

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GENE COMPANY PTY LTD,
Petitioner,

v.

THE TRUSTEES OF COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK,
Patent Owner.

IPR2024-00312
Patent 9,486,432 B2

Before ZHENYU YANG, TINA E. HULSE, and TAWEN CHANG,
Administrative Patent Judges.

HULSE, *Administrative Patent Judge.*

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

I. INTRODUCTION

Gene Company Pty Ltd (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–28 of U.S. Patent No. 9,486,432 B2 (Ex. 1001, “the ’432 Patent”). Paper 2 (“Pet.”). The Trustees of Columbia University in the City of New York (“Patent Owner”) did not file a Preliminary Response to the Petition.

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). Upon considering the argument and evidence presented in the Petition, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition. Accordingly, we institute an *inter partes* review of the challenged claims of the ’432 Patent.

A. *Real Parties-in-Interest*

Petitioner identifies itself as the real party-in-interest. Pet. 20.

Patent Owner identifies itself and the exclusive licensee, Alkeus Pharmaceuticals, Inc., as the real parties-in-interest. Paper 5, 2.

B. *Related Proceedings*

Petitioner states there are no related matters to this proceeding. Pet. 20. Patent Owner identifies IPR2024-00313 (“the -313 IPR”), which involves U.S. Patent No. RE47,045 E, as a related matter that would affect, or be affected by a decision in this proceeding. Paper 5, 2.

C. *The ’432 Patent*

The ’432 Patent, entitled “Compositions and Methods for Treating Macular Degeneration,” was filed as U.S. Application No. 14/510,975 on

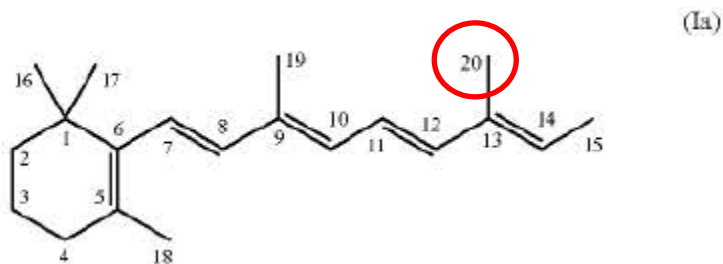
October 9, 2014, and claims the benefit of U.S. Patent Application No. 12/733,631, which was filed on September 12, 2008, and U.S. Provisional Application No. 60/993,379, filed on September 12, 2007. Ex. 1001, codes (54), (21), (22), (60), (62); 1:7–14.

Macular degeneration is the deterioration of cells in the macula, which is located in the back of the eye in the center of the retina. Ex. 1001, 1:36–41. As a result, central vision is lost, along with the ability to read, write, drive, and see color. *Id.* at 1:37–40. Macular degeneration is marked by the accumulation of lipofuscin in the retinal pigment epithelium (“RPE”) cell layer of the retina. *Id.* at 1:58–60. The Specification states that the only compounds that have been characterized to date from RPE lipofuscin are A2E (N-retinylidene-N-retinylethanolamine) and ATR-dimer (all-trans-retinal dimer). *Id.* at 1:60–63. A2E and ATR-dimer are derived from reactions of all-trans-retinal, an isomer of 11-cis-retinal, the chromophore of the visual pigments. *Id.* at 1:63–65. These toxic compounds have been shown to cause RPE cell death, causing photoreceptor cell degeneration and vision loss. *Id.* at 1:65–2:1.

The ’432 Patent relates to compounds and compositions for treating an ophthalmologic disorder such as macular degeneration by slowing or limiting the accumulation of age pigments or lipofuscin in the RPE cells of the retina. *Id.* at 1:23–28. The Specification explains that recently proposed therapeutic approaches to limit lipofuscin formation are based on slowing the visual cycle. *Id.* at 3:25–26. But the Specification describes several disadvantages to slowing the visual cycle, including poor night vision, loss of vision due to prolonged slowing of the visual cycle, toxic side effects of vitamin A analogs, and the requirement for relatively large doses, which lead to increased side effects. *Id.* at 3:26–4:13.

The Specification states that “it would be advantageous to provide treatments for ophthalmologic disorders, e.g., macular degeneration, that do not have, or limit one or more of, the side effects summarized above.” *Id.* at 5:13–16. Specifically, the Specification states it would be advantageous “to provide compounds, compositions, and methods for impeding or halting the accumulation of lipofuscin or age pigments in the RPE cells of the retina without slowing, or slowing minimally, the visual cycle.” *Id.* at 5:16–20.

Accordingly, the '432 Patent describes selectively replacing atoms on vitamin A to hamper the formation of A2E and ATR dimer, while preserving the chemical structure of vitamin A and minimally disturbing its participation in the visual cycle. *Id.* at 7:24–30. The Specification provides the numbering scheme for retinoids in Formula Ia, reproduced below, which we have annotated by circling C₂₀.



Formula Ia depicts the numbering scheme for the chemical formula of retinoids, with C₂₀ circled in red. *Id.* at 9:65–10:10. The Specification states that when C₂₀ hydrogens are replaced by deuteriums, there is a kinetic isotope effect that results in A2E formation that is about seven times slower and ATR-dimer formation that is about 15 times slower. *Id.* at 8:13–17; *see also id.*, FIG. 3, FIG. 4. According to the Specification, deuterated vitamin A is widely used in humans and shows no toxicity. *Id.* at 8:17–18. Thus, the Specification states “a treatment using a C₂₀-D₁₋₃-retinoid should be an

effective and non-toxic therapy to treat or ameliorate macular degeneration without adverse visual effects.” *Id.* at 8:18–21.

D. Illustrative Claim

Petitioner challenges claims 1–28 of the ’432 Patent, of which claim 1 is the only independent claim. Claim 1 is illustrative and reproduced below:

1. A pharmaceutical composition comprising a substituted C₂₀-D₁₋₃-retinoid and a pharmaceutically acceptable carrier, wherein the C₂₀-D₁₋₃-retinoid is selected from the group consisting of C₂₀-D₁₋₃-retinol, C₂₀-D₁₋₃-retinol ester, C₂₀-D₁₋₃-retinal and a C₂₀-D₁₋₃-pro-vitamin A carotenoid.

Ex. 1001, 24:5–9 (claim 1).

E. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–28 are unpatentable on the following grounds:

Claims Challenged	32 U.S.C. § ¹	Reference(s)/Basis
1–6, 28	103	Bergen ² and Furr ³

¹ 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. Because the ’432 Patent has an effective filing date before March 16, 2013, the pre-AIA version of § 103 applies. Our decision, however, would be the same under either version.

² Bergen et al., *Synthesis of Tri-, Tetra-, and Penta-deuterated Forms of Vitamin A*, 25 J. LABELLED COMPOUNDS AND RADIOPHARMS. 11–21 (1988) (Ex. 1006, “Bergen”). We note that Petitioner refers to Ex. 1006 as “Olson 1988.” We refer to Ex. 1006 as “Bergen,” according to the Board’s convention of using the first author’s last name and to avoid confusion with “Olson 1989.” The parties should follow the Board’s convention in their future papers.

³ Furr et al., *Vitamin A Concentrations in Liver Determined by Isotope Dilution Assay with Tetradeuterated Vitamin A and by Biopsy in Generally Healthy Adult Humans*, 49 AM. J. CLIN. NUTR. 713–16 (1989) (Ex. 1007, “Furr”). Petitioner refers to Ex. 1007 as “Olson 1989.” We refer to Ex. 1007 as “Furr,” according to the Board’s convention and to avoid confusion

Claims Challenged	32 U.S.C. § ¹	Reference(s)/Basis
1–6, 8–23, 25, 27, 28	103	Ortho Pharma ⁴ and Bergen
7, 24, 26	103	Ortho Pharma, Bergen, and Widder ⁵

Petitioner also relies on the Declarations of F. Peter Guengerich, Ph.D. (Ex. 1002) and Andrew Calman, M.D., Ph.D. (Ex. 1004).

