

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FORTE BIOSCIENCES, INC.,
Petitioner,

v.

UNIVERSITY OF MASSACHUSETTS,
Patent Owner.

PGR2023-00014
Patent 11,278,505 B2

Before GEORGIANNA W. BRADEN, ROBERT A. POLLOCK, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

BRADEN, *Administrative Patent Judge*.

DECISION
Granting Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

Forte Biosciences, Inc. (“Petitioner”) filed a Petition requesting a post-grant review of claims 1–5 (the “challenged claims”) of U.S. Patent No. 11,278,505 B2 (Ex. 1001, “the ’505 patent”). Paper 2 (“Pet.”). University of Massachusetts (“Patent Owner”) filed a Preliminary Response. Paper 6 (“Prelim. Resp.”).

We have authority to determine whether to institute a post-grant review under 35 U.S.C. § 324 and 37 C.F.R. § 42.4. A post-grant review may not be instituted unless it is determined that “the information presented in the petition filed under section 321, if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable.” 35 U.S.C. § 324 (2018); *see also* 37 C.F.R. § 42.4(a) (2022) (“The Board institutes the trial on behalf of the Director.”). The “more likely than not” standard requires greater than 50% chance of prevailing. Consolidated Trial Practice Guide 58 (Nov. 2019), *available at* <https://www.uspto.gov/TrialPracticeGuideConsolidated>.

For the reasons provided below and based on the record before us, we determine Petitioner has demonstrated that it is more likely than not that it would prevail in showing the unpatentability of at least one of the challenged claims. We decline to deny the Petition on a discretionary basis as requested by Patent Owner. Accordingly, we institute a post-grant review of the ’505 patent and all of the asserted challenges to patentability.

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner states that it “is the real party-in-interest.” Pet. 21. Patent Owner lists itself, Villarís Therapeutics, Inc., and Incyte Corporation, as real parties-in-interest. Paper 4 (Patent Owner’s Mandatory Notice), 1.

B. Related Proceedings

The parties do not list any related proceedings. *See* Pet. 21; Paper 4, 1. Patent Owner lists U.S. Patent Application No. 17/667,699 as “a divisional application of the ’505 patent.” Paper 4, 1.

C. The ’505 Patent (Ex. 1001)

The ’505 patent is titled “Diagnosis and Treatment of Vitiligo,” and issued on March 22, 2002. Ex. 1001, codes (45), (54). It is the U.S. National Stage Application of PCT/US2018/029185 and relies on provisional application No. 62/489,191, which was filed on April 24, 2017. *Id.* at codes (22), (60), (86).

1. Written Description

The ’505 patent relates methods for treating vitiligo. Ex. 1001, code (57); 6:31–33. The ’505 patent explains that vitiligo “is a chronic, progressive autoimmune skin disease characterized by white or depigmented patches of skin.” *Id.* at 6:34–35. The disease is caused by cluster of differentiation 8 positive (“CD8⁺”) T cells that target melanocytes (melanin-forming cells) for destruction. *Id.* at 1:29–31. The ’505 patent explains that a specific class of CD8⁺ T cells, tissue resident memory (“Trm”) T cells “are present in both mouse and human vitiligo skin lesions.” *Id.* at 1:49–50; *see id.* at 5:33–45 (citing Harris (Ex. 1006)). According to the ’505 patent, “depleting Trm or inhibiting their function is a highly effective and durable treatment for vitiligo.” *Id.* at 1:63–64. The ’505 patent further explains that “others have shown” that interleukin-15 (“IL-15”) “is required for the generation of CD8⁺ Trm in viral models in mice” and “is much more potent at generating CD8⁺ Trm pools than residual [interleukin-2 (‘IL-2’)] signaling in skin tissue.” *Id.* at 6:3–9. According to the ’505 patent “[t]he present data support targeting this cytokine as a strategy to clear autoreactive

memory cells from the tissue, resulting in a long-lasting, durable response to treatment.” *Id.* at 6:22–24.

The ’505 patent describes methods for treating vitiligo as including “delivery of a therapeutically effective amount of an inhibitor of IL-15, the IL-15 receptor, a Spingosine-1-receptor inhibitor, and/or the downstream signaling molecules [Janus kinase (‘JAK’)]1 and 3” to a vitiligo subject in need of treatment. *Id.* at 7:19–33. The ’505 patent lists various diverse types of inhibitors of IL-15 and the IL-15 receptor, including small molecules, fusion proteins, peptides, antibodies, and nucleic acids. *See id.* at 7:34–8:37.

In one embodiment, “mice with longstanding, stable vitiligo (>12 weeks after disease initiation) were treated with an anti-mouse IL-15R β antibody, which blocks IL-15 signaling.” *Id.* at 33:17–22. The ’505 patent reports “significant repigmentation in treated mice compared to controls (FIG. 6A–6C)” after 8 weeks of systemic treatment. *Id.* at 33:22–26. Mice treated with IL-15R β antibody for only 2 weeks also had significant repigmentation over a 10-week period, indicating a durable treatment option. *Id.* at 33:35–41 (citing Fig. 6F–I).

2. Illustrative Claims

As noted previously, Petitioner challenges claims 1–5 of the ’505 patent, of which claim 1 is independent. Pet. 1; Ex. 1001, 44:13–27. Claim 1 is illustrative of the challenged subject matter and is reproduced below.

1. A method of treating a subject who has a vitiligo lesion, the method comprising:
identifying a subject in need of treatment; and

administering a therapeutically effective amount of an inhibitor of IL-15 or the IL-15 receptor to the subject.

Ex. 1001, 44:12–17.

D. Asserted Challenges to Patentability and Evidence of Record

Petitioner challenges the patentability of claims 1–5 of the '505 patent on the following bases:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–5	112(a)	written description
1–5	112(a)	enablement
1–5	103	Harris ¹ , Xing ²

In support of its patentability challenge, Petitioner relies on, *inter alia*, the Declaration of Abul Abbas, MBBS (“Dr. Abbas”) (Ex. 1002) and R. Todd Plott, M.D. (“Dr. Plott”) (Ex. 1004).

III. PRELIMINARY MATTERS

A. Post-Grant Eligibility

Post-grant reviