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Paper 21
Date: November 10, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

IPR2021-00880
Patent 9,669,069 B2

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

NEW, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner Mylan Pharmaceuticals Inc. ("Petitioner") has filed a Petition (Paper 1, "Pet.") seeking *inter partes* review of claim 1 and 8–12 of US Patent 9,669,069 B2 (Ex. 1001, the "'069 patent"). Patent Owner Regeneron Pharmaceuticals, Inc. ("Patent Owner") timely filed a Preliminary Response. Paper 10 ("Prelim. Resp."). With our authorization (*see* Paper 13), Petitioner filed a Reply to the Preliminary Response (Paper 16 ("Reply")), and Patent Owner filed a Sur-Reply. Paper 19 ("Sur-Reply").

Under 35 U.S.C. § 314, the Board "may not authorize an *inter partes* review to be instituted unless … the information presented in the petition … and any response … shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Upon consideration of the Petition, Preliminary Response, Reply, Sur-Reply, and the evidence of record, we determine that the evidence presented demonstrates a reasonable likelihood that Petitioner would prevail in establishing the unpatentability of at least one challenged claim of the '069 patent.

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner identifies Viatris Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, and Johnson & Johnson as the real parties-in-interest. Paper 18. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 5, 2.

B. Related Matters

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00881 (PTAB May 5, 2021) (the "-881 petition") as a related matter. Pet. 4; Paper 5, 2. The -881 petition challenges claims of U.S. Patent No. 9,254,338 B2 ("the '338 patent"). The parties further identify *Chengdu Kanghong Biotechnol. Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB Jan. 7, 2021) challenging the claims of U.S. Patent No. 10,828,345 B2 ("the '345 patent"), which is related to the '069 patent and the '338 patent. Pet. 5. This latter proceeding has been terminated. *See Chengdu*, PGR2021-00035, Paper 8.

Petitioner also identifies additional patents and patent applications that claim priority to the '069 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. 5.

C. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1 and 8–12 of the '069 patent are unpatentable, based upon the following grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
I	1, 9–12	102	Dixon[1]

[1] 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.

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
II	1, 9–12	102	Heier 2009[2]
III	1, 9–12	102	Regeneron I[3]
IV	1, 8–12	102 and/or 103	Dixon
V	1, 8–12	103	Heier-2009 and Mitchell[4] or Dixon, and optionally, Papadopolous[5] or Dix[6]

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

[2] J.S. Heier, *Intravitreal VEGF Trap for AMD: An Update*, October 2009 RETINA TODAY 44–45 (2009) ("Heier 2009") Ex. 1020.

[3] Press Release, *Bayer and Regeneron Extend Development Program for VEGF Trap-Eye to Include Central Retinal Vein Occlusion*, April 30, 2009 ("Regeneron I") Ex. 1028.

[4] P. Mitchell et al., *Ranibizumab (Lucentis) in Neovascular Age-Related Macular Degeneration: Evidence from Clinical Trials*, 94(2) Br. J. Ophthalmol. 2–13 (2010) Ex. 1030.

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

[6] Dix et al., (US 2006/0217311 A1, May 20, 2008) ("Dix") Ex. 1033.

D. The '069 Patent

The '069 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 the sole independent claim of the '069 patent, 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 on an as needed/ pro re nata (PRN) basis, based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional;

> wherein the VEGF antagonist is a 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, col. 21, ll. 42–60.

F. Prosecution History of the '069 Patent

The '069 patent issued from U.S. Application Ser. No. 14/972,560 (the "'560 application") filed on December 17, 2015, and claims the priority benefit of, *inter alia*, provisional Application Ser. No. Provisional application No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

The claims of the '069 patent, including claims 1 and 8–12 were allowed on March 6, 2017, and the patent issued on June 6, 2017. Ex. 1017, 162; Ex. 1001, code (45).

III. ANALYSIS

A. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the

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

Petitioner proposes constructions for the claim terms "initial dose," "secondary dose," "tertiary dose," "4 weeks," "*pro re nata* (PRN)," "VEGFR1 Component," "VEGFR2 Component," and "Multimerization Component." Pet. 13-19. Patent Owner responds that, although it does not agree with Petitioner's proposed constructions for these terms, Patent Owner does not advance claim construction positions for these terms at this time because construction of these terms is not necessary to resolve the arguments presented in its Preliminary Response. Prelim. Resp. 19 (citing *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017)).

Having reviewed the pleadings and evidence of record, we agree with Patent Owner that no construction of these claim terms is necessary for the purposes of this Decision to Institute a trial.

B. A Person of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art would typically possess 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 (1) developing treatments for angiogenic eye disorders (such as AMD), including through the use of VEGF antagonists, or (2) treating of angiogenic eye disorders (such as age-related macular degeneration ("AMD")), including through the use of VEGF antagonists. Pet. 25 (citing Ex.1002 ¶¶ 26–28).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Preliminary Response, although Patent Owner contends that such a skilled artisan could not necessarily perform the limitation of claim 1 reciting "based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional." *See, e.g.*, Prelim. Resp. 28. We address Patent Owner's contentions with respect to this limitation in our analysis below. For the purposes of this decision, because we find Petitioner's definition to be consistent with the level of skill in the art (see, e.g., Exs. 1006, 1020), and in the absence of a different proposed definition of the level of skill in the art by Patent Owner, we consequently adopt Petitioner's definition.

C. Discretionary Denial of Institution under 35 U.S.C. § 325(d)

Patent Owner urges us to exercise our discretion to deny institution of trial under 35 U.S.C. §325(d). Prelim. Resp. 10. Under § 325(d), we have discretion to deny a petition that presents the same or substantially the same prior art or arguments as previously presented to the Office. *See* 35 U.S.C. § 325(d). In evaluating whether the factual predicate under § 325(d) is met, we consider a number of non-exclusive factors, as set forth in our decision in

Becton, Dickinson and Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential) ("the *Becton Dickinson* factors"):

(a) the similarities and material differences between the asserted art and the prior art involved during examination;

(b) the cumulative nature of the asserted art and the prior art evaluated during examination;

(c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;

(d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;

(e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and

(f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson, IPR2017-01586, Paper 8 at 17–18.

In performing an analysis under § 325(d), "the Board uses the following two-part framework: (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and (2) if either condition of first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims. . . . If, after review of [*Becton, Dickinson*] factors (a), (b), and (d), it is determined that the same or

substantially the same art or arguments previously were presented to the Office, then factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office." *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential). Consequently, we first turn to an analysis of *Becton-Dickinson* factors (a), (b), and (d) to determine whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office.

1. Part One of the *Advanced Bionics* Analysis

Becton Dickinson factors (a), (b), and (d) require us to determine, respectively: (a) "the similarities and material differences between the asserted art and the prior art involved during examination;" (b) "the cumulative nature of the asserted art and the prior art evaluated during examination," and (d) "the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art." *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17.

Patent Owner points out that Dixon is listed as a reference in the '069 patent (*see* Ex. 1001 code (56)), and was submitted to the Office in an IDS during prosecution and marked "considered" by the Examiner. Prelim. Resp. 10–11 (citing Ex. 1017, 121, 168). Patent Owner acknowledges that Heier 2009, Mitchell, Regeneron I, and Papadopolous, were not present before the Examiner during prosecution of the '560 application, but argues that each of these references is cumulative of Dixon because each reference

is "substantially the same as" Dixon. *Id.* at 11–14 (citing *NXP USA, Inc. v. Impinj, Inc.*, IPR2020-00519, 2020 WL 4805424, at *4-5 (Aug. 17, 2020)).