II. ANALYSIS

A. *Person of Ordinary Skill in the Art*

Petitioner contends that a person of ordinary skill in the art at the time of the invention (“POSA”) would have had “an advanced degree (e.g., Ph.D., M.D., M.S., or equivalent), in chemistry, biochemistry, pharmaceutical science, medicine, or a related field.” Pet. 7. Petitioner further contends that that POSA “may have worked in consultation with a team including, e.g., a practicing physician who diagnoses and treats macular degeneration” and would have had “practical knowledge about biological studies, pharmaceutical formulation, and the deuterium isotope effect.” *Id.* (citing Ex. 1002 ¶¶ 47–50; Ex. 1004 ¶¶ 38–40).

We adopt Petitioner’s definition as it appears to be consistent with the prior art’s demonstration of the level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required “where the prior art itself reflects an appropriate level and a need

with “Olson 1988.” The parties should follow the Board’s convention in their future papers.

⁴ DE 20 2006 014 588 U1, filed September 20, 2006 and published January 18, 2007 (English translation) (Ex. 1008, “Ortho Pharma”).

⁵ Widder et al., WO 2006/007314 A1, published Jan. 19, 2006 (Ex. 1009, “Widder”).

for testimony is not shown” (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

In an *inter partes* review, the Board applies the same claim construction standard that would be used to construe claims in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b). 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).

Petitioner states that no construction is necessary for purposes of this decision. Petitioner also notes that the Specification confirms that the claim term “pharmaceutically acceptable carrier” “encompasses a wide variety of conventional carriers, including water, saline solution, corn oil, and starch.” Pet. 22 (citing Ex. 1001, 15:9–27; Ex. 1002 ¶¶ 26–30; Ex. 1004 ¶ 27).

At this stage of the proceeding, we agree with Petitioner that no construction of any claim terms is necessary for purposes of our Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’” (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

C. Alleged Obviousness over Bergen and Furr

Petitioner asserts that claims 1–6 and 28 are unpatentable as obvious over the combination of Bergen and Furr. Pet. 22–38.

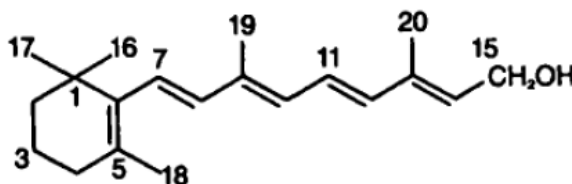
On this record—and without the benefit of a response from Patent Owner—we determine that Petitioner has established a reasonable likelihood

that it would prevail in showing the challenged claims are unpatentable over the combination of cited references.

1. Bergen (Ex. 1006)

Bergen is a journal article entitled, “Synthesis of Tri-, Tetra-, and Penta-deuterated Forms of Vitamin A,” which appears to have been published in the *Journal of Labelled Compounds and Radiopharmaceuticals* in 1988. Ex. 1006.

Bergen provides Scheme 1, reproduced below:



Scheme 1. Numbering system for retinol (vitamin A alcohol).

Scheme 1 depicts the numbering system for retinol (vitamin A alcohol). *Id.* at 12. Bergen describes the synthesis of 20,20,20-trideutero analogs of retinoic acid ethyl ester and retinyl acetate. *Id.*, Summary, 15–19. Bergen explains that nonradioactive deuterated compounds of high purity are desired “[f]or studying the metabolism of vitamin A in humans.” *Id.* at 11. Bergen states that such deuterated compounds “should contain three or more deuteriums in metabolically and chemically stable positions to provide adequate analytical sensitivity.” *Id.*

2. Furr (Ex. 1007)

Furr is a journal article entitled “Vitamin A concentrations in liver determined by isotope dilution assay with tetradeuterated vitamin A and by biopsy in generally healthy adult humans,” which appears to have been published in *The American Journal of Clinical Nutrition* in 1989. Ex. 1007, 713.

Furr describes a study for estimating the total body reserves of vitamin A in humans using a relatively noninvasive procedure. *Id.* Specifically, Furr describes administering to healthy patients 45 mg all-trans 10,19,19,19-tetradeuterated retinyl acetate in corn oil that was synthesized and purified as described in Bergen. *Id.* at 714, 716 (citing Ex. 1006 in endnote 9). Furr teaches measuring the ratio of deuterated retinol to ¹H-retinol in plasma over time and then calculating the total body reserves and liver concentrations of vitamin A. *Id.*, Abstract. Furr concludes that the predictive nature of its approach is satisfactory for detecting deficient or marginal vitamin A status. *Id.* at 716.

