Trials@uspto.gov
571-272-7822

Paper 14
Date: August 13, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES S.A. and
DR. REDDY'S LABORATORIES, INC.,
Petitioner,

v.

EYE THERAPIES, LLC,
Patent Owner.

IPR2024-00467
Patent 11,833,245 B2

Before ZHENYU YANG, ROBERT A. POLLOCK, and RYAN H. FLAX, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge*.

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

I. INTRODUCTION

Dr. Reddy's Laboratories S.A. and Dr. Reddy's Laboratories, Inc. (collectively, "Petitioner") filed a Petition (Paper 2, "Pet.") seeking *inter partes* review of claims 1, 2, 4–9, 11–17, 20–22, 25, and 27 of U.S. Patent No. 11,833,245 B2 (Ex. 1001,[1] "the '245 patent"). Eye Therapies, LLC ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp."). With our authorization (Ex. 3001), Petitioner filed a Reply (Paper 12), and Patent Owner filed a Sur-reply (Paper 13).

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a).

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Accordingly, we institute *inter partes* review of all challenged claims based on the ground raised in the Petition.

A. Real Parties in Interest

Petitioner identifies Dr. Reddy's Laboratories SA, Dr. Reddy's Laboratories, Inc., Slayback Pharma LLC, and Slayback Pharma India LLP as the real parties in interest. Pet. 65. Patent Owner identifies Eye Therapies, LLC, Bausch & Lomb, Inc., and Bausch & Lomb Ireland Limited as the real parties in interest. Paper 4, 2.

---

[1] Both parties filed exhibits with only numbers. Any exhibit filed in the future must be given a short, descriptive name in addition to the number. For example, for Exhibit 1001, the description may be "the '245 patent."

B. Related Matters

According to the parties, the ’245 patent was asserted in the consolidated action *In re Lumify*, Case No. 3:21-cv-16766 (D.N.J.). Pet. 65; Paper 4, 2.

Petitioner represents that in the same action, two other patents were also asserted: U.S. Patent No. 8,293,742 (Ex. 1002, “the ’742 patent”) and No. 11,596,600 (“the ’600 patent”). The ’600 patent is the parent of the ’245 patent. Ex. 1001, code 63. The ’742 patent and the ’245 patent claim priority to the same set of provisional applications. *Id.*, code 60; Ex. 1002, code 60.

Slayback Pharma, LLC, one of Petitioner’s real parties in interest,[2] previously filed IPR2022-00142, challenging the claims of the ’742 patent. Ex. 2021. In the ’142 IPR, the Board found all challenged claims unpatentable as obvious over the same combination of prior art asserted in this proceeding. Ex. 1003, 40–68. Patent Owner’s appeal of the Board’s Final Written Decision in the ’142 IPR (“the ’142 FWD”) is currently pending before the Federal Circuit. Pet. 65; Paper 4, 2.

A month after filing the Petition in the instant proceeding, Petitioner filed IPR2024-00563, challenging claims 1, 12, and 28 of the ’600 patent.

C. The ’245 Patent

The ’245 patent relates generally to compositions and methods for inducing vasoconstriction, and specifically, to “using low doses of highly

[2] Henceforth, “Petitioner” refers to both Petitioner in the ’142 IPR and Petitioner in this proceeding.

selective a[lpha]-2 adrenergic receptor agonists to achieve vasoconstriction with significantly reduced hyperemia."[3] Ex. 1001, 2:52–57.

According to the '245 patent, dilation of small blood vessels causes undesirable events, including surface hemorrhage and ocular hyperemia (i.e., eye redness) following Lasik surgery and eye redness (conjunctival hyperemia). *Id.* at 1:22–27.

Adrenergic receptors, including a-1 (or α-1 or alpha-1) and a-2 (or α-2 or alpha-2) types, are involved in a variety of physiological functions, including functions of the cardiovascular and central nervous systems. *Id.* at 1:28–35. At the time of the '245 patent, agonists of alpha-2 adrenergic receptors were used in the treatment of hypertension, glaucoma, spasticity, and cancer pain. *Id.* at 1:41–45.

Brimonidine was a known compound having selective alpha-2 agonist activity and was used pharmaceutically for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. *Id.* at 1:65–2:1, 2:16–18. According to the '245 patent, "[i]t is a known property of all a[lpha] adrenergic receptor agonists, including brimonidine, to cause vasoconstriction." *Id.* at 2:7–9; *see also id.* at 1:45–47 ("Vascular constriction is known to be mediated by a[lpha]-adrenergic receptors.").

The '245 patent notes, however, that "known formulations of brimonidine and other known a[lpha]-2 adrenergic receptor agonists are associated with a high incidence of rebound hyperemia,[4] or other side

---

[3] The parties agree that ocular hyperemia refers to eye redness caused by vasodilation. Pet. 21; Prelim. Resp. 7.

[4] The '245 patent states that "[r]ebound hyperemia refers to induced vasodilation (instead of intended vasoconstriction) occurring, often with a

effects, in clinical use." *Id.* at 2:9–12. Specifically, brimonidine "is associated with significant rebound hyperemia (primary or delayed onset vasodilation) in its current concentration range for treating glaucoma of about 0.1% to 0.2%." *Id.* at 2:16–21.

The '245 patent also states that commercially available general alpha agonists for topical ophthalmic use have high alpha-1 receptor agonist activity and are known to cause rebound hyperemia. *Id.* at 2:22–27. Thus, their clinical use is typically limited to several hours or days, even though users with ocular hyperemia from chronic conditions, such as dry eye, contact lens wear, and allergic conjunctivitis, require longer-term agonist use. *Id.* at 2:28–36.

The '245 patent explains that "there is a need for new methods and formulations that would provide safe and long term vasoconstriction with reduced or minimized side effects, such as rebound hyperemia." *Id.* at 2:45–48. According to the '245 patent, its invention uses highly selective alpha-2 agonists at low concentrations, which "allows reducing, minimizing, and/or eliminating rebound hyperemia while optimally providing clinically equal or more effective vasoconstriction." *Id.* at 4:41–45; *see also id.* at 2:53–57 ("One of the key discoveries of the present invention lies in using low doses of highly selective a[lpha]-2 adrenergic receptor agonists to achieve vasoconstriction with significantly reduced hyperemia.").

D. Illustrative Claims

Of the challenged claims, claims 1 and 8 are independent. Claim 1 is illustrative of the claimed subject matter and is reproduced below.

---

lag time, after an application or, more typically, repeated applications of vasoconstrictors." Ex. 1001, 4:46–49.

> 1. A method for reducing eye redness in a human subject having ocular hyperemia, consisting of topically administering to an eye of said human in need of said reduction of eye redness a composition in the form of an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient, and one or more non-therapeutic components including benzalkonium chloride, wherein the ocular drop has a pH between 5.5 to 6.5, wherein the ocular hyperemia is reduced.

Ex. 1001, 22:36–44.

Claim 8 is similar to claim 1, except (1) it recites "comprising," instead of "consisting of," topically administering brimonidine; and (2) it requires that brimonidine is "the sole redness reducing active ingredient." *Id.* at 22:65–23:6.

E. Asserted Challenge to Patentability

Petitioner asserts the following challenge to patentability:

Claims Challenged	35 U.S.C. §[5]	References
1, 2, 4–9, 11–17, 20–22, 25, 27	103	Norden,[6] Gil,[7] Dean,[8] Alphagan,[9] Federal Register[10]

As support for its patentability challenge, Petitioner relies on the Declarations of Reza Dana, M.D., MSc, MPH (Ex. 1012), Paul A. Laskar, Ph.D. (Ex. 1013), John Galanis, M.D., FACS (Ex. 1014), and Radojka Savic, Ph.D. (Ex. 1015).