Petitioner replies that Dixon was "neither applied against the claims nor discussed by the [E]xaminer." Reply 3 (citing *Amazon.com, Inc. v. M2M Solutions LLC*, IPR2019-01205, Paper 14 at 16 (PTAB Jan. 27, 2020) (finding that "a reference that 'was neither applied against the claims nor discussed by the Examiner' does not weigh in favor of exercising the Board's discretion under § 325(d) to deny a petition.")). Petitioner asserts that the Examiner issued a single office action, issuing several rejections upon the grounds of obviousness-type double patenting over several prior patents, none of which disclosed CLEAR-IT-2. *Id.* (citing Ex.1017, 105–09).

In fact, Petitioner argues, Dixon was not presented in full to the Examiner. Reply 4. According to Petitioner, the EFS Acknowledgment Receipt shows that the Examiner received only a single page. *Id.* (citing Ex. 1017, 126). Petitioner also points to the certified file history as confirming that Patent Owner submitted only a one-page copy of Dixon. *Id.* (citing Ex. 1087, 1). Petitioner asserts that, under 37 C.F.R. § 1.98(a)(2)[7], Patent Owner thus informed the Examiner that its one-page copy represented the "portion which caused [Dixon] to be listed," affirmatively excluding the rest of the reference. *Id.* Petitioner contends that the submitted page, however,

[7] 37 C.F.R. § 1.98(a)(2) states, in relevant part: "Any information disclosure statement filed under § 1.97 shall include the items listed in paragraphs (a)(1), (a)(2) and (a)(3) of this section…. A legible copy of… [e]ach publication *or that portion which caused it to be listed*, other than U.S. patents and U.S. patent application publications unless required by the Office. (Emphasis added).

does not disclose (or even mention) the prior art regimens described extensively in the complete Dixon reference. *Id.* *See* Ex. 1087, 1.

Patent Owner acknowledges that only one page of Dixon, instead of the whole paper, was filed, and asserts that it was unaware that Dixon was submitted as a single page prior to Petitioner's Reply. Sur-Reply 8. Patent Owner contends that the full citation to the Dixon paper was presented in an IDS, that the reference was publicly available, and that it was marked considered by the Examiner. *Id.* (citing Ex. 1017 at 121, 168; MPEP § 609.05(b)). Patent Owner notes that the record does not suggest that the Examiner found Patent Owner's disclosure of Dixon to be defective or incomplete, because the Examiner did not draw a line through the citation on the IDS. *Id.* at 9.

Patent Owner argues further that the Dixon disclosures relied upon by Mylan, *viz.*, the CLEAR-IT-2 dosing regimen and results are also disclosed in the Thomson Reuters Integrity Press Release of September 28, 2008[8] ("Thomson Reuters"), which was presented to, and considered by, the Examiner, and which was cited in the '069 patent. *Id.* (citing Ex. 1017 at 68, 114; Ex. 1001, code (56)). Patent Owner repeats that Petitioner's secondary references are also cumulative of art that was considered by the Office. *Id.*

We are not persuaded that Patent Owner has demonstrated that Becton-Dickinson factors (a), (b), and (d) have been satisfied. The evidence of record shows that the Dixon reference before the Examiner consisted of merely the first page of Dixon. *See* Ex. 1087. The single page of Dixon that

[8] Thomas Reuters Integrity, *VEGF Trap-Eye Final Phase II Results in Age-Related Macular Degeneration Presented at 2008 Retina Society Meeting*, (Sep. 28, 2008). Ex. 2007.

was before the Examiner provides no disclosure of the claimed dosing regimen. It would consequently have been impossible for the Examiner to analyze the limitations of the challenged claims in view of the complete teachings of Dixon under these circumstances.

We consequently find that the disclosure of Dixon that form the basis of Petitioner's Grounds I and IV (of which Dixon is the sole reference) were not before the Examiner as prior art during examination (because the relevant disclosures were missing or omitted), and that there could therefore be no overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art.

Furthermore, we also reject Patent Owner's argument that the Heier 2009, Mitchell, Regeneron I, and Papadopolous references are cumulative of Dixon because, as we have explained, the single page of Dixon that was actually before the Examiner during prosecution does not teach all of the limitations of the challenged claims, nor does it disclose all of the relevant limitations that Petitioner relies upon those references as disclosing. The remaining references do not, consequentially, disclose the same, or substantially the same, subject matter as the one-page version of Dixon that was before the Examiner during prosecution.

2. Summary

Because we find that the evidence of record demonstrates that *Becton-Dickinson* factors (a), (b), and (d) have not been satisfied, our analysis ends at this point, and we need not proceed to step two of the *Advanced Bionics* framework. *See Advanced Bionics*, IPR2019-01469, Paper 6 at 8. We

consequently decline to exercise our discretion to deny institution of Grounds I and IV. Furthermore, because, for the reasons we shall explain, we institute trial on at least one of the challenged claims, we similarly decline to exercise our discretion to deny institution on the remaining Grounds II, III, and V. *See SAS Institute, Inc. v. Iancu*, 138 S.Ct. 1348, 1354–55 (2018) (holding that, when *inter partes* review is instituted, the Board shall issue a final written decision with respect to the patentability of any patent claim challenged by the petitioner).

D. Grounds I and II: Alleged Anticipation of Claims 1 and 9-12 by Dixon or Heier 2009

1. Overview of Dixon

Dixon was published in October, 2009, and is prior art to the '069 patent. Ex. 1006, 9. 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.*

Relevantly, Dixon discloses that, structurally, VEGF Trap-Eye is a fusion protein of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fe fragment. Ex. 1006, 3, Fig. 1. Dixon also discloses the CLEAR-IT-1, CLEAR-IT-2, and VIEW1/VIEW2 clinical trials. (Ex. 1006, 3–4, 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, 2, 5; 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 PRN administration. *Id.*, 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, 5). 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 4. Dixon also discloses that "[p]atients initially treated with 2.0 or 0.5 mg of VEGF TrapEye monthly achieved mean improvements of 9.0 ($p < 0.0001$) and 5.4 ($p < 0.085$) ETDRS letters with 29 and 19% gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." *Id.*

Dixon also describes the then-ongoing VIEW 1 and VIEW 2 phase III clinical trials. Ex. 1006, 4. 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. Overview of Heier 2009

Heier 2009 was published in October, 2009, and is prior art to the '069 patent. Ex. 1020, 1. As in Dixon, Heier 2009 describes the CLEAR-IT 2 trial, a phase 2 study of the safety and efficacy of VEGF Trap-Eye in patients with neovascular age-related macular degeneration (AMD). *Id.*

Heier 2009 discloses that:

> VEGF Trap-Eye is a purified formulation of VEGF Trap, a vascular endothelial growth factor (VEGF) receptor fusion protein that binds all forms of VEGF-A. VEGF Trap-Eye, formulated for intraocular use, is being developed for the treatment of neovascular AMD, diabetic macular edema, and other ocular pathologies.

Ex. 1020, 1–2 (internal reference omitted).

With respect to the CLEAR-IT 2 trial, Heier 2009 relates that:

> CLEAR-IT 2 was a double-masked multicenter trial in which patients with neovascular AMD were randomly assigned to receive monthly intravitreal injections of VEGF Trap-Eye 0.5

> mg or 2.0 mg or quarterly injections of 0.5, 2.0 or 4.0 mg for an initial 3-month fixed-dose period, after which they received the same doses on an as needed basis at monthly visits out to 1 year.

Ex. 1020, 2. Heier 2009 further discloses that:

> At 1 year, for all treated groups combined (n=157), there was a significant improvement in BCVA from baseline (mean improvement 5.3 letters; P<.0001). Patients who received three monthly doses of 2.0 mg followed by as-needed dosing achieved mean improvements in BCVA of 9.0 letters from baseline (P<.0001 vs baseline).
> ….
> Patients receiving initial monthly doses of VEGF Trap-Eye achieved mean decreases in retinal thickness vs baseline at 1 year. In addition, treatment with VEGF Trap-Eye was associated with a reduction in the size of the total active choroidal neovascular membrane (CNV).

Id. at 2.

3. Anticipation of claims 1 and 9–12 by Dixon (Ground I) and Heier 2009 (Ground II).

a. Petitioner's contentions

i. Claim 1

Petitioner argues that the disclosures of Dixon and Heier 2009 both anticipate each of the limitations of independent claim 1 and dependent claims 9–12. Pet. 26–33. Petitioner has provided a claim chart of the limitations of claim 1, and what it contends are the corresponding disclosures of each reference, which, for convenience, is reproduced below:

Claim 1	Heier-2009:	Dixon:
1. A method for treating an angiogenic eye disorder in a patient	"The CLEAR-IT 2 trial was a phase 2 study of the safety and efficacy of VEGF Trap-Eye . . . in patients with [AMD]." (Ex.1020, Heier-2009, 44). "At 1 year . . . there was a significant improvement in BCVA from baseline . . . ." (*Id.*, 45). "Patients who received three monthly doses of 2.0 mg followed by as-needed dosing achieved mean improvements in BCVA of 9.0 letters from baseline." (*Id.*). (Ex.1002, Albini, ¶¶ 116, 120).	"VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and Phase II trial data indicating safety, tolerability and efficacy for the treatment of [AMD]." (Ex.1006, Dixon, 1573; *id.*, 1575). "Phase I data demonstrated acceptable safety and tolerability of VEGF Trap-Eye in the treatment of neovascular AMD." (*Id.*, 1577). Phase 2 patients "treated with 2.0 mg or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p<0.0001$) and 5.4 ($p<0.085$) ETDRS letters." (*Id.*, 1576). "[P]atients . . . demonstrated stabilization of their vision that was similar to previous studies of ranibizumab at 1 year." (*Id.*, 1577).

Claim 1	Heier-2009:	Dixon:
		(Ex.1002, Albini, ¶¶ 116, 120).
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;	"Patients with neovascular AMD were randomly assigned to receive monthly intravitreal injections of VEGF Trap-Eye 0.5 mg or 2.0 mg . . . for an initial 3-month fixed-dose period, after which they received the same doses on [a PRN] basis at monthly visits out to 1 year." (Ex.1020, Heier-2009, 45). (Ex.1002, Albini, ¶¶ 121-23).	"Two groups received monthly doses of either 0.5 or 2.0 mg for 12 weeks (at weeks 0, 4, 8 and 12) . . . . Following this fixed dosing period, patients were treated with the same dose of VEGF Trap-Eye on a p.r.n. basis." (Ex.1006, Dixon, 1576).[16] (Ex.1002, Albini, ¶¶ 121-123).
wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and	(Ex.1020, Heier-2009, 45). (Ex.1002, Albini, ¶¶121-23).	(Ex.1006, Dixon, 1576). (Ex.1002, Albini, ¶¶ 121-23).

Claim 1	Heier-2009:	Dixon:
wherein each tertiary dose is administered on an as-needed/pro re nata (PRN) basis, based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional;	(Ex.1020, Heier-2009, 45). (Ex.1002, Albini, ¶¶ 121-23).	"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 . . . 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." (Ex.1006, Dixon, 1576).
wherein the VEGF antagonist is a 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	"VEGF Trap-Eye is a purified formulation of VEGF Trap, a vascular endothelial growth factor (VEGF) receptor fusion protein that binds all forms of VEGF-A." (Ex.1020, Heier-2009, 44-45 (Fig.1)).[17]	VEGF Trap-Eye is "a fusion protein of binding domains of VEGF receptors-1 and -2 attached to the Fc fragment of human IgG." (*Id.*, 1576 (Fig.1)). "VEGF Trap-Eye and aflibercept (the oncology product) have the same

Claim 1	Heier-2009:	Dixon:
130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2.	(Ex.1002, Albini, ¶ 125).	molecular structure." (*Id.*, 1575). (Ex.1002, Albini, ¶ 125).

Pet. 46–49.

ii. Claims 9 and 10

Claim 9 is exemplary and recites:

> 9. The method of claim **1**, wherein the angiogenic eye disorder is selected from the group consisting of: age related macular degeneration, diabetic retinopathy, diabetic macular edema, central retinal vein occlusion, branch retinal vein occlusion, and corneal neovascularization.

Ex. 1001 col. 22, ll. 53–57. Petitioner argues that Dixon discloses the employing the PRN regimen and results of CLEAR-IT 2 (Phase 2) in the treatment of AMD. Pet. 49 (citing Ex. 1006, 1, 4, 7). Similarly, Petitioner contends, Heier 2009 discloses CLEAR-IT-2 data confirming that the trial's PRN regimen was successful at treating AMD. *Id.* (citing Ex. 1020, 2). Dixon similarly discloses the PRN regimen and results of CLEAR-IT-2 (Phase 2) to treat AMD. (Ex. 1006, Dixon, 1573, 1576, 1579).

iii. Claim 11

Dependent claim 11 recites:

> 11. The method of claim **1**, wherein all doses of the VEGF antagonist are administered to the patient by topical administration or by intraocular administration.

Ex. 1001 col. 22, ll. 60–62.

Petitioner contends that "intraocular administration" refers to administration to the eye generally, whereas intravitreal administration, a subset of intraocular administration, refers to administration directly into the vitreous chamber of the eye. Pet. 49 (citing Ex. 1002 ¶¶ 132–33; Ex. 1001 col. 2, ll. 39–41). Petitioner argues that Heier 2009 and Dixon both disclose monthly intravitreal injections of VEGF Trap-Eye. *Id.* (citing Ex. 1020 1–2; Ex. 1006 3; Ex. 1002 ¶¶ 134-35).

iv. Claim 12

Claim 12 recites:

> 12. The method of claim 1, wherein the VEGF antagonist is VEGFR1R2-FcΔC1(a) encoded by the nucleic acid sequence of SEQ ID NO: 1.

Ex. 1001 col. 22, ll. 63–65.

Petitioner argues that both the amino acid and nucleotide sequences of VEGF Trap-Eye were disclosed in the prior art and were well known to skilled artisans. Pet. 50 (citing Ex. 1002 ¶¶ 136–37; Ex. 1010, Figs. 24A–C (disclosing the nucleotide sequence and deduced amino acid sequence), col. 10, ll. 15–17 (specifying that this molecule is termed "VEGFR1R2-FcΔC1(a)"); Ex. 1033, SEQ ID NO:3; Ex. 1083). Petitioner asserts that the

CLEAR-IT 2 trials disclosed by both Heier 2009 and Dixon employed VEGF Trap-Eye, and therefore disclose the "VEGF antagonist" recited by claim 12. *Id.*

b. Patent Owner's Preliminary Response

i. "Assessed by a physician or other qualified medical professional"

Patent Owner argues that Petitioner has failed to show that Heier 2009 or Dixon discloses, either expressly or inherently, the limitation of claim 1 reciting: "assessed by a physician or other qualified medical professional." Prelim. Resp. 24.

Patent Owner contends that Petitioner relies upon Dixon's disclosure that:

> 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.