3. *Analysis*

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. 35 U.S.C. § 103(a); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) where in evidence, objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

“[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 550 U.S. at 418. “[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention

does.” *Id.* Moreover, a person of ordinary skill in the art must have had a reasonable expectation of success of doing so. *PAR Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

a) *Claims 1–4*

Petitioner asserts that the combination of Bergen and Furr teaches each limitation of claims 1–4. Pet. 24–27. On this record, we are persuaded that Petitioner has shown sufficiently that the combination of cited references teaches each limitation of those claims. For example, regarding claim 1, Petitioner asserts that Furr teaches administering to patients a pharmaceutical composition comprising a purified, deuterated form of vitamin A—which was synthesized according to Bergen—in corn oil, which is a pharmaceutically acceptable carrier. *Id.* at 24 (citing Ex. 1007,⁶ Abstract, 714; Ex. 1002 ¶¶ 191–193). Petitioner also notes that Bergen specifically created its deuterated vitamin A compounds for biological studies. *Id.* (citing Ex. 1006, 11). Finally, Petitioner asserts that Bergen teaches the retinoid limitation of the claim, because it teaches making and purifying the claimed C₂₀-D₁₋₃-retinoids, including C₂₀-D₁₋₃-retinol and C₂₀-D₁₋₃-retinol ester (e.g., C₂₀-D₃-retinol acetate). *Id.* at 24 (citing Ex. 1006, Abstract, 12, 15–19; Ex. 1002 ¶¶ 199–207).

Regarding dependent claims 2 and 3, Petitioner asserts that Bergen teaches making and purifying the claimed C₂₀-D₃-retinol and C₂₀-D₃-retinol acetate. Pet. 26–27 (citing Ex. 1006, Abstract, 15–19). And regarding

⁶ Petitioner cites Ex. 1006, but, based on the sentence it supports and the parenthetical quotations, it is clear Petitioner should have cited Ex. 1007 (Furr). We caution Petitioner, however, that the Board will generally not be an archaeologist of the record to determine the correct exhibit for miscitations.

dependent claim 4, Petitioner asserts that Furr teaches a unit dosage form because it teaches administering an oral dose of 45 mg of deuterated retinyl acetate in corn oil. *Id.* at 27 (citing Ex. 1007, 714; Ex. 1002 ¶¶ 213–216; Ex. 1004 ¶ 144).

Petitioner asserts that a POSA would have had a reason to combine Bergen and Furr with a reasonable expectation of success. Pet. 31–32. Specifically, Petitioner argues that a POSA would have understood by September 2007 that making use of Bergen’s deuterated compounds for biological studies would have involved formulation in a pharmaceutically acceptable carrier, as corroborated by Furr’s success in doing so. *Id.* (citing Ex. 1002 ¶¶ 225–226). Moreover, Petitioner asserts that a POSA would have had a reasonable expectation of success in making a pharmaceutical composition comprising the claimed C₂₀-D₃-retinol acetate and a pharmaceutically acceptable carrier because Bergen had already synthesized the retinoid and Furr had already formulated deuterated vitamin A retinoids in a pharmaceutical composition comprising a pharmaceutically acceptable carrier. Pet. 36–37 (citing Ex. 1002 ¶ 235).

Accordingly, at this stage of the proceeding, having considered the arguments and evidence set forth in the Petition, we find Petitioner has shown a reasonable likelihood of prevailing on its assertion that Claims 1–4 would have been obvious in light of the combination of Bergen and Furr. *See* Pet. 24–26, 30–38; Ex. 1006, Abstract, 15–19; Ex. 1007, Abstract, 714; Ex. 1002 ¶¶ 191–216, 223–238; Ex. 1004 ¶¶ 127–144.

b) Claims 5, 6, 28

Dependent claims 5, 6, and 28 further recite limitations wherein the aldehyde of C₂₀-D₃-all-trans-retinol acetate forms A2E about 7 times slower

and inhibits the formation of A2E as compared to the non-deuterium-enriched retinoid. Ex. 1001, Claims 5, 6, 28.