---

[5] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. § 103, effective March 16, 2013. On its face, the '245 patent claims priority to several applications filed before the effective date of AIA. Ex. 1001, codes (60), (63). Petitioner does not challenge the priority claim and states that "[p]re-AIA patent law applies to this Petition." Pet. 5 n.1. At this stage, Patent Owner does not address which version of the statute applies in this proceeding. Accordingly, we apply the pre-AIA version of § 103. We, however, note that the '245 patent was examined under the provisions of the AIA without Patent Owner's protest. Ex. 1010, 93, 208. Our analysis does not substantively depend on which version of the statute is applied.

[6] R.A. Norden, *Effect of Prophylactic Brimonidine or Bleeding Complications and Flap Adherence after Laser in Situ Keratomileusis*. 18 J. REFRACTIVE SURG. 468–71 (2002) (Ex. 1006, "Norden").

[7] Gil et al., US 6,294,553 B1, issued Sept. 25, 2001 (Ex. 1004, "Gil").

[8] Dean et al., US 6,242,442 B1, issued June 5, 2001 (Ex. 1007, "Dean").

[9] *ALPHAGAN® (brimonidine tartrate ophthalmic solution) 0.2%.* Physicians' Desk Reference, 52th ed., 487 (1998) (Ex. 1008, "Alphagan").

[10] 53 Fed. Reg. 7076–93 (Mar. 4, 1988) (Ex. 1009, "Federal Register").

F. Prior Art Disclosures

At this stage of the proceeding, Patent Owner does not dispute that the references asserted by Petitioner and discussed below qualify as prior art. *See generally* Prelim. Resp.

1. Gil

Gil relates to the topical use of brimonidine to treat ocular pain and neurogenic inflammation. Ex. 1004, 1:11–13. Gil explains that the first step leading to the sensation of pain is the activation of nociceptive primary afferents (i.e., pain receptors) by some form of stimuli. *Id.* at 1:20–22. The stimulation of primary afferents leads to the release of neuropeptides, which "enhance inflammatory reactions in the injured tissue, contributing to vasodilation, edema, and increased vascular permeability, this phenomenon is called 'neurogenic inflammation.'" *Id.* at 1:40–43.

Gil teaches that a topical formulation having between 0.01% and 0.5% (weight/volume) of brimonidine is anticipated to provide ocular pain relief. *Id.* at 3:46–49; *see also id.* at 3:53–66 ("For ophthalmic application, preferably solutions are prepared typically containing from about 0.01% to about 0.5% of active ingredient, and a physiological saline solution as a major vehicle.").

In Example 1, Gil teaches administering 0.03% brimonidine to patients who underwent radial keratotomy.[11] *Id.* at 4:47–49. In the study, each subject received one drop of brimonidine every four hours while awake

[11] According to Dr. Dana, an ophthalmologist, radial keratotomy "is a refractive surgical procedure aimed at correcting myopia (nearsightedness) by creating radial incisions in the cornea, altering its shape and thereby improving distance visual acuity by making the cornea flatter." Ex. 1012 ¶ 25.

one day before surgery and again every twenty minutes for the two hours just before surgery. *Id.* at 4:54–57. After surgery, each subject received one drop of brimonidine every hour hours while awake for 14 days. *Id.* at 4:58–60. Efficacy was assessed by evaluating pain intensity and pain relief, and "[s]ymptoms of ocular inflammation (i.e., burning/stinging, tearing, etc.) are also recorded." *Id.* at 4:62–65. According to Gil, the result "appears to suggest that brimonidine, administered preoperatively, blocks the perception of pain." *Id.* at 5:1–2.

In Example 4, Gil studies the effect of brimonidine on ocular pain using a rabbit model, specifically the ability of brimonidine at concentrations ranging from 0.01% to 0.5% to reduce neurogenic responses. *Id.* at 5:20–45. According to Gil, "[o]cular responses characteristic of neurogenic inflammation[include] redness," and "[b]rimonidine is effective in reducing such neurogenic responses." *Id.* at 5:39–45.

2. Norden

Norden teaches that brimonidine is a relatively selective α-2 adrenergic agonist and that α-2 adrenergic agonist drugs are considered to be "strong vasoconstrictors." Ex. 1006, 4. According to Norden, there are many anecdotal reports that the use of topical brimonidine before LASIK surgery can help prevent bleeding-related problems in the anterior segment. *Id.* Norden states that "some refractive surgeons now administer [brimonidine] prophylactically to reduce subconjunctival hemorrhage and improve the post-operative appearance." *Id.* Norden explains that its study was designed to "objectively assess the effect of brimonidine administration before LASIK on subconjunctival hemorrhage, hyperemia, and micropannus bleeding." *Id.*

Norden describes a study in which "LASIK was performed on 61 eyes of 31 patients."[12] *Id.* at 5. Patients received one drop of 0.2% brimonidine fifteen minutes before LASIK surgery and a second drop five minutes before surgery. *Id.* The drops were administered to one eye only. *Id.* After LASIK surgery, the amount of subconjunctival hemorrhage, hyperemia, bleeding from the micropannus, and flap slippage/wrinkling were recorded. *Id.*

Norden reports that subconjunctival hemorrhage was observed in 22 of 61 eyes, and hyperemia developed in all but three of 61 eyes. *Id.* at 6. Norden reports that the three eyes without hyperemia were in the brimonidine group and for the others, the amount of hyperemia was "notably lower in the eyes treated prophylactically with brimonidine." *Id.* Norden concluded "brimonidine administered before LASIK can significantly reduce subconjunctival hemorrhage as well as the amount of hyperemia." *Id.* at 7.

3. Dean

Dean relates to the treatment of ocular diseases and conditions caused by compromised blood flow with novel formulations of brinzolamide combined with brimonidine and the use of the two compounds administered separately. Ex. 1007, 1:4–8; *see also id.* at 2:27–29 (stating the two compounds "can be used either alone, in separate compositions dosed within 5 to 10 min of each other, or together in a single formulation").

Dean teaches that brimonidine is a "potent and relatively selective α2 agonist" and that "[u]pon topical administration, brimonidine causes vasoconstriction in scleral vessels." *Id.* at 2:33–36. Dean notes that although

[12] One patient had LASIK in one eye. Ex. 1006, 5.

brimonidine is a "relatively safe compound[,] it has been shown to cause the side effects of sedation and ocular hyperemia in an allergic like reaction in some patients." *Id.* at 2:38–41. Dean explains that the side effects "are thought to be due to the relatively high concentration of the drug administered topically." *Id.* at 2:41–43.

Specifically, Dean states that "[i]t is likely that the frequent instillation of relatively high drug concentrations" that causes hyperemia. *Id.* at 2:45–47. Thus, Dean suggests that "lowering the overall dose of brimonidine while maintaining [intra-ocular pressure] IOP control would be advantageous." *Id.* at 2:48–50.

Dean teaches that

> [w]hen two separate formulations of brinzolamide and brimonidine are used, the preferred administration sequence is brimonidine first and brinzolamide second. In this case, brinzolamide serves to constrict ocular vessels and thereby reducing the flux of blood through the anterior portion of the eye. When brinzolamide is administered[,] the reduced circulation in the eye should result in an increase in the bioavailability . . . .

Id. at 2:55–62.

Dean teaches that brimonidine, when administered alone, "is preferably formulated as a topical ophthalmic solution with a pH of about 4.5–7.8" and "will normally be contained in the formulation at a concentration of 0.01%–0.2% by weight." *Id.* at 5:20–23.

4. Alphagan

Alphagan 0.2% is a brimonidine tartrate ophthalmic solution "indicated for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension." Ex. 1008, 3. It includes benzalkonium chloride as the preservative and the pH is at 6.3–6.5. *Id.*

5. Federal Register

Federal Register is a publication of the final rule establishing conditions for branding of over-the-counter ophthalmic drug products. Ex. 1009, 1. It states that a vasoconstrictor can be identified as an "eye redness reliever." *Id.* at 7. It identifies several vasoconstrictors, including naphazoline hydrochloride (0.01 to 0.03%) and tetrahydrozoline hydrochloride (0.01 to 0.05%). *Id.* at 14.

G. The '142 IPR

We briefly summarize the '142 IPR because it involved similar issues and arguments in the instant case.

In the '142 IPR, Petitioner challenged claims 1–6 of the '742 patent. Ex. 2021. Petitioner asserts, and Patent Owner does not dispute, that the '742 patent and the '245 patent are commonly owned, share the same specification, and claim priority to the same priority application. Pet. 5, 65. Claim 3 of the '742 patent is reproduced below:

> 3. A method for reducing eye redness consisting essentially of topically administering to a patient having an ocular condition a composition consisting essentially of brimonidine into ocular tissue, wherein pH of said composition is between about 5.5 and about 6.5, wherein said brimonidine concentration is between about 0.001% and about 0.025% weight by volume and wherein said composition is formulated as an ocular drop.

Ex. 1002, 22:25–32.

In the '142 IPR, the Board concluded that claims 1–6 would have been obvious over the same prior art asserted in the current proceeding: Gil,

Norden, Dean, Alphagan, and Federal Register. Ex. 1003, 40–68. In reaching that conclusion, the Board determined:

(1) the preamble "is limiting and requires that the claimed brimonidine composition be administered with the intentional purpose of reducing eye redness, whether or not eye redness is actually reduced" (*id.* at 11–12);

(2) the transitional phrase "consisting essentially of" "does not preclude the use of additional active agents that may also cause vasoconstriction and reduction of hyperemia along with low-dose brimonidine" (*id.* at 15–16);

(3) the term "about 0.025%" includes 0.03% brimonidine (*id.* at 29); and

(4) the term "ocular condition" includes, but is not limited to, eye redness (*id.* at 31).

The Board found Norden, as evidenced by Federal Register, "teaches a method for reducing eye redness by administering prophylactic brimonidine to LASIK patients, which resulted in reducing subconjunctival hemorrhage and hyperemia." *Id.* at 53.

The Board also found Gil "teaches administering 0.03% brimonidine—which is within the claimed range—and suggests that doing so will reduce eye redness in radial keratotomy patients, particularly as evidenced by Federal Register and Dean." *Id.* But even if the claim term "about 0.025%" did not encompass 0.03% brimonidine, the Board continued, Gil's preferred range of "about 0.01% to about 0.5%" overlaps with the claimed range of "about 0.001% to about 0.025%," and thus, "creates a presumption of obviousness, which [wa]s not rebutted upon considering the totality of the evidence of record." *Id.* at 53–54.

The Board further found that Norden and Gil teach a composition "consisting essentially of brimonidine" because they "teach or suggest that brimonidine alone is effective in reducing eye redness," even though they "may also teach the possibility of co-administering pain medication, steroids, and antibiotics." *Id.* at 54.

Lastly, the Board found Alphagan teaches the claimed pH range. *Id.* at 54–55.

Thus, the Board determined that an ordinarily skilled artisan "would have had a reason to combine the pH of Alphagan with the 0.03% brimonidine of Gil to reduce redness as taught by Gil and Norden, as evidenced by Federal Register and Dean, with a reasonable expectation of success." *Id.* at 55.

The Board rejected Patent Owner's argument that an ordinarily skilled artisan "would not have been motivated to use brimonidine to reduce ocular redness with a reasonable expectation of success." *Id.* at 55–58. The Board also rejected Patent Owner's argument that an ordinarily skilled artisan "would have had no reason to consider brimonidine at a concentration between 0.001% and about 0.025%, and the prior art taught away from doing so." *Id.* at 58–59. The Board found that, in making these arguments, Patent Owner overlooked the express teachings of the asserted prior art. *Id.* at 56–59.

The Board evaluated Patent Owner's evidence of objective indicia but found it "does not outweigh the strong evidence of obviousness." *Id.* at 62–67. Specifically, the Board accorded "little weight" to the evidence of unexpected results because they were compared with commercial redness relievers like Visine, which are not the closest prior art. *Id.* at 62–64.

The Board further found no nexus between the other evidence of objective indicia and the alleged invention of the ’742 patent. *Id.* at 65–67. The Board stated that “Patent Owner’s evidence of industry praise, commercial success, licensing, and copying is not probative of nonobviousness (or at best carry little weight), as Lumify’s success was not the result of the novel features of the claim.” *Id.* at 66. In addition, the Board found Lumify’s success was also due to the sales and marketing campaigns unrelated to the alleged invention. *Id.* at 67.

As a result, the Board concluded that claims 1–6 of the ’742 patent are unpatentable as obvious over the combination of Gil, Norden, Dean, Alphagan, and Federal Register. *Id.* at 68.

H. Prosecution History of the ’245 Patent

The application that issued as the ’245 patent was filed on January 30, 2023, after the Board instituted review in the ’142 IPR. Ex. 1001, code 22. The applicant requested prioritized examination of the application, and the Office granted the request. Ex. 1010, 18, 90.

During prosecution, the examiner rejected the claims on the ground of nonstatutory double patenting as being unpatentable over, among others, claims 1–5 of the above-discussed ’742 patent, the subject of the ’142 IPR. *Id.* at 95–96. According to the examiner, “[a]lthough the claims at issue are not identical, they are not patentably distinct from each other.” *Id.* at 96.

In response, the applicant did not contest the rejection, but filed a terminal disclaimer over, among others, the ’742 patent to overcome the rejection. *Id.* at 176–78, 189–90. The applicant also amended the claims. *Id.* at 185–88. For example, for pending claim 29 (issued as claim 1), the applicant added that the ocular drop “further comprises benzalkonium

chloride." *Id.* at 185. The applicant also introduced the phrase "consisting of" into that claim, stating that

> [b]y consisting of, it is meant that brimonidine is the sole active ingredient administered in the method for reducing redness of claim 29, though inactive ingredients/excipients (such as benzalkonium chloride as recited in the claim) would not be excluded; however, it is clear that other active ingredients (such as steroids, anesthetics, carbonic anhydrase inhibitors, or NSAIDS, for example) would be excluded.

Id. at 189.

The applicant further added the phrase "wherein the redness is reduced" into both independent claims, stating with that language, "all claims require actual redness reduction." *Id.* at 185, 186, 189.

In addition to the terminal disclaimer and the amendments, the applicant submitted an IDS, listing the '142 FWD. *Id.* at 194.

The examiner rejected the amended claims under § 112 and proposed certain language. *Id.* at 209–10. The applicant largely adopted the suggested edits. *Id.* at 283, 288. Thereafter, the examiner allowed the claims. *Id.* at 294.

II. DISCRETIONARY DENIAL

Institution of an *inter partes* review is discretionary. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) (explaining that because 35 U.S.C. § 314 includes no mandate to institute review, "the agency's decision to deny a petition is a matter committed to the Patent Office's discretion"); *see also Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (stating that under § 314(a), "the PTO is permitted, but never compelled, to institute an IPR proceeding").

A. § 325(d)

Under 35 U.S.C. § 325(d), in determining whether to institute an *inter partes* review, "the Director may take into account whether, and reject the

petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office." Our § 325(d) analysis employs a two-prong framework: (1) whether the arguments presented in the petition are the same or substantially the same as those previously presented to the Office; and (2) if so, whether the petitioner has demonstrated a material error by the Office in its prior consideration of those arguments. *Advanced Bionics, LLC v. Med-El Electromedizinishe Geräte GmbH*, IPR2019-01469, Paper 6 ("*Advanced Bionics*"), 8 (PTAB Feb. 13, 2020) (precedential). "If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review." *Id.* at 8–9. "At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* at 9.

Patent Owner argues that we should exercise our discretion to deny institution under § 325(d). Prelim. Resp. 60–64. Patent Owner points out that during the prosecution of the '245 patent as well as the parent '600 patent, the applicant "submitted an IDS listing *all* of the references Petitioner presently asserts against the '245 patent claims," together with the expert declarations submitted with the petition and reply in the '142 IPR. *Id.* at 61–62. Patent Owner emphasizes that during the prosecution of the '245 patent, the applicant submitted another IDS, listing the '142 FWD. *Id.* at 62. Under the current Office policy, we agree with Patent Owner that the first prong of the *Advanced Bionics* framework is satisfied. *See id.*

We next evaluate whether Petitioner has demonstrated a material error by the Office in its prior consideration of the previously presented art.

Advanced Bionics, 8. As explained above, during prosecution of the '245 patent, the examiner issued a nonstatutory double patenting rejection because the claims were "not patentably distinct from" the '742 patent claims.[13] *See supra* Section I.H (citing Ex. 1010, 96). Petitioner argues that "[i]t was material error for the Examiner to both acknowledge that the '245 claims were patentably indistinct from the '742 claims and yet ignore the FWD and allow the claims despite the Board's prior findings." We find Petitioner's argument persuasive.

To determine whether Petitioner has sufficiently shown material error, we look at, for example, "the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection." *Advanced Bionics*, 9 (citing *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8, 10–11 (Dec. 15, 2017)). Petitioner asserts Gil, Norden, Dean, Alphagan, and Federal Register in this

[13] Under 37 C.F.R. § 42.73(d)(3)(i), "[a] patent applicant or owner is precluded from taking action inconsistent with the adverse judgment, including obtaining in any patent . . . [a] claim that is not patentably distinct from a finally refused or canceled claim." Despite the boiler plate language "without acquiescing to the propriety of the [nonstatutory double patenting] rejection," the applicant filed a terminal disclaimer over the '742 patent without substantively challenging the examiner's "not patentably distinct" characterization of the pending claims. Ex. 1010, 95–96, 176–77, 189–90. Nonetheless, because the appeal of the '142 FWD was pending while the application was on an expedited examination, the '742 patent claims were not "finally refused or canceled." Thus, § 42.73(d)(3)(i) did not apply during prosecution of the '245 patent. In addition, because the Rule only precludes an applicant from "obtaining" a new claim, we do not apply § 42.73(d)(3)(i) to the issued claims in this proceeding. *SoftView LLC v. Apple Inc.*, No. 2023-1005, 2024 WL 3543902, at *6 (Fed. Cir. July 26, 2024).

proceeding. During prosecution of the '245 patent, the examiner did not discuss or apply these references, or for that matter, any prior art.

Patent Owner points out that during prosecution of the parent '600 patent, the examiner "rejected the claims as obvious over a published application (USPA 2001/0031754) corresponding to Gil in view of Dean." Prelim. Resp. 61 (citing Ex. 2001, 168–73). It is, however, undisputed that Norden, Alphagan, and Federal Register were not discussed and were not the bases of any rejection, during prosecution of either the '245 patent or the '600 patent.

Patent Owner argues that the examiner "indisputably considered" these references, "particularly Norden," given his initial on the IDS. *Id.* at 63. Patent Owner does not present, and we do not find, any evidence to show that the examiner considered "particularly Norden." As Petitioner correctly points out, "unlike Gil and Dean, Norden explicitly includes statistically significant data showing that brimonidine reduces hyperemia in human patients after topical administration." Reply 7 (citing Ex. 1006, 6). Thus, the examiner's failure to address Norden's express teaching that "brimonidine administered before LASIK can significantly reduce subconjunctival hemorrhage as well as the amount of hyperemia" amounts to a material error. *See* Ex. 1006, 7.

Moreover, we do not equate an examiner's initial on an IDS with meaningful evaluation and appreciation of the prior art, especially in this case. Indeed, Patent Owner contends that the examiner "indisputably considered . . . the detailed analysis presented in the expert declarations and FWD" from the '142 IPR. *Id.* But all the expert declarations and the '142 FWD analyzed Gil, an issued patent; yet, peculiarly, the only

art-based rejection Patent Owner points to was based on "a published application (USPA 2001/0031754) corresponding to Gil." *Id.* at 61 (citing Ex. 2001, 168–73). We are hard pressed to accept that the examiner, after reviewing the materials from the '142 IPR, would choose to not rely on the prior art patent analyzed therein, but search for an earlier published application. In other words, circumstances of this case suggest that the examiner overlooked the prior art analyzed and determinations made in the '142 FWD. *See Keysight Techs., Inc. v. Centripetal Networks, Inc.*, IPR2022-01421, Paper 14, 6–8 (Aug. 24, 2023) (Director Review Decision vacating the Board's decision denying institution under § 325(d), finding the examiner misapprehended or overlooked an earlier Board's final written decision involving the same prior art and substantially overlapping subject matter, despite "some differences between the language" of the claims challenged in the two proceedings).

In sum, because the Office erred in a manner material to the patentability of the challenged claims, we will not exercise our discretion to deny the Petition under § 325(d).

B. § 314(a)

The Board has held that the advanced state of a parallel district court action is a factor that may weigh in favor of denying a petition under § 314(a). *See NHK Spring Co. v. Intri-Plex Techs., Inc.*, IPR2018-00752, Paper 8 at 20 (PTAB Sept. 12, 2018) (precedential); Patent Trial and Appeal Board, Consolidated Trial Practice Guide, 58 & n.2 (Nov. 2019) ("Trial Practice Guide")[14]. We consider the following factors to assess "whether

[14] Available at https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf.

efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding":

1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
3. investment in the parallel proceeding by the court and the parties;
4. overlap between issues raised in the petition and in the parallel proceeding;
5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
6. other circumstances that impact the Board's exercise of discretion, including the merits.

Apple Inc. v. Fintiv, Inc., IPR2020-00019, Paper 11 at 5–6 (PTAB Mar. 20, 2020) (precedential) ("*Fintiv*"). In evaluating these factors, we "take[] a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review." *Id.* at 6; *see also Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation* (June 21, 2022).[15]

Patent Owner presents evidence showing that the district court previously denied its motion to stay. Ex. 2029. Thus, factor 1 weighs in favor of denying institution.

Patent Owner represents that it has requested a trial date in February 2025. Sur-reply 8. Although it states it would "provide an update

[15] Available at https://www.uspto.gov/sites/default/files/documents/interim_proc_discretionary_denials_aia_parallel_district_court_litigation_memo_20220621_.pdf

after the schedule is finalized," as of today, more than a month after the June due date of the parties' joint status letter, no update has been filed. *See* Prelim. Resp. 65. Meanwhile, Petitioner, citing evidence to show that the average time to trial in the District of New Jersey is more than three years, argues that "a trial may not be held until 2026—well after a FWD would be expected in this proceeding." Pet. 15 (citing Ex. 1027, 2); Reply 8. We find factor 2 weighs in favor of institution.

Patent Owner contends that the district court and the parties have made significant investments in the parallel proceedings. Prelim. Resp. 65. But those investments relate to the preliminary injunction proceeding, and not the validity of the challenged claims. *Id.* Tellingly, the district court declined to "wade into" the validity analysis because it would "only muddy the waters as the Federal Circuit considers the same arguments" in the '142 appeal. Ex. 2030, 53. Thus, factor 3 weighs in favor of institution.

Patent Owner asserts that "[t]he claims, grounds, arguments, and evidence relied upon in the Petition are fully subsumed within" those in the parallel proceedings. Prelim. Resp. 66. Petitioner counters that only claims 1, 2, and 15 are at issue in the district court proceeding, whereas additional claims, including independent claim 8 are challenged in this proceeding. Pet. 1, 15, 16 n.5. We find factor 4 neutral.

Petitioner and the defendant in the parallel district court proceeding are the same party. Thus, factor 5 weighs in favor of denying institution.

Patent Owner asserts that "[t]he Petition submits art and arguments that Patent Owner has already overcome in prosecution and following the Board's FWD" in the '142 IPR. Prelim. Resp. 66. As explained above,

however, circumstances of this case suggest that the examiner misapprehended or overlooked the '142 FWD. *See supra* Section II.A.

Petitioner points out that it promptly filed the Petition less than two months after Patent Owner asserted the '245 patent, and that the district court case is at an early stage. Pet. 15–16. Petitioner also emphasizes that the Board has already found substantially overlapping subject matter in the '742 patent obvious over the same prior art combination. *Id.* at 11, 16. We agree with Petitioner that "[t]he Board is the tribunal best positioned to ensure that the issues presented in this Petition are decided consistently with the Federal Circuit's ultimate disposition of the [pending] appeal of IPR2022-00142." *Id.* at 11. Under these circumstances, we find factor 6 weighs in favor of institution.

A holistic balancing of the *Fintiv* factors weighs in favor of institution. Thus, we decline to exercise our discretion to deny the Petition in view of the parallel district court proceeding.

III. ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe a claim term "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b)." 37 C.F.R. § 42.100(b) (2020). Under that standard, the words of a claim "are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Petitioner proposes that we construe the term "consisting of" in claim 1 and the term "low incidence of rebound hyperemia" in claim 2. Pet. 17–19. Patent Owner argues that we do not need to construe these terms. Prelim. Resp. 18.

We agree with Patent Owner. Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to expressly construe any claim term.

Patent Owner appears to suggest, although it does not explicitly argue, that the claims require "a single drop of [0].025% brimonidine." *See* Prelim. Resp. 6; *see also id.* at 27 (arguing Gil is "with multi-dosed 0.03% brimonidine"); *id.* at 28 (arguing Dean is with "multi-dosed concentrations"). To the extent our understanding is correct, Patent Owner should expressly discuss at trial any construction that would so limit the claim. Such discussion should be set forth in a separate section of a response, if filed, designated for claim construction; claim construction positions should not be merely included in arguments over the merits on patentability.

B. Level of Ordinary Skill in the Art

Petitioner asserts that:

> A person of ordinary skill in the art ("POSA") would have been a composite person (or team) that included a medical doctor and pharmaceutical formulator. EX-1014, ¶¶60-61; EX-1013, ¶¶16, 22-24. The medical doctor would be an ophthalmologist with at least three to four years of experience in clinical trials and FDA regulation of eye products and would have experience in the use of topical brimonidine and apraclonidine and topical vasoconstrictors such as naphazoline and tetrahydrozoline.

> EX-1014, ¶60. The pharmaceutical formulator would have a doctorate in pharmaceutics or a related degree and at least three to five years of experience developing eye drop formulations for clinical trial and regulatory approval. EX-1013, ¶16.

Pet. 16–17. Patent Owner does not, at this point, dispute this proposed definition of the ordinarily skilled artisan. *See generally* Prelim. Resp. For purposes of this Decision, we adopt Petitioner's definition of the person of ordinary skill in the art as it appears consistent with the skill level reflected in the prior art of record and the disclosure of the '245 patent.

C. Alleged Obviousness the Challenged Claims

Petitioner asserts that claims 1, 2, 4–9, 11–17, 20–22, 25, and 27 would have been obvious over the combination of Gil, Norden, Dean, Alphagan, and Federal Register. Pet. 36–55, 62–64. We focus our analysis on independent claim 1.

The parties dispute whether an ordinarily skilled artisan, in view of the asserted prior art, would have (1) used brimonidine as the sole active agent for reducing eye redness, and (2) used 0.025% brimonidine and reasonably expected it to reduce eye redness. *Id.* at 36–50; Prelim. Resp. 19–57. The parties also dispute whether the prior art teaches "wherein the ocular hyperemia is reduced" by administering 0.025% brimonidine. Pet. 54–55; Prelim. Resp. 57–60. Based on this record, and for at least the following reasons, we find Petitioner's arguments sufficiently persuasive for institution purposes. Thus, we determine Petitioner has established a reasonable likelihood that it would prevail in showing the obviousness of claim 1.

1. Brimonidine as the Sole Active Agent

Petitioner asserts that both Gil and Norden teach using brimonidine to reduce eye redness before the priority date of the '245 patent. Pet. 37–39 (citing Ex. 1004, 1:40–43, 4:45–65, 5:44–45; Ex. 1006, 4–5, 7). Petitioner contends that Norden and Gil evaluate the effect of brimonidine alone on eye redness, and "conclude that topical administration of brimonidine—without any other step or ingredient—is effective at reducing eye redness." *Id.* at 39–41 (citing Ex. 1004, 1:11–13, 4:46–61; Ex. 1006, 4, 6). Petitioner also argues that even without the express disclosures of Norden and Gil on this issue, Dean teaches that brimonidine alone is effective as a vasoconstrictor. *Id.* at 41 (citing Ex. 1007, 2:23–25, 2:55–65). According to Petitioner, Dean's teaching, in view of Federal Register's characterization of vasoconstrictor as "redness reliever," would have motivated an ordinarily skilled artisan to use brimonidine alone to reduce eye redness. *Id.* at 41–42 (citing Ex. 1009, 17).

Patent Owner disagrees. Patent Owner argues that "Norden and Gil are ocular trauma models, necessarily combining brimonidine with other redness-reducing agents." Prelim. Resp. 19 (heading normalized); *see also id.* at 22 (citing Ex. 2013 ¶ 126)[16] (quoting the declaration of Dr. Galanis, one of Petitioner's experts, in which he testified that "[t]he patients in Norden and Gil received other drugs as a necessity—the patients were undergoing surgical procedure on their eyes"). Similarly, Patent Owner

[16] Exhibit 2013 is a declaration of Dr. Galanis submitted during the preliminary injunction proceeding before the district court. The testimony in paragraph 126 of Exhibit 2013 is substantively the same as that in paragraph 82 of Exhibit 1014. We cite Exhibit 1014, as it is filed in support of the Petition in this proceeding.

contends that Dean's "entire inventive concept is the combined administration of brimonidine with brinzolamide for treating glaucoma." *Id.* at 27–28 (citing Ex. 1007, 2:51–54). According to Patent Owner, "modifying Norden, Gil, or Dean to use brimonidine alone would have made them inoperative for their intended purpose." *Id.* at 26 (heading normalized). Thus, Patent Owner concludes that "only in hindsight would a POSA have used brimonidine as the sole active agent for reducing eye redness." *Id.* at 19 (heading normalized).

On this record, we find Petitioner's arguments more persuasive. As an initial matter, Petitioner asserts an obviousness challenge, not anticipation. Thus, the issue we need to address is whether Petitioner has shown a reasonable likelihood that the prior art would have suggested—even if it does not expressly disclose—administering an ocular drop, with brimonidine as the sole active ingredient, to reduce eye redness.

In Norden, each patient received in both eyes ofloxacin (antibiotic) and diclofenac (non-steroidal anti-inflammatory drug (NSAID)) before, proparacaine (anesthetic) during, and prednisolone (steroidal anti-inflammatory drug) after LASIK surgery. Ex. 1006, 4–5. To "assess the effect of brimonidine" on subconjunctival hemorrhage and hyperemia, each patient received, in one eye only, brimonidine drops before surgery. *Id.*

In other words, the test and the control groups both "underwent the same protocol—both groups received the same drugs (other than brimonidine), in the same amounts, at the same times," and "[t]he only variable between the two groups was the administration of brimonidine." Pet. 40 (citing Ex. 1014 ¶ 82). Norden reported that all eyes in the control group developed hyperemia. Ex. 1006, 6. In the test group, three eyes did

not develop hyperemia, and for the others, the amount of hyperemia was "notably lower," i.e., reduced. *Id.* Norden concluded that "brimonidine administered before LASIK," and not the other drugs, "can significantly reduce subconjunctival hemorrhage as well as the amount of hyperemia." *Id.* at 7.

Gil teaches using brimonidine "for treating ocular pain and neurogenic inflammation." Ex. 1004, 1:11–13. In Example 1, the test group received brimonidine, while the control group received placebo. Id. at 4:46–48. Thus, we agree with Petitioner that "the only variable between the two groups of radial keratotomy patients is the administration of 0.03% brimonidine or placebo." Pet. 40 (citing Ex. 1004, 4:46–61; Ex. 1014 ¶ 82). Gil teaches that brimonidine "blocks the perception of pain." Ex. 1004, 5:1–2. Gil also teaches that vasodilation is characteristic of neurogenic inflammation. *Id.* at 1:40–43. In Example 4, Gil teaches that, in a rabbit model, brimonidine, the only active ingredient of the ophthalmic formulation, "is effective in reducing such neurogenic responses," including redness. Ex. 1004, 5:39–45; Pet. 38–39 (citing Ex. 1004, 5:44–45; Ex. 1014 ¶¶ 66, 67, 79).

Finally, although Dean teaches using a combination of brinzolamide and brimonidine to treat certain ocular diseases and conditions, it also teaches that the two agents can be used "alone, in separate compositions." Ex. 1007, 1:4–8, 2:27–28. Dean teaches that, when separate formulations are used, it is preferred to administer brimonidine first because "brinzolamide serves to constrict ocular vessels and thereby reducing the flux of blood through the anterior portion of the eye." *Id.* at 2:55–60. As Petitioner correctly argues, the purpose of Dean's sequential dosing "is to allow

brimonidine to act as a vasoconstrictor on blood vessels toward the front of the eye to increase the bioavailability and effect of brinzolamide." Pet. 41 (citing Ex. 1007, 2:60–65). On the current record, we understand that it is vasodilation at the front of the eye that causes eye redness. *See id.* at 20–21; Prelim. Resp. 7–8. Thus, we agree with Petitioner that Dean teaches "brimonidine alone is a known vasoconstrictor," or as Federal Register characterizes it, a "redness reliever." Pet. 41–42 (citing Ex. 1009, 17; Ex. 1014 ¶ 143).

In sum, for institution purposes, Petitioner has shown sufficiently that the asserted prior art suggests using brimonidine as the sole active ingredient to reduce eye redness. On this record, Patent Owner's arguments are unavailing for several reasons. First, citing the testimony from its expert during the preliminary injunction proceeding, Patent Owner contends that "although Norden reports measuring 'hyperemia,' a POSA would have understood that Norden's hyperemia is not vasodilation, but rather micro-vessel hemorrhage (i.e., blood leakage in the subconjunctival space making eyes appear hyperemic)." Prelim. Resp. 20 (citing Ex. 2009, 32:1–14, 57:21–59:4, 59:20–61:8, 64:11–65:17, 67:13–68:17). Based on the current record, we are not persuaded by this argument.

Norden assessed the effect of brimonidine on not only hyperemia, but also subconjunctival hemorrhage and micropannus bleeding. Ex. 1006, 5–6. Patent Owner does not sufficiently explain why Norden would record and report the amounts of subconjunctival hemorrhage and hyperemia separately, if they were the same. In fact, Dr. Galanis's testimony at the district court, which Patent Owner also cites as support (Prelim. Resp. 20

(citing Ex. 2014, 739:23–741:21), appears to contradict Patent Owner's argument.

Dr. Galanis explained that Norden evaluated four things: subconjunctival hemorrhage, hyperemia, micropannus bleeding, and flap slippage. Ex. 2014, 741:8–14. According to Dr. Galanis,

> [Norden i]s evaluating those four things. And he makes a distinction between those four things. The subconjunctival hemorrhage is bleeding underneath the conjunctiva. The micropannus bleeding is actually bleeding that goes outside of the eye. And then hyperemia is actually dilation of the blood vessels. And then the other thing is slipping of the flap has nothing to do with bleeding. So there are separate things.

Id. at 741:13–20. In view of Norden's clear distinction of subconjunctival hemorrhage and hyperemia, we are not persuaded by Patent Owner's argument that "a POSA would have thus understood Norden's 'hyperemia' to necessarily be micro-vessel hemorrhage." *See* Prelim. Resp. 21.

Second, in an obviousness analysis, we determine whether an ordinarily skilled artisan would have had a reason to modify the teachings of the prior art references, not to meet the requirements of the references "that are not requirements of the claims at issue," but to achieve the claimed invention. *Axonics, Inc. v. Medtronic, Inc.*, 73 F.4th 950, 957 (Fed. Cir. 2023); *see also Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007) (stating a patent challenger must show that "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention").

Thus, the proper inquiry in this case is whether Norden, Gil, and Dean suggest using brimonidine alone to reduce eye redness, not whether using brimonidine alone would have worked in the alleged ocular trauma models or the glaucoma treatment of the prior art. As a result, we are not persuaded

by Patent Owner's argument that "modifying Norden, Gil, or Dean to use brimonidine alone would have made them inoperative for their intended purpose." Prelim. Resp. 26.

Third, for the rest of its arguments, Patent Owner heavily relies on the evidence presented during the preliminary injunction proceeding before the district court. According to Patent Owner, "the District Court found that 'there was ample testimony from Patent Owner's highly credentialed experts which presented a very different view of the prior art teachings' than Petitioner and its experts." Prelim. Resp. 5 (citing Ex. 2030, 50). Patent Owner asserts that the district court credited the testimony from Patent Owner's experts, "in stark contrast to Petitioner's experts." *Id.*

We read the district court's decision denying preliminary injunction differently. In our view, the District Court merely recited the expert testimonies related to validity without addressing their substance. Indeed, if describing the testimonies amounted to the court's approval of them, then the court, by restating the prior art, also found "Norden tends to support [Petitioner's] position," and the prior art references, coupled with the case law, "support [Petitioner's] argument." Ex. 2030, 50. But, that was not the case.

Instead, the district court explicitly stated that its "finding as to the validity of the '245 Patent is unnecessary to its ruling on the preliminary injunction." *Id.* at 52. In addition, "in light of the pending ['142] appeal," the district court declined to "wade into" the validity analysis because it would "only muddy the waters as the Federal Circuit considers the same arguments." *Id.* at 52–53.

Thus, we agree with Petitioner that, in its decision denying preliminary injunction, "[t]he District Court did not weigh the evidence from both sides, did not weigh the credibility of the experts on both sides, and did not reach any conclusions regarding the validity of the '245 patent."[17] Reply 1. At the preliminary stage of this proceeding, without any opportunity to evaluate credibility of expert testimonies submitted in the district court, and without the benefit of the district court's credibility determination, we accord those testimonies limited weight.