Prelim. Resp. 27 (citing Pet., 48 (quoting Ex. 1006, 4). Petitioner argues that Dixon provides no disclosure of who is assessing the disclosed retreatment criteria, and contends that Petitioner has not made any showing that this is inherent in Dixon. *Id.* at 27–28. Furthermore, argues Patent Owner, since Petitioner's definition of a person of ordinary skill in the art includes, *inter alia*, a person with "an advanced degree, such as an M.D. or

Ph.D. … with practical academic or medical experience," a person of ordinary skill in the art need not be "a physician or other medical qualified medical professional." *Id.* at 28. Patent Owner therefore contends that it cannot be assumed and is not necessarily the case that a "physician or other qualified medical professional" assessed the disclosed retreatment criteria in Dixon. *Id.*

Similarly, argues Patent Owner, Petitioner relies upon the following passage of Heier 2009 as disclosing the limitation at issue:

> [P]atients with neovascular AMD were randomly assigned to receive monthly intravitreal injections of VEGF Trap-Eye 0.5 mg or 2.0 mg or quarterly injections of 0.5, 2.0 or 4.0 mg for an initial 3-month fixed-dose period, after which they received the same doses on an as needed basis at monthly visits out to 1 year.

Prelim. Resp. 24–25 (citing Pet., 48 (quoting Ex. 1020, 2). According to Patent Owner, Heier 2009 fails to disclose a method where the administration is "based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional." *Id.* at 25. Patent Owner argues that, in fact, Petitioner never argues that this limitation is disclosed, either expressly or inherently, in Heier 2009. *Id.*

Patent Owner argues that Petitioner relies upon unsupported statements from one of its Declarants, Dr. Thomas Albini. Prelim. Resp. 25 (citing Pet. 48). Specifically, Patent Owner points to Dr. Albini's statement that:

> [T]o determine the need for an injection at each visit during the trial, a physician or other qualified medical professional would have to make an assessment, and that would have been well understood by persons of ordinary skill in the art to include visual

> and/or anatomical outcomes, such as visual acuity and retinal swelling measurements.

Id. (quoting Ex. 1002, ¶ 121). Patent Owner contends that Dr. Albini's testimony is not credible because it is unsupported by any underlying facts. *Id.* at 26 (citing Patent Trial and Appeal Board, *Consolidated Trial Practice Guide*, November 2019, 40–41).

Patent Owner argues further that Dr. Albini attests that Heier 2009 discloses "several measures that physicians were to use in assessing patients for PRN dosing." Prelim. Resp. 26 (quoting Ex. 1002, ¶ 121 (citing Ex. 1020, 2)). However, argues Patent Owner, the only discussion of these measures, i.e., best corrected visual acuity ("BCVA") and retinal thickness in Heier 2009 relate to the 1-year outcomes of the clinical trial, not PRN retreatment criteria. *Id.* (citing Ex. 1020, 2). Therefore, asserts Patent Owner, Heier 2009 does not disclose that PRN dosing in the clinical trial was "based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional," as required by the challenged claims. *Id.*

ii. Lack of enablement

Patent Owner next contends that neither the Dixon nor Heier 2009 prior art references are enabled, and therefore cannot anticipate the '609 patent. Prelim. Resp. 29.

Petitioner asserts that the challenged claims require that each tertiary dose is administered as-needed/PRN "based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional." Prelim. Resp. 30 (quoting Ex. 1001 col. 21, ll. 50–53). Patent

Owner points out that Petitioner defines a person of ordinary skill in the art as including, *inter alia*, a person with "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." *Id.* (quoting Pet. 25). Patent Owner contends that Petitioner fails to show that such a skilled artisan, which includes individuals without medical training, could have used the disclosure of Heier 2009 or Dixon to practice the claimed method without undue experimentation. *Id.* Patent Owner contends that Petitioner provides no evidence to suggest that a Ph.D.-trained individual with no clinical training or experience would be qualified to assess visual and/or anatomical outcomes, even with the disclosure of retreatment criteria, let alone qualified to make assessments or decisions about whether or when to administer a tertiary dose. *Id.* at 31.

iii. Disclosure of "VEGF Trap-Eye"

Patent Owner next argues that Petitioner relies on the unproven assumption that "VEGF Trap-Eye" was known in the art to possess the same amino acid sequence as aflibercept. Prelim. Resp. 32. However, Patent Owner asserts, none of Petitioner's cited anticipatory references discloses the amino acid sequence of "VEGF Trap-Eye." *Id.*

Specifically, Patent Owner argues, claim 1 requires the administration of a VEGF antagonist comprising amino acids 27–457 of SEQ ID NO:2. Prelim. Resp. 32 (citing Ex. 1001 col. 21, ll. 54–60). Patent Owner contends that Petitioner has not identified any prior art that discloses the amino acid sequence for "VEGF Trap-Eye." *Id.* at 33. According to Patent Owner,

Petitioner argues that both Dixon's and Heier 2009's use of the term "VEGF Trap-Eye" would have been understood by a person of ordinary skill in the art as referring to aflibercept — and only to aflibercept — and that aflibercept's amino acid sequence was well-known in the art. *Id.* (citing Pet. 48–49, 52).

Patent Owner contends that the prior art's use of the term "VEGF Trap-Eye" was inconsistent, and argues that Petitioner fails to show a clear or uniform understanding that "VEGF Trap-Eye" was just another name for "aflibercept" in the art. Prelim. Resp. 33 (citing *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)). Rather, Patent Owner contends, Petitioner ignores evidence that a skilled artisan would not have understood that "VEGF Trap-Eye" and aflibercept necessarily have the same amino acid sequence, such as evidence discussed below showing different molecular weights "VEGF Trap-Eye" and "aflibercept", and inconsistent descriptions of "VEGF Trap," "VEGF Trap-Eye," and "aflibercept" in the art. *Id.* at 33–34.

Specifically, Patent Owner argues that Petitioner relies heavily on a statement in Dixon that "VEGF Trap-Eye" and aflibercept (the oncology product) share a "molecular structure." Prelim Resp. 35 (quoting Ex. 1006, 1). But, Patent Owner asserts, Dixon does not state that "VEGF Trap-Eye" and aflibercept have an identical amino acid sequence, and Petitioner provides no evidence that a shared "molecular structure" indicates an identical amino acid sequence. *Id.* Patent Owner points to the preceding paragraph of Dixon, which discloses that: "Structurally, VEGF Trap-Eye is a fusion protein of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment (Fig. 1)." *Id.* (quoting Ex. 1006, 3).

Patent Owner contends that Heier 2009 provides even less information regarding the nature of "VEGF Trap-Eye" than Dixon. Prelim. Resp. 35–36. Patent Owner asserts that Heier 2009 states only that: "VEGF Trap-Eye is a purified formulation of VEGF Trap, a vascular endothelial growth factor (VEGF) receptor fusion protein that binds all forms of VEGF-A." *Id.* at 36 (citing Ex. 1020, 1–2, Fig. 1).

Patent Owner contends that Petitioner attempts to connect the dots by arguing that "VEGF Trap-Eye" and "aflibercept" were different names for the very same protein: "Aflibercept, VEGF Trap, VEGF Trap-Eye, VEGF-TrapR1R2, and AVE0005 are simply different names for the same molecule." Prelim. Resp. 36 (quoting Pet., 26; also citing Ex. 1002, ¶ 39). However, argues Patent Owner, by equating "VEGF Trap Eye" with all variations of "VEGF Trap" nomenclature, including VEGF Trap names that were known in the art to refer to a genus of proteins, Petitioner and its Declarant, Dr. Albini, only underscore the uncertainty confronting a skilled artisan regarding the identity and sequence of "VEGF Trap-Eye." *Id.*

Patent Owner argues further that "VEGF Trap-Eye" was used to describe many different fusion proteins. Prelim. Resp. 36–37. By way of example, Patent Owner asserts that "VEGF Trap" was known in the art to encompass a genus of engineered fusion proteins, each having a different amino acid sequence. *Id.* at 37. Patent Owner points to Holash[9], which describes several different Regeneron-developed VEGF-Traps (e.g., VEGF $Trap_{parental}$, VEGF-$Trap_{\Delta B1}$, VEGF-$Trap_{\Delta B2}$, VEGF $Trap_{R1R2}$). *Id.* (citing Ex.

[9] J. Holash et al., VEGF-Trap: *A VEGF Blocker with Potent Antitumor Effects*, 99(17) PROC. NAT'L ACAD. SCIS. 11393–98 (2002) ("Holash") Ex. 1004.

1004, 11394). Notably, Patent Owner points out, Holash never uses the term "VEGF Trap-Eye" (or aflibercept) for any of the VEGF Trap fusion proteins it describes, and none of VEGF $Trap_{parental}$, VEGF-$Trap_{\Delta B1}$, or VEGF$Trap_{\Delta B2}$ satisfies the sequence limitation of the challenged claims. *Id.* Therefore, argues Patent Owner, a person of ordinary skill in the art would have known of Regeneron "VEGF-Trap" molecules, including many that do not comprise SEQ ID NO:2. *Id.*

Patent Owner argues still further that, as of the priority date, a person of ordinary skill in the art would have been aware of inconsistent reports in the literature regarding the molecular weight of "VEGF Trap-Eye." Prelim. Resp. 38. Patent Owner points to Stewart[10], which reports that "VEGF Trap-Eye is a 110-kDa recombinant protein," whereas Ni[11] reports that "VEGF Trap-Eye (Regeneron Inc.) is a 115-kDa recombinant fusion protein." *Id.* (quoting Ex. 2011, 667; Ex. 1075, 403; also citing Ex. 2012, 49; Ex. 2013, 144 ("VEGF Trap is a 115 kDa recombinant fusion protein….").

Conversely, Patent Owner contends, the molecular weight of aflibercept was routinely reported as 115 kDa. Prelim. Resp. 38 (citing, e.g., Ex. 2014, 596 (molecular weight of aflibercept 115 kDa…"); Ex. 2015 ¶¶ 3, 10). Patent Owner therefore suggests that a person of ordinary skill in the art would have understood that differences in protein molecular weights can

[10] M.W. Stewart et al., *Predicted Biological Activity of Intravitreal VEGF Trap*, 92 BR. J. OPHTHALMOL. 667–68 (2008) ("Stewart") Ex. 2011.

[11] Z. Ni et al., *Emerging Pharmacologic Therapies for Wet Age-Related Macular Degeneration*, 223 OPHTHALMOLOGICA 401–10 (2009) Ex. 1075.

reflect differences in the amino acid sequences of proteins, and, specifically, 5,000 Da could equate to a sequence difference of approximately 42 amino acids. *Id.* at 39 (citing Ex. 2016, 1272; Ex. 2017, 11). Patent Owner asserts that the Petition is devoid of evidence indicating how a skilled artisan would have understood these varying prior art disclosures regarding the identity of the term "VEGF Trap-Eye." *Id.*

c. Analysis

We conclude that Petitioner has established a reasonable likelihood of success in prevailing at trial on Grounds 1 and 2, and that Patent Owner's arguments are insufficient, based upon the current record, to overcome that likelihood of success. Petitioner's claim chart maps out the correspondence between the limitations of claim 1 and the disclosures of Dixon and Heier 2009 in a manner that persuasively demonstrates that the disclosures of both references disclose all of the limitations. Patent Owner does not dispute Petitioner's showing that the references anticipate, with three exceptions. We address each of those arguments in turn.

i. "Assessed by a physician or other qualified medical professional"

Patent Owner contends that neither Dixon nor Heier 2009 teaches the limitation of claim 1 reciting "wherein each tertiary dose is administered on an as needed/ pro re nata (PRN) basis, based on visual and/or anatomical

outcomes *as assessed by a physician or other qualified medical professional*." (emphasis added). We disagree.[12]

> Dixon teaches:
>
> 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*.

Ex. 1006, 4 (emphasis added). Dixon thus expressly discloses that patients were treated on a "p.r.n. basis" (i.e., an "as needed basis") for additional doses, and details the criteria by which the physical symptoms were assessed to determine whether another dose was warranted.

It is true that Dixon does not expressly state that it is a physician who performs this assessment of the patient in question. But we find that a person of ordinary skill in the art, as defined by Petitioner, would understand that the preforming of diagnostic procedures and analysis, and the prescription of the appropriate medication, would necessarily need to be performed by a physician or other qualified medical professional licensed by

[12] Patent Owner also argues that, *contra* Petitioner's assertion, this limitation is a positive limitation of the claim that should be afforded patentable weight. *See* Prelim. Resp. 20–24. For the purposes of this Decision, we accept Patent Owner's contention that the limitation reciting "assessed by a physician or other qualified medical professional" is entitled to patentable weight. As we explain, however, Patent Owner's argument that this limitation is not disclosed by the cited prior art is unpersuasive.

the state. That is, almost by definition, the practice of medicine, and is certainly well known in this art. *See In re Graves*, 69 F.3d 1147, 1152 (Fed. Cir. 1995) (holding that the teachings of a reference may be taken in combination with knowledge of the skilled artisan to put the artisan in possession of the claimed invention within 35 U.S.C. § 102 even though the patent does not specifically disclose certain features); *see also Continental Can*, 948 F.2d at 1269 (holding that anticipation requirement that every element of a claim appears in a single reference accommodates situations where the common knowledge of "technologists" is not recorded in a reference, i.e., where technical facts are known to those in the field of the invention). We therefore find that a person of ordinary skill in the art, as defined by Petitioner, would understand that only a licensed physician could competently perform the procedures disclosed by Dixon in the quoted passage.

> With respect to the disclosures of Heier 2009, the reference discloses:
>
> [P]atients with neovascular AMD were randomly assigned to receive monthly intravitreal injections of VEGF Trap-Eye 0.5 mg or 2.0 mg or quarterly injections of 0.5, 2.0 or 4.0 mg for an initial 3-month fixed-dose period, *after which they received the same doses on an as needed basis at monthly visits out to 1 y*ear.

Ex. 1020, 2 (emphasis added). We agree with Patent Owner that Heier 2009 does not expressly disclose either that the patients were assessed based on visual and/or anatomical outcomes, or that the assessment is performed by a physician. Nevertheless, we conclude that both elements of the limitation are inherent to Heier 2009's disclosure of "after which [patients] received the same doses on an as needed basis," (*see* Ex. 1020, 2), because a person of ordinary skill in the art would understand that they are necessary to that

process. *See Therasense, Inc. v. Becton, Dickinson and Co.*, 593 F.3d 1325, 1332–33 (Fed. Cir. 2010).

"*Pro re nata*" (p.r.n.) is defined, in its medical context, as "when necessary ([ ] for an occasion that has arisen, as circumstances require, as needed)." MedicineNet, *Pro re nata*, available at: https://www.medicinenet.com/prn/definition.htm (last visited October 20, 2021). Inherent to the determination of whether a dose is to be administered *pro re nata*, is a determination whether administration of such dose is necessary. *See, e.g.*, Ex. 1002 ¶ 43. We find that a person of ordinary skill in the art would understand, in the present context, that the way to determine whether an as-needed dose of VEFG Trap-Eye is required is to perform a visual and/or anatomical test to determine the outcome, i.e., whether the dose is actually needed. We conclude that a skilled artisan would understand that an assessment of whether dosage is required is a necessary part of treatment *pro re nata*, and is consequently inherent to that claim term. *See Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1337 (Fed. Cir. 2010) (holding that a reference may anticipate inherently if a claim limitation that is not expressly disclosed "is necessarily present, or inherent, in the single anticipating reference").

We have also explained why a person of ordinary skill in the art would understand that only a qualified medical professional could perform such an assessment and prescribe a course of treatment. Therefore, a skilled artisan would understand that a person administering treatment *pro re nata* would necessarily, and thus inherently, be a physician or other qualified medical professional. We consequently find, based upon the current record, that both Dixon and Heier 2009 inherently disclose the limitation of claim 1

reciting "wherein each tertiary dose is administered on an as needed/ pro re nata (PRN) basis, based on visual and/or anatomical outcomes as assessed by a physician or other qualified medical professional."

ii. Enablement

Patent Owner next argues that neither Dixon nor Heier 2009 is enabled, because a person of ordinary skill in the art, as defined by Petitioner, can be a person possessing "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." *See* Pet. 25. Patent Owner argues that certain persons of ordinary skill in the art as defined by Petitioner, for example, a person holding a Ph.D. and practical academic experience, would be unable to practice the disclosures of the references, because they would not possess a medical degree or qualifications (i.e., the legal right to practice medicine).

In some respects, Patent Owner's argument appears to be more of a challenge to Petitioner's proposed definition of the level of ordinary skill in the art than to the enablement of the cited prior art. In that regard, we note that:

> A person may not need to be a person of ordinary skill in the art in order to testify as an expert under Rule 702, but rather must be "qualified in the pertinent art." *Sundance, Inc. v. DeMonte Fabricating Ltd.*, 550 F.3d 1356, 1363–64 (Fed. Cir. 2008). For example, the absence of an advanced degree in a particular field may not preclude an expert from providing testimony that is helpful to the Board, so long as the expert's experience provides sufficient qualification in the pertinent art.

PTAB, *Consolidated Trial Practice Guide*, November 2019 at 34.

In terms of enablement of the prior art, Patent Owner concedes that the disclosures of Dixon and Heier 2009 are sufficiently specific for qualified medical professionals to perform the disclosed methods. That is all that is required of the references for enablement. *See Koito Mfg. Co., Ltd. v. Turn-Key-Tech*, LLC, 381 F.3d 1142, 1155 (Fed. Cir. 2004). Further, because an expert, as defined by Petitioner, even one without a medical qualification, would understand how the disclosures of Dixon and Heier 2009 were performed, and could be performed by medical practitioners, such testimony is helpful to the Board. *See* Consolidated Trial Practice Guide at 34. We therefore conclude that, for the purposes of institution of *inter partes* review, Patent Owner has failed to demonstrate persuasively that the references are not enabled.

iii. Disclosure of "VEGF Trap-Eye"

Finally, Patent Owner argues that Petitioner has not identified any prior art that discloses the amino acid sequence for "VEGF Trap-Eye." Patent Owner contends that a skilled artisan would not have understood that "VEGF Trap-Eye" and aflibercept necessarily have the same amino acid sequence, such as evidence discussed below showing different molecular weights "VEGF Trap-Eye" and "aflibercept," and inconsistent descriptions of "VEGF Trap," "VEGF Trap-Eye," and "aflibercept" in the art. *Id.* at 33–34.

We disagree. As an initial matter, Dixon expressly teaches:

> 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, 3 (emphasis added). Dixon thus teaches that VEGF Trap-Eye and aflibercept (the active agent in VEGF Trap-Eye) have the same molecular structure, but that VEGF Trap-Eye undergoes additional preparatory steps to make it more acceptable as an agent for intraocular injection. Nevertheless, based on the testimony of Dr. Albini, we find that a person of ordinary skill would understand that proteins with the same molecular structure would necessarily possess the same amino acid sequence.

More specifically, Dixon teaches that "[s]tructurally, VEGF Trap-Eye is a fusion protein of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fe fragment (Figure 1)." Ex. 1006, 3. This, too, was well known in the art at the time of invention, as demonstrated by Holash, which teaches that:

> The parental VEGF-Trap was created by fusing the first three Ig domains of VEGFR1 to the constant region (Fc) of human IgG1…. VEGF-Trap$_{R1R2}$ was created by fusing the second Ig domain of VEGFR1 with the third Ig domain of VEGFR2. All of the VEGF-Trap variants were produced and purified from Chinese hamster ovary cells.

Ex. 1004, 1. Patent Owner, in discussing Holash, argues that none of VEGF $Trap_{parental}$, VEGF-$Trap_{\Delta B1}$, or VEGF$Trap_{\Delta B2}$ satisfies the sequence limitation of the challenged claims (*see* Prelim. Resp. 37), but the Preliminary Response is silent with respect to VEFG-$TRAP_{R1R2}$, which corresponds to the description of VEGF Trap-Eye in Dixon.

Furthermore, Papadopoulos, as relied upon by the Examiner, teaches:

> Preferred embodiments of the invention include a fusion polypeptide capable of binding a VEGF polypeptide comprising (a) a VEGF receptor component operatively linked to (b) a multimerizing component, wherein the VEGF receptor component is the only VEGF receptor component in the fusion polypeptide and consists essentially of the amino acid sequence of Ig domain 2 of the extracellular domain of a first VEGF receptor and the amino acid sequence of Ig domain 3 of the extracellular domain of a second VEGF receptor.

Ex. 1010 col. 7, ll. 1–9. Furthermore, Papadopoulos expressly teaches "VEGFR1R2-FcΔC1(a) encoded by the nucleic acid sequence of SEQ ID NO: 1," as recited in dependent claim 12. This is not disputed by Patent Owner.

With respect to Heier 2009, we acknowledge that the reference discloses only that "VEGF Trap-Eye is a purified formulation of VEGF Trap." Ex. 1020. As we have related *supra*, Heier 2009 is a brief report of clinical trials employing VEGF Trap-Eye. Nevertheless, by the time VEGF Trap-Eye was in clinical trials, it was very almost certainly well known in the art what its chemical composition (including its amino acid sequence) was, if only to avoid regulatory and clinical confusion.

Finally, Petitioner's Declarant, Dr. Albini, opines that:

> [T]he last element of claim 1— "wherein the VEGF antagonist is a 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"—was disclosed well before January 2011. (See, e.g., Ex.1020, Heier-2009, 44-45; Ex.1006, Dixon, 1575, 1576 (Fig.1); Ex.1010, '758 patent, Fig.24A-C (disclosing the nucleotide sequence and deduced amino acid sequence, as well as a description of each molecular component therein (i.e., the signal sequence, the FLT1 Ig domain 2, the FLK1 Ig domain 3, and the FcΔC1 domain), 10:15-17 (specifying that this molecule is termed "VEGFR1R2-FcΔC1(a).")); Ex.1033, Dix, SEQ ID NO:4; Ex.1083; Ex.1039, '095 patent, 1:45-54; Ex.1040, WHO Drug Info, 118-19; Ex.1021, 2009 10-Q, 20; Ex.1041, Regeneron (26-February-2009), 1-2 (using VEGF Trap and aflibercept interchangeably and explaining that "VEGF Trap-Eye is a specially purified and formulated form of VEGF Trap for use in intraocular applications."); Ex.1007, Adis, 261 (indicating in the title that aflibercept, VEGF Trap (R1R2), and VEGF Trap-Eye, among other terms, were understood by a person of ordinary skill in the art to refer, interchangeably, to the same drug)).