Petitioner asserts that those claims “merely recite properties that naturally result from deuteration at C-20.” Pet. 28 (citing Ex. 1002 ¶¶ 217–219; Ex. 1004 ¶ 145). Petitioner notes that the ’432 Patent states that the seven times slower formation of A2E and the slower formation of ATR-dimer as compared to the non-deuterium-enriched retinoid is the result of deuterating carbon 20. *Id.* (citing Ex. 1001, 6:9–38, Figs. 2–4). Petitioner also asserts that because Bergen teaches making the claimed C₂₀-D₃-retinol acetate, which the body naturally converts to all-trans-retinal, “the claimed reductions in A2E and ATR-dimer formation is an inherent property of the C₂₀-D₃-retinoids disclosed in [Bergen.]” *Id.* at 29 (citing Ex. 1002 ¶ 219). Dr. Guengerich explains that this property “flows naturally from the C-20 deuterium substitution and the kinetic isotope effect that . . . is a result of the increased size, lower bond frequency, high energy of activation for bond cleavage, and thus slower bond cleavage of the carbon deuterium bond as compared to the carbon hydrogen bond.” Ex. 1002 ¶ 218.

To establish that a prior art reference inherently teaches a claim limitation, Petitioner must show that “the limitation at issue necessarily must be present, or [is] the natural result of the combination of elements explicitly disclosed by the prior art.” *PAR Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014). On this record—and without the benefit of Patent Owner’s response—we are persuaded that Petitioner has shown sufficiently that the A2E reduction limitations of claims 5, 6, and 28 are the natural result of administering C₂₀-D₃-retinol acetate, as taught by the combination of Bergen and Furr, for the reasons stated by Petitioner and its expert Dr. Guengerich. *See* Pet. 28–29; Ex. 1002 ¶¶ 218–222.

c) Conclusion

On this record at this stage of the proceeding, we find Petitioner has shown a reasonable likelihood that it would prevail on its assertion that claims 1–6 and 28 are unpatentable as obvious over the combination of Bergen and Furr.⁷

D. Alleged Obviousness over Ortho Pharma and Bergen

Petitioner asserts that claims 1–6, 8–23, 25, 27, and 28 are unpatentable as obvious over the combination of Ortho Pharma and Bergen. Pet. 38–55.

On this record—and without the benefit of a response from Patent Owner—we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the challenged claims are unpatentable over the cited references.

We incorporate here our earlier findings and analysis of Bergen.

1. Ortho Pharma (Ex. 1008)

Ortho Pharma is an English translation of German Patent Application No. DE 20 2006 014 588 U1, published January 18, 2007, entitled “Carotenoid-containing product.” Ex. 1008, codes (10), (43), (54).

Ortho Pharma relates to a carotenoid-containing product that is suitable for dietary supplements for age-related eye diseases such as age-related macular degeneration. *Id.* ¶ 1. Ortho Pharma states that supportive care, especially for elderly patients, is known to prevent vitamin and nutrient deficiencies to the eye. *Id.* ¶ 3. Ortho Pharma states, however, that a “disadvantage of available preparations is that they often have high

⁷ Patent Owner has not yet presented evidence of secondary considerations of nonobviousness. We will consider and weigh any such evidence—if presented at trial—in our Final Written Decision.

proportions of individual antioxidant vitamins, but do not take into account a comprehensive supply of vitamins and minerals to the eye.” *Id.* ¶ 4.

According to Ortho Pharma, “there is a need for an agent that provides a comprehensive supply of antioxidant substances, vitamins, trace elements, and nutrients to the eye.” *Id.* ¶ 6.

Thus, Ortho Pharma discloses a carotenoid-containing product comprising vitamin A together with other vitamins such as vitamins C, E, and D, antioxidants such as carotenoids, and minerals such as zinc. *Id.* ¶ 8.

2. *Analysis*

a) *Claims 1–6, 28*

Petitioner asserts that the combination of Ortho Pharma and Bergen teaches each limitation of claims 1–6 and 28. Pet. 39–44. Petitioner relies on Ortho Pharma for the teaching of a pharmaceutical composition comprising vitamin A in a pharmaceutically acceptable carrier (e.g., water) in a unit dosage form (e.g., a solution in a drinking vial). *Id.* (citing Ex. 1008 ¶¶ 9, 12–15, 56–58). And, like Ground 1, Petitioner relies on Bergen’s teaching of the making and purification of C₂₀-D₃-retinol acetate for the retinoid limitations. *Id.* (citing Ex. 1006, Abstract, 15–19). At this stage of the proceeding, we are persuaded Petitioner has shown sufficiently that the combination of Ortho Pharma and Bergen teaches each limitation of claims 1–6 and 28.