2. 0.025% Brimonidine

Petitioner asserts that the prior art teaches 0.025% brimonidine reduces eye redness. Pet. 44–49. Petitioner contends that Gil teaches brimonidine in concentrations from 0.01% to 0.5% "is effective in reducing neurogenic responses, including eye redness." *Id.* at 45 (citing Ex. 1004, 3:63–66, 5:20–46). Petitioner also refers to Dean for teaching brimonidine in concentrations from 0.01% to 0.2% can constrict ocular vessels. *Id.* (citing Ex. 1007, 5:20–23). Petitioner further points out that Gil teaches 0.03% brimonidine and Dean teaches 0.02% brimonidine. *Id.* at 45–46 (citing Ex. 1004, 4:49–53; Ex. 1007, 6:45–55). According to Petitioner, the range of 0.01% to 0.2% "disclosed in the prior art overlaps with the claimed amount of 0.025%, and thus renders the limitation *prima facie* obvious." *Id.* at 46. Petitioner also asserts that an ordinarily skilled artisan, starting with

[17] Patent Owner contends that the district court heard "credible testimony from Dr. Robert Noecker." Sur-reply 2 (citing Ex. 2030, 32, 50) (brackets omitted). The court, however, limited its credibility finding to Patent Owner's infringement argument on page 32, and did not appear to discuss Dr. Noecker's testimony on page 50. Ex. 2030, 32, 50.

Norden's 0.2% brimonidine, would have had several reasons to lower the concentration to reduce eye redness. *Id.* at 47–49.

Patent Owner disagrees. According to Patent Owner, "neither Dean nor Gil makes 0.025% brimonidine claimed use presumptively obvious." Prelim. Resp. 40 (heading normalized). Patent Owner further contends that its evidence, including teaching away and unexpected results, would rebut such presumption of obviousness, even if it applies. *Id.* at 47–57. Patent Owner asserts that Petitioners' other proffered reasons for lowering brimonidine concentration also fail. *Id.* at 39–40.

On this record, we find Petitioner's arguments more persuasive. Dean teaches that brimonidine causes vasoconstriction, and thus, should be administered before brinzolamide to increase the bioavailability of the latter. Ex. 1007, 2:33–36, 2:55–62. It teaches that brimonidine, when administered alone, is formulated "at a concentration of 0.01%–0.2% by weight." *Id.* at 5:20–23. Dean suggests that lowering the dose of brimonidine "would be advantageous" because high concentrations cause side effects, such as ocular hyperemia. *Id.* at 2:38–50. For institution purposes, we accept Petitioner's position that Deans' brimonidine concentration range overlaps with the claimed concentration, and thus, creates a presumption of obviousness.

On this record, Patent Owner's arguments to the contrary are unavailing. First, Patent Owner argues that Dean's working conditions "fundamentally differ" from the claimed method. Prelim. Resp. 42–43. Patent Owner contends that Dean is "limited to co-administration of brimonidine with brinzolamide," whereas the claimed method is a brimonidine monotherapy. *Id.* at 42. But, Dean's teaching that "brimonidine causes vasoconstriction" is independent of the co-administration Patent

Owner emphasizes. Ex. 1007, 2:33–36. In fact, Dean specifically teaches using brimonidine first, and thus, alone, "to constrict ocular vessels." *Id.* at 2:55–62. Similarly, Dean teaches the range of 0.01%–0.2% brimonidine in a formulation having brimonidine alone. *Compare id.* at 5:20–23 ("Brimonidine is preferably formulated as a topical ophthalmic solution . . . at a concentration of 0.01–0.2% by weight"), *with id.* at 5:28–35 ("The combinations of brinzolamide and brimonidine are preferably formulated as topical ophthalmic suspensions").

Second, Patent Owner contends that Dean's range of 0.01%–0.2% does not create the presumption of obviousness because it is "so broad as to encompass a very large number of possible distinct compositions." Prelim. Resp. 44–45 (citing *Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1306 (Fed. Cir. 2011)). *Genetics Institute* is apposite. As Patent Owner recognizes, the prior art in *Genetics Institute* motivated researchers to make smaller proteins, not the claimed larger proteins. *Id.* at 45 (citing *Genetics Inst.*, 655 F.3d at 1306). In contrast, Dean explicitly teaches lowering the "relatively high concentration" of brimonidine, which according to Patent Owner, is 0.2% in the commercially available Alphagan. *Id.* at 46; Ex. 1007, 2:38–50. Moreover, whether a range of 0.01%–0.2% is "very broad"[18] is a question of fact. At this stage of the proceeding, Patent Owner has not pointed to any persuasive evidence to support this attorney argument.

---

[18] Patent Owner argues that "it is well-established that the 'disclosure of a range is no more a disclosure of the end points of the range than it is of each of the intermediate points.'" Prelim. Resp. 45 (quoting *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 1000 (Fed. Cir. 2006)). *Atofina*, however, addressed the issue of anticipation, not obviousness. 441 F.3d at 1000.

Third, at this stage of the proceeding, we are not persuaded that the record evidence overcomes the presumption of obviousness. Relying on the information presented in the new drug application ("NDA") for Alphagan and labels of Alphagan products, Patent Owner argues that the prior art teaches away from selecting 0.025% brimonidine for reducing eye redness. Prelim. Resp. 49.

Specifically, Patent Owner points out that 50% of the patients reported conjunctival blanching when administered with 0.5% brimonidine, 3.5% of the patients reported conjunctival blanching when administered with 0.2% brimonidine, and no patient reported conjunctival blanching when administered with 0.1% and 0.15% brimonidine. *Id.* at 49 (citing Ex. 1030, 13, 52, 109; Ex. 1067, 4, 9; Ex. 1068, 4); *see also id.* ("Derick found '[c]onjunctival blanching was observed to occur more frequently in both the 0.2% and 0.5% treatment groups than in the 0.08% group or the vehicle control group.'") (quoting Ex. 1029, 4). According to Patent Owner, there is a "dose response relation" for conjunctival blanching. *Id.* (citing Ex. 1029, 4–5). Thus, Patent Owner concludes that the prior art would have directed an ordinarily skilled artisan to higher concentration of brimonidine to reduce eye redness. *Id.* at 50.

In making these arguments, Patent Owner appears to equate conjunctival blanching with reducing ocular hyperemia. Petitioner disagrees on this issue, arguing that "[c]ontrary to Patent Owner's implication, blanching is not synonymous with vasoconstriction." Pet. 49 (citing Ex. 1012 ¶¶ 46–49; Ex. 1014 ¶ 131). We find this is another fact issue that can benefit from further record development. We, however, make a few relevant observations.

Patent Owner asserts that in the '142 IPR, Petitioner "cited prior art's reporting on brimonidine's 'conjunctival blanching' was an 'excellent reason' to use brimonidine for redness reduction." Prelim. Resp. 34 (citing Ex. 2005, 5; Ex. 2021, 20–21, 53; Ex. 2022 ¶¶ 37, 99, 150; Ex. 2023 ¶¶ 43, 93). That assertion is inaccurate. Both the prior art and the petition in the '142 IPR relate to skin blanching on the cheek, not conjunctival blanching. *See* Ex. 2005, 5; Ex. 2021, 20–21, 53; Ex. 2022 ¶¶ 37, 99, 150; Ex. 2023 ¶¶ 43, 93.

Patent Owner disputes Petitioner's argument that "the ALPHAGAN data reported 'conjunctival blanching' as an 'adverse' event, and a POSA would not have been motivated to pursue concentrations that led to side effects reported as 'adverse.'" Prelim. Resp. 34 (quoting Pet. 49).[19] It is undisputed that conjunctival blanching is listed as an adverse event in the NDA and label for Alphagan. Ex. 1030, 52, 109; Ex. 1067, 4, 9. Dr. Dana testifies that "[t]he intent of a redness reliever is not to cause blanching, however, but to moderately reduce redness by suppressing vascular engorgement. A POSA would have therefore been motivated to reduce the concentration of brimonidine considerably to achieve a more moderate whitening effect." Ex. 1012 ¶ 49. For purposes of institution, we find this testimony reasonable.

Patent Owner emphasizes that no patient reported conjunctival blanching when administered 0.1% and 0.15% brimonidine. Prelim.

---

[19] Petitioner argues that the Board in the '142 FWD made this finding. Pet. 49. Patent Owner contends that "[t]he FWD made so such finding." Prelim. Resp. 34. We agree with Patent Owner. Nonetheless, Petition cites sufficient evidence to support its argument in this proceeding. *See* Pet. 49 (citing Ex. 1014 ¶¶ 131–133; Ex. 1012 ¶¶ 46–50).

Resp. 49 (citing Ex. 1068, 4). Dr. Dana testifies that "a POSA would not have considered the absence of conjunctival blanching as an adverse effect in the Alphagan P label as evidence of a lack of vasoconstrictive effect." Ex. 1012 ¶ 50. According to Dr. Dana, "a moderate whitening effect would not have been evidence of a potentially dangerous adverse event (like blanching) and would not have been recorded by clinicians studying glaucoma treatment." *Id.*

Dr. Dana's testimony appears to be consistent with the prior art, which reports that "[i]n some cases, the conjunctival blanching was the surgeon's description of what, in fact, appears to be a 'normal-looking' eye." Ex. 1032, 4. Because determination of conjunctival blanching is subjective (*see* Ex. 1029, 2), we find it reasonable that "a POSA would not have interpreted the lack of reported blanching" as "evidence that low doses of brimonidine did not cause vasoconstriction." Ex. 1012 ¶ 50.

Patent Owner further contends that "the claimed invention's unexpected superior redness reduction, coupled with its excellent safety profile, overcome any presumption of obviousness." Prelim. Resp. 50 (heading normalized). According to Patent Owner, Lumify, which embodies the claimed invention, showed unexpected, superior redness reduction compared to Visine, the prior art standard of care. *Id.* at 53–57.

The Board addressed the same argument in the '142 FWD. The Board determined that "[t]he only similarity between the commercial redness relievers like Visine and the claimed invention is redness reduction. But just because Visine and similar commercial products have been 'market leaders for decades' does not elevate those products to the level of closest prior art." Ex. 1003, 63. Instead, the Board found Gil is the closest prior art because it

"discloses the use of low-dose 0.03% brimonidine and that low-dose brimonidine is effective in reducing ocular responses characteristic of neurogenic inflammation, such as redness. Ex. 1004, 1:11–13, 40–43, 5:38–45." *Id.* at 63–64. For the purpose of institution, we agree with the Board's previous determination and adopt it as our own. As a result, we find that Patent Owner's evidence of unexpected results compared to Visine, instead of the closest prior art, is insufficient to overcome the presumption of obviousness created by the overlapping range.

3. "Wherein the Ocular Hyperemia Is Reduced"

Petitioner argues that the wherein limitation "adds nothing to the claimed method and claims no more than an inherent result of administering 0.025% brimonidine." *Id.* (citing Ex. 1014 ¶ 96). Patent Owner counters that "Petitioner has not established that all brimonidine concentrations within the ranges disclosed by Gil (0.01-0.5%) and Dean (0.01-0.2%) necessarily and inevitably reduce ocular hyperemia." Prelim. Resp. 59.

On this record, we find Petitioner has the better position. Inherency may supply a missing claim limitation in an obviousness analysis. *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1194–95 (Fed. Cir. 2014). "An inherent characteristic of a formulation can be part of the prior art in an obviousness analysis even if the inherent characteristic was unrecognized or unappreciated by a skilled artisan." *Endo Pharm. Sols., Inc. v. Custopharm Inc.*, 894 F.3d 1374, 1381 (Fed. Cir. 2018); *see also In re Kubin*, 561 F.3d 1351, 1357 (Fed. Cir. 2009) (explaining that even if no prior art of record explicitly discusses the allegedly inherent limitation, the applicant's application itself instructs that the limitation "is not an additional requirement imposed by the claims" on the claimed invention, "but rather a

property necessarily present" in the claimed invention); *Alcon Rsch., Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012) (stating claim language "stabilizing conjunctival mast cells" does not impose any additional requirement because the patent-at-issue itself defines mast cell stabilization as a property that is necessarily present).

Here, the '245 patent states that "[o]ne of the key discoveries of the present invention lies in using low doses of highly selective a[lpha]-2 adrenergic receptor agonists," such as brimonidine, "to achieve vasoconstriction with significantly reduced hyperemia." Ex. 1001, 2:52–57. As Dr. Galanis testifies,

> [t]he [claimed] single-step method is simply topical administration of brimonidine in the form of an ocular drop, with 0.025% brimonidine being the sole active ingredient in the ocular drop. The claimed method adds no more, no less. If the POSA performs the single step of the method, the claimed inherent result will be achieved.

Ex. 1014 ¶ 96.

On this record, we find Petitioner has sufficiently shown, for institution purposes, that reducing ocular hyperemia is an inherent result of administration of 0.025% brimonidine. Patent Owner does not cite any legal authority to support its position that, even though the claim requires 0.025% brimonidine, Petitioner must show all brimonidine concentrations within the prior art ranges necessarily and inevitably reduce ocular hyperemia. *See* Prelim. Resp. 58–59.

4. Summary

In sum, on this record, we determine Petitioner has established a reasonable likelihood that it would prevail in its assertion that claim 1 would

have been obvious over the combination of Gil, Norden, Dean, Alphagan, and Federal Register.

Petitioner also asserts that the combination of the asserted prior art renders claims 2, 4–9, 11–17, 20–22, 25, and 27 obvious. Pet. 55–62. Patent Owner does not argue these claims separately. *See generally* Prelim. Resp. 19–60. In any event, we institute *inter partes* review of all claims challenged in the Petition. *See SAS Institute, Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018); *see also* 37 C.F.R. § 42.108(a) ("When instituting *inter partes* review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim.").

IV. CONCLUSION

Based on the current record, and for the reasons explained above, we find Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one claim challenged in the Petition. We therefore institute an *inter partes* review of all challenged claims on all asserted grounds.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review is hereby instituted on all challenged claims of the '245 patent based on the assert ground set forth in the Petition; and

FURTHER ORDERED, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), notice is hereby given of the institution of a trial commencing on the entry date of this decision.

FOR PETITIONER:

Linnea Cipriano
Christopher Cassella
Goodwin Procter LLP
lcipriano@goodwinlaw.com
ccassella@goodwinlaw.com
extDG-Brimonidine@goodwinlaw.com

FOR PATENT OWNER:

Bryan Diner
Justin Hasford
Joshua Goldberg
Kassandra Officer
Christina Ji-Hye Yang
Ryan McDonnell
Jason Zhang
Finnegan, Henderson, Farabow,
Garrett & Dunner, LLP
bryan.diner@finnegan.com
justin.hasford@finnegan.com
joshua.goldberg@finnegan.com
kassandra.officer@finnegan.com
christina.yang@finnegan.com
ryan.mcdonnell@finnegan.com
jason.zhang@finnegan.com