Trap-Eye have the “same molecular

structure" demonstrated that Dixon inherently disclosed the claimed amino acid sequence of VEGF Trap-Eye (aflibercept). *See* -00881 IPR, Paper 94 at 32–40. The Board found that the disclosures of Dixon, the prosecution history, and Patent Owner's own documents, demonstrated that aflibercept and VEGF Trap-Eye were the same well-characterized single drug, rather than, as Patent Owner suggested, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye." *Id.* at 39.

Patent Owner makes essentially the same arguments in the present *inter partes* review (*see* PO Resp. 54–65) and, in view of the evidence of record, and our reasoning in the -00881 and -01225 Decisions, these arguments fare little better than before. Of particular note is Patent Owner's argument that its publications and Dixon, consistently refer to "VEGF Trap-Eye" as an ophthalmology drug and aflibercept as an oncology product. PO Resp. 65 (citing Ex. 2057 ¶¶ 37, 45, 118–119).

We disagree, and add that we addressed this issue extensively in the -00881 and -01225 Decisions. *See* Ex. 3001, 32–40. Dixon discloses that:

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

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

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

Moreover, Dixon also expressly discloses in its Abstract that "[o]ne promising new drug is aflibercept (VEGF Trap-Eye)," showing that persons of ordinary skill in the art knew that the VEGF Trap-Eye disclosed by Dixon and aflibercept, the molecular sequence of which was reported in the 2006 WHO index,[10] refer to the same molecule as that recited in the challenged claims. (*See, e.g.*, Pet. Reply 19, Ex. 1080, 5–6).

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

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

IPR2021-00880, Paper 89 at 58.

We incorporate by reference and adopt the reasoning of the -00881 and -01225 Decisions in the present case, and conclude that the preponderance of the evidence demonstrates that Dixon inherently discloses the "VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of

---

[10] "Aflibercept" in 20(2) WHO DRUG INFORMATION 118–19 (2006) (WHO index") (Ex. 1080).

SEQ ID NO:2," also known as aflibercept or VEGF Trap-Eye, as recited in challenged claims 1 and 14.

Patent Owner additionally contends that the challenged claims would not have been obvious over the cited prior art references because: (1) a person of ordinary skill in the art would not have had a reasonable expectation of success in using the claimed method to treat an angiogenic eye disorder based upon the disclosures of Dixon; and (2) objective secondary indicia of nonobviousness support the patentability of the challenged claims.[11] PO Response 28–32, 65–68.

We find neither of these arguments persuasive. Ground 1, the sole ground of the present *inter partes* review, alleges that the challenged claims would have been obvious over the cited prior art, including Dixon. As we have related, we have previously concluded, in both the -00881 and -01225 IPRs, that the same challenged claims are anticipated by Dixon.[12] We conclude that, because the challenged claims are anticipated by Dixon, they are also obvious over Dixon. *See In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002) (holding that "[i]t is well settled that 'anticipation is the epitome of obviousness'" (quoting *Connell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548, (Fed. Cir. 1983)).

---

[11] Patent Owner made these same arguments with respect to the '681 patent in its Response in the -01225 IPR. *See* -01225 IPR, Paper 41 at 48–55, 65–68.

[12] Again, the remaining references, CATT, MACTEL, and PIER are cited by Petitioner as demonstrating the obviousness of the exclusion criteria. Because we have again concluded that the exclusion criteria are not limiting upon the challenged claims, these references play no part in our analysis.

Furthermore, although the record may establish evidence of secondary considerations that are indicia of nonobviousness, the record may also establish such a strong case of obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness. *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 769 (Fed. Cir. 1988), *cert. denied*, 493 U.S. 814 (1989). *See also Pfizer Inc. v. Apotex Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007) (unexpected results not sufficient to outweigh a strong showing of obviousness). There can be no stronger evidence of obviousness than anticipation. *McDaniel*, 293 F.3d at 1385. Therefore, because we have previously concluded that the challenged claims are anticipated, we need not consider Patent Owner's arguments concerning secondary considerations. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cir. 2008) (holding that "secondary considerations are not an element of a claim of anticipation").

For the reasons explained in Section IV.A.3 above, we conclude that the exclusion criteria are entitled to no patentable weight. Because independent challenged claims 1 and 14 are otherwise identical to claims 1 and 14 of the '338 patent of the -00881 Decision, we conclude, for the same reasons set forth in the -00881 and -01225 Decisions, that Petitioner has demonstrated, by a preponderance of the evidence, that challenged claims 1 and 14 of the '681 patent are unpatentable as being anticipated by, and thus obvious over, Dixon.

4. <u>Challenged dependent claims 3–11, 13, 16–24, and 26</u>

In the -01225 IPR, we noted that each of challenged claims 3–11, 13, 16–24, and 26 of the '681 patent are identical to dependent claims 3–11, 13,

16–24, and 26 of the ’338 patent, which were all found to be unpatentable as anticipated by Dixon in the -00881 Decision. *See* -01225 IPR, Paper 96 at 61. We further found that the only difference between the challenged dependent claims of the ’681 patent and those of the ’338 patent is the incorporation into the former of the exclusion criteria into the dependent claims from independent claims 1 or 14. *See Monsanto Co. v. Syngenta Seeds, Inc.*, 503 F.3d 1352, 1357 (Fed. Cir. 2007) (holding that “[a] claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers” (quoting 35 U.S.C. § 112 ¶ 4 (2000))).

We have explained, in Section IV.A.3. above, why we again conclude that the exclusion criteria are not accorded patentable weight. We therefore incorporate by reference and adopt the Board’s reasoning and conclusions from the -00881 and -01225 Decisions with respect to the challenged claims in this *inter partes* review, and we conclude, for the same reasons, that Petitioner has shown, by a preponderance of the evidence, that dependent claims 3–11, 13, 16–24, and 26 of the ’681 patent are anticipated by Dixon. Moreover, because we have concluded that these claims are anticipated by Dixon, they are also obvious over Dixon, and consequently unpatentable.

V. CONCLUSION

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

VI. ORDER

In consideration of the foregoing, it is hereby:

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

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

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

Claims	35 U.S.C. §	References	Claims Shown Unpatentable	Claims Not shown Unpatentable
1, 3–11, 13, 14, 16–24, 26	103	Dixon, CATT, MACTEL, PIER	1, 3–11, 13, 14, 16–24, 26	

For PETITIONER:

Raymond Nimrod
Matthew Traupman
Landon Smith
QUINN EMANUEL URQUHART & SULLIVAN, LLP
raynimrod@quinnemanuel.com
matthewtraupman@quinnemanuel.com
landonsmith@quinnemanuel.com

For PATENT OWNER:

Deborah Fishman
David Caine
Alice Ho
David Denuyl
Abigail Struthers
ARNOLD & PORTER KAYE SCHOLER, LLP
deborah.fishman@arnoldporter.com
david.caine@arnoldporter.com
alice.ho@arnoldporter.com
david.denuyl@arnoldporter.com
abigail.struthers@arnoldporter.com