Petitioner asserts that a POSA would have had a reason to use Bergen’s C₂₀-D₃-retinol acetate in place of the non-deuterated forms of vitamin A in Ortho Pharma’s formulations for age-related macular degeneration because a POSA would have understood that doing so would inhibit reactions that involve cleavage of a hydrogen from C-20 through a 1,5-sigmatropic shift (e.g., in A2E formation). Pet. 51 (citing Ex. 1002

¶ 311; Ex. 1010, 7158). Petitioner asserts that a POSA would have therefore understood that a pharmaceutical composition with C₂₀-D₃-retinol acetate may reduce lipofuscin formation to treat or prevent macular degeneration. *Id.* at 52–53 (citing Ex. 1010, 7154; Ex. 1002 ¶¶ 312–314; Ex. 1004 ¶¶ 168–171). Finally, Petitioner asserts that a POSA would have had a reasonable expectation of success in making such a pharmaceutical composition as vitamin A formulations (including deuterated forms of vitamin A) in a pharmaceutically acceptable carrier were known in the art. *Id.* at 53 (citing Ex. 1008, Abstract; Ex. 1007, 714).

At this stage of the proceeding, having considered the arguments and evidence presented in the Petition, we find Petitioner has shown a reasonable likelihood of prevailing in its assertion that a POSA would have had a reason to modify Ortho Pharma’s oral dosage formulations by substituting the non-deuterated vitamin A with Bergen’s C₂₀-D₃-retinol acetate to reach claims 1–6 and 28 with a reasonable expectation of success for the reasons stated in the Petition. *See* Pet. 39–43, 50–55.

b) Dependent Claims 8–23, 25, and 27

Dependent claims 8–23, 25, and 27 recite additional additives of the pharmaceutical composition in various amounts. Ex. 1001, claims 8–23, 25, 27. We have considered the arguments and evidence presented by Petitioner regarding those claims and find Petitioner has shown sufficiently that the combination of Ortho Pharma and Bergen teaches or suggests the additional limitations of those claims—including overlapping ranges of additive amounts—and that a POSITA would have had a reason to combine the references with a reasonable expectation of success for the reasons stated in the Petition. *See* Pet. 44–50 (citing, e.g., Ex. 1008, Abstract, ¶¶ 8, 36; Ex. 1002 ¶¶ 279–308; Ex. 1004 ¶¶ 178–198); *see also* *UCB, Inc. v. Actavis*

Labs. UT, Inc., 65 F.4th 679, 689–90 (Fed. Cir. 2023) (“A presumption of obviousness applies ‘[w]here a claimed range overlaps with a range disclosed in the prior art.’” (citation omitted)).

3. Conclusion

On this record at this stage of the proceeding, we find Petitioner has shown a reasonable likelihood that it would prevail on its assertion that claims 1–6, 8–23, 25, 27, and 28 are unpatentable as obvious over the combination of Ortho Pharma and Bergen.

E. Alleged Obviousness over Ortho Pharma, Bergen, and Widder

Petitioner argues that claims 7, 34, and 26 are unpatentable as obvious over the combination of Ortho Pharma, Bergen, and Widder. Pet. 55–64.

On this record—and without the benefit of a response from Patent Owner—we determine that Petitioner has established a reasonable likelihood that it would prevail in showing that the challenged claims are unpatentable over the cited references.

We incorporate here our earlier findings and analysis regarding Ortho Pharma and Bergen.

1. *Widder (Ex. 1009)*

Widder is a published PCT application entitled “Methods and Compositions for Treating Ophthalmic Conditions with Retinyl Derivatives,” which was published on January 19, 2006. Ex. 1009, codes (54), (43).