Ex. 1002 ¶ 125. Dr. Albini's testimony is thus supported by factual evidence, and is not directly contradicted by Patent Owner. Although Patent Owner may elect to challenge Dr. Albini's testimony at trial, we find it persuasive for the purposes of this Decision.

We acknowledge that this issue is susceptible to further development of proof concerning the knowledge of a person of ordinary skill in the art as to the chemical composition of aflibercept/VEGF Trap-Eye. As Patent Owner points out, there appears to be some discrepancy concerning the molecular weight of aflibercept and VEGF Trap-Eye. Nevertheless, we find that, for the purposes of this Decision to Institute, the evidence of record

supports Petitioner's position that the molecular structure of aflibercept/VEGF Trap-Eye was known in the art at the time of invention, not least because it was in clinical trials, and that Dixon and Heier 2009, both of which disclose the use of VEGF Trap-Eye in clinical trials, thus inherently disclose the limitation of claim 1 reciting "wherein the VEGF antagonist is a 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."

c. Summary

Having determined that Petitioner has established a reasonable likelihood of success in establishing at trial that claims 1 and 9–12 are unpatentable under 35 U.S.C. § 102 as anticipated by either Dixon (Ground I) or Heier 2009 (Ground 2), we consequently institute trial on claims 1 and 8–12 for all of the Grounds set forth in the Petition. *See SAS*, 138 S.Ct. at 1354–55 (2018) (holding that, when *inter partes* review is instituted, the Board shall issue a final written decision with respect to the patentability of any patent claim challenged by the petitioner). We add below our comments on the remaining grounds for guidance to the parties.

D. Ground III: Alleged Anticipation of Claims 1 and 9-12 by Regeneron I

1. Overview of Regeneron I

Regeneron I was published on April 30, 2009, and is prior art to the '069 patent. Ex. 1028, 1. Regeneron I, a press release, discloses that "Bayer HealthCare AG and Regeneron Pharmaceuticals, Inc. (Nasdaq: REGN) today announced that the companies are extending their global development program for VEGF Trap-Eye, an investigational agent for the treatment of certain eye diseases." *Id.*

Specifically, Regeneron I discloses that:

> In the Phase 3 CRVO program for VEGF Trap-Eye, Regeneron and Bayer HealthCare will conduct two identical multinational clinical studies: COPERNICUS (COntrolled Phase 3 Evaluation of Repeated iNtravitreal administration of VEGF Trap-Eye In Central retinal vein occlusion: Utility and Safety…. [in which] [p]atients in both studies will receive 6 monthly intravitreal injections of either VEGF Trap-Eye at a dose of 2 milligrams (mg) or sham control injections. The primary endpoint of both studies is improvement in visual acuity versus baseline after 6 months of treatment. At the end of the initial 6 months, all patients will be dosed on a PRN (as needed) basis for another 6 months. All patients will be eligible for rescue laser treatment.

Ex. 1028, 1.

2. Anticipation of claims 1 and 9–12 by Regeneron I

i. Claim 1

Petitioner argues that the disclosures of Regeneron I anticipate each of the limitations of independent claims 1 and 9–12. Pet. 50–53. Petitioner has provided a claim chart of the limitations of claim 1, and what it contends are the corresponding disclosures of Regeneron I, which, for convenience, is reproduced below:

Claim 1	Regeneron (30-April-2009):
1. A method for treating an angiogenic eye disorder in a patient	"[A] Phase 3 program evaluating the efficacy and safety of VEGF Trap-Eye in the treatment of CRVO . . . ." (Ex.1028, Regeneron (30-April-2009), 1). "[A]nti-VEGF treatment may help decrease vascular permeability and edema and prevent the growth of abnormal new blood vessels in the retina in patients with CRVO." (*Id.*).
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;	"Patients in both studies will receive 6 monthly intravitreal injections . . . . At the end of the initial 6 months, all patients will be dosed on a PRN (as needed) basis for another 6 months." (*Id.*).[18]
wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and	(*Id.*).
wherein each tertiary dose is administered on an as-needed/pro re nata (PRN) basis, based on visual and/or anatomical outcomes as	(*Id.*).

Claim 1	Regeneron (30-April-2009):
assessed by a physician or other qualified medical professional;	
wherein the VEGF antagonist is a 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.	"VEGF Trap-Eye is a fully human, soluble VEGF receptor fusion protein that binds all forms of VEGF-A along with the related Placental Growth Factor (PIGF). Investigational VEGF Trap-Eye is a specific blocker of VEGF-A and PIGF that has been demonstrated in preclinical models to bind these growth factors with greater affinity than their natural receptors." (*Id.*).[19]

Pet. 51–52.

ii. Claims 9 and 10

As for Grounds I and II, Petitioner argues that Regeneron I also discloses VEGF Trap-Eye clinical trials for AMD and thus anticipates claim 10. Pet. 52 (*see* Ex. 1028, 1).

iii. Claim 11

Petitioner argues that Regereron I expressly discloses intravitreal injection used in Phase 3 CRVO studies, and thus anticipates claim 11. Pet. 52–53 (*see* Ex. 1028, 1).

iv. Claim 12

Petitioner again argues that the amino acid and nucleotide sequences for aflibercept were disclosed in the prior art and well known to skilled

artisans. Pet. 53 (citing Ex. 1002 ¶¶ 154–55; Ex. 1010 col. 10, ll.15–17, Figs. 24A–C; Ex. 1033, SEQ ID NO:3; Ex. 1083). Petitioner contends that the studies reported in Regeneron I are directed to VEGF Trap-Eye and, consequently, Regeneron I discloses the "VEGF antagonist" required by claim 12.

3. Analysis

Patent Owner essentially relies upon the same arguments advanced with respect to Grounds I and II and, for the same reasons, we do not find them sufficient, for the purposes of this Decision, to overcome the reasonable likelihood of success established by Petitioner's evidence of record. In particular, Patent Owner argues that Regeneron I provides no disclosure of any retreatment criteria (e.g., "visual and/or anatomical outcomes") or who is assessing such retreatment criteria. Prelim. Resp. 29. Patent Owner also contends that Petitioner makes no attempt to establish that the requirement that the PRN administration is by "a physician or other qualified medical professional" is disclosed expressly or inherently in Regeneron I.

Regeneron I expressly teaches that VEGF Trap-Eye is being employed in phase II clinical trials in human patients. We find that a person of ordinary skill would understand that such trials, performed in a clinical setting, are necessarily performed by, or under the direct supervision of, a physician. Furthermore, and as we have explained, the very nature of *pro re nata* administration, which is expressly disclosed by Regeneron I, requires the assessment and diagnosis of whether additional administration of the drug is required. Consequently, and for the same reasons we have explained

above, we conclude that Petitioner has established a reasonable likelihood of success at trial.

E. Ground IV: Alleged Anticipation or Obviousness of Claims 1 and 8–12 over Dixon

1. Claims 1 and 9–12

We have explained our reasons for concluding that Petitioner has established a reasonable likelihood of prevailing in demonstrating that claims 1 and 9–12 are anticipated by Dixon. Similarly, and for the same reasons, we conclude that the Petitioner has concurrently established a reasonable likelihood of prevailing in demonstrating that claims 1 and 9–12 are 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 *In re Fracalossi*, 681 F.2d 792, 794 (C.C.P.A. 1982)).

2. Claim 8

Claim 8 depends from claim 1 and recites "[t]he method of claim 1, wherein only two secondary doses are administered to the patient, and wherein each secondary dose is administered 4 weeks after the immediately preceding dose." Ex. 1001 col. 22, ll. 49–52.

Petitioner contends that, whereas Patent Owner acknowledges that challenged claims encompass the VIEW1/VIEW2 dosing regimen, as disclosed by Dixon, Dixon expressly discloses the claim 8 limitation. Pet. 55–57 (quoting Ex. 1006, 4 ("three monthly doses," i.e., an initial dose at day

0 and two secondary doses at weeks 4 and 8); also citing Ex.1002 ¶¶ 175–78).

Patent Owner makes no separate argument with respect to claim 8. Rather, Patent Owner argues, Dixon's VIEW1/2 disclosure fails to disclose a "tertiary dose" that "is administered on an as-needed/ PRN basis." Prelim. Resp. 42. Patent Owner argues that Petitioner's reliance upon Dixon's disclosure of a two-part Phase 3 study that "will evaluate the safety and efficacy of … 2.0 mg at an 8-week dosing interval (following three monthly doses)" is inapposite. *Id.* (citing Pet., 55).

Patent Owner contends that Petitioner premises its anticipation argument on Patent Owner's prosecution history statements, which Petitioner argues, equated the 8-week dosing regimen of VIEW with a PRN treatment protocol:

> Dixon discloses the exact VIEW1/VIEW2 dosing regimens that Regeneron told the Examiner represented a "PRN treatment protocol" "as claimed" in independent claim 1. Applying Regeneron's interpretation of the Challenged Claims, Dixon discloses each and every element of Challenged Claim 1….

Prelim Resp. 43 (citing Pet. 54).

It is Patent Owner's contention that Petitioner misconstrues the Applicant's tatements in prosecution, and ignores important differences between Dixon's disclosures, relied upon by Petitioner, and the Heier 2012 paper that was discussed in prosecution. Prelim. Resp. 44. According to Patent Owner, the Applicant did not argue during prosecution that 8-week dosing and PRN dosing were the same thing. *Id.* Pet. at 12. Instead, Patent

Owner explained that the Heier 2012 reference[13] showed that extended dosing regimens with VEGF Trap-Eye were unexpectedly non-inferior to the prevailing standard of care (i.e., monthly injections of ranibizumab). *Id.* at 43–44 (citing Ex. 1017, 136).

Dixon discloses two relevant clinical testing regimes: the CLEAR-IT-2 phase II clinical trial, and the VIEW1/2 phase III clinical trials. Ex. 1006, 4. In the CLEAR-IT-2 trial regime:

> 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.

Id. The View1/2 testing regimes:

> [W]ill 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.

It is evident from these disclosures that neither the CLEAR-IT-2 nor VIEW1/2 regimes teaches the limitation of claim 8 reciting "only two secondary doses are administered to the patient, and wherein each secondary dose is administered 4 weeks after the immediately preceding dose." We

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

consequently conclude that Petitioner is unlikely, at trial, to prevail in demonstrating that Dixon anticipates claim 8 of the '069 patent.

Whether the dosing regimen of claim 8 limiting the secondary dosages to only two doses is obvious over the teachings of Dixon is a closer question. However, because we institute trial on at least one of the claims and Grounds in the Petition, this argument, including secondary considerations of non-obviousness (*see* Pet. 69–72; Prelim. Resp. 52–57) can be further developed and argued by the parties at trial.

F. Ground V: Alleged Obviousness of Claims 1 and 8–12 over Heier2009 and Mitchell, or Dixon, and optionally, Papadopolous or Dixon

1. Claims 1 and 9–12

We have explained our reasons for concluding that Petitioner has established a reasonable likelihood of prevailing in demonstrating that claims 1 and 9–12 are anticipated by Heier 2009. Patent Owner largely repeats the arguments presented with respect to Ground II, *supra*. See Prelim. Resp. 31. Similarly, and for the same reasons, we conclude that the Petitioner has concurrently established a reasonable likelihood of prevailing in demonstrating that claims 1 and 9–12 are obvious over Heier 2009. *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 *In re Fracalossi*, 681 F.2d 792, 794 (C.C.P.A. 1982)).

2. Claim 8

Petitioner contends that the regimen recited in claim 8 is the same loading dose regimen used in the ranibizumab PrONTO and SUSTAIN trials by Mitchell, as well as, the VEGF Trap-Eye VIEW Phase 3 trials disclosed in Dixon. Pet. 66 (citing Ex. 1030, 6–7; Ex.1006, 4; Ex.1002 ¶¶ 204–07).

Patent Owner does not expressly argue that Petitioner has not demonstrated a reasonable expectation of prevailing at trial in demonstrating that claim 8 is obvious over the combined cited prior art.

Patent Owner argues further that it would not have been obvious to combine the teachings of the references, because: (1) Petitioner fails to provide a motivation to explore fewer loading doses, but relies upon describing a motivation to reduce the number of maintenance injections required to treat a chronic disorder; and (2) the results of CLEAR-IT-2 demonstrate the importance of loading doses in establishing the best visual acuity and anatomical outcomes; and (3) Petitioner fails to explain why Dixon's disclosure of the VIEW1/2 regimen, which was designed to evaluate fixed monthly or 8-week dosing for the first year following the loading doses, would motivate the POSA to alter the loading dose period for a monthly loading dose direct-to-PRN regimen. Prelim. Resp. 41–47.

As we have explained, we do not agree that Dixon teaches the same dosing regimen recited in claim 8. Mitchell is a summary of various clinical trials evaluating the drug ranibizumab (Lucentis) in the treatment of neovascular age-related macular degeneration. Ex. 1030, 1. Relevantly, Mitchell teaches that in a:

> [S]mall, open-label, prospective, single-centre, non-randomised, investigator-sponsored PrONTO study assessed three consecutive monthly injections followed by OCT-guided variable dosing (at ≥ 1 month intervals). Retreatment criteria

> were: five-letter loss in the presence of fluid at the macula detected by optical coherence tomography (OCT); ≥ 100 pm increase in central retinal thickness (CRT); new-onset classic choroidal neovascularization (CNV); new macular haemorrhage; or persistent macular fluid detected by OCT…. Although small and open label, this study suggests that flexible OCT-guided retreatment could sustain visual gain with fewer injections.

Ex. 1030, 8 (internal references omitted). Mitchell thus teaches at least one clinical trial in which the VEGF antagonist ranibizumab is administered, such that "only two secondary doses are administered to the patient, and wherein each secondary dose is administered 4 weeks after the immediately preceding dose," as recited in claim 8. Notably, Petitioner makes no argument concerning why a person of ordinary skill would have been motivated to apply the clinical trial regiment for administrating ranibizumab to a regimen for the similar VEGF antagonist VEFG Trap-Eye, in treating age-related macular degeneration. We expect that the parties will further develop and argue this issue at trial.

IV. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has established a sufficiently persuasive showing that the cited prior art references disclose, teach, or suggest the elements of claims 1 and 8–12 of the '069 patent, as set forth in the asserted Grounds I–V. 35 U.S.C. § 314. Furthermore, and also for the reasons set forth, we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of *inter partes* review.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED, pursuant to 35 U.S.C. § 314(a), that the Petition for *inter partes* review of the challenged claims of US Patent 9,669,069 B2 is GRANTED with respect to all grounds in the Petition; and

FURTHER ORDERED that *inter partes* review is instituted.

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