Widder teaches methods, composition and formulations for treating ophthalmic conditions and controlling symptoms that are associated with such ophthalmic conditions. *Id.* at 2:25–26. In one embodiment, Widder teaches formulations comprising retinyl derivatives to treat macular degeneration. *Id.* at 2:25–27. Widder also teaches that its formulations are

used to limit the formation of all-trans-retinal, A2E, and lipofuscin. *Id.* at 2:29–33. Widder describes administering vitamin A with fenretinide to inhibit the development or reoccurrence of macular degeneration. *Id.* at 47:21–27. Widder also explains that the use of certain negatively charged phospholipids has been shown to help patients with macular degeneration. *Id.* at 33:1–2. Examples of suitable negatively charged phospholipids that can be used with vitamin A include cardiolipin and phosphatidylglycerol. *Id.* at 33:3–5.

2. *Analysis*

Petitioner asserts that Widder teaches the additional limitations of dependent claims 7, 24, and 26. Pet. 56–64. On this record, we find Petitioner has shown sufficiently that Widder teaches the additional limitations of those claims. For example, regarding claim 7, Petitioner asserts that Widder teaches a pharmaceutical composition comprising an effective amount of fenretinide co-administered with vitamin A to inhibit the development or reoccurrence of macular degeneration. *Id.* at 56–57 (citing, e.g., Ex. 1009, 47:21–27). Regarding claim 24 (which depends from claim 21), Petitioner asserts that Widder teaches a pharmaceutical composition comprising cardiolipin and phosphatidylglycerol. *Id.* at 59 (citing, e.g., Ex. 1009, 33:1–7). And regarding claim 26, Petitioner asserts that Widder teaches that the composition can be an aqueous solution, which can be presented in the form of eye drops. *Id.* at 61–62 (citing, e.g., Ex. 1009, 25:16–26:40).

Petitioner asserts that a POSA would have had a reason to combine Widder with the composition of Ortho Pharma and Bergen because a POSA would have understood that Widder teaches that fenretinide and negatively charged phospholipids such as cardiolipin and phosphatidylglycerol have

been shown to benefit patients with macular degeneration. Pet. 57–58 (citing Ex. 1004 ¶¶ 215–218), 59–60 (citing Ex. 1004 ¶¶ 204–205).

Petitioner also asserts that a POSA would have had a reason to make the pharmaceutical composition of Ortho Pharma and Bergen suitable for administration to the eye, because Widder teaches that local administration directly to the eye was desirable to concentrate the active ingredient in the targeted tissue more specifically than systemic administration. Pet. 62–63 (citing Ex. 1004 ¶¶ 210–214).

At this stage of the proceeding, having considered Petitioner’s arguments and evidence, we are persuaded that Petitioner has shown sufficiently that a POSA would have combined Widder’s composition with Ortho Pharma and Bergen to reach the invention of claims 7, 24, and 26 with a reasonable expectation of success. *See* Pet. 55–64; Ex. 1004 ¶¶ 199–220.

3. Conclusion

On this record at this stage of the proceeding, we find Petitioner has shown a reasonable likelihood that it would prevail on its assertions that claims 7, 24, and 26 are unpatentable as obvious over the combination of Widder, Ortho Pharma, and Bergen.

III. CONCLUSION

For the foregoing reasons, we determine that Petitioner has established a reasonable likelihood of prevailing on its assertion that at least one of the challenged claims of the ’432 Patent is unpatentable. Accordingly, we institute an *inter partes* review of claims 1–28 of the ’432 Patent on each of the grounds raised in the Petition.

Our determination in this Decision is not a final determination on the construction of any claim term or the patentability of any challenged claim and, thus, leaves undecided any factual issues necessary to determine

whether sufficient evidence supports Petitioner’s contentions by a preponderance of the evidence in the final written decision. *See TriVascular, Inc. v. Samuels*, 812 F.3d 1056, 1068 (Fed. Cir. 2016) (noting that “there is a significant difference between a petitioner’s burden to establish a ‘reasonable likelihood of success’ at institution, and actually proving invalidity by a preponderance of the evidence at trial”) (quoting 35 U.S.C. § 314(a) and comparing § 316(e)). Any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–28 of U.S. Patent No. 9,486,432 B2 is instituted with respect to all challenged claims and all grounds set forth in the Petition; and

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

IPR2024-00312
Patent 9,486,432 B2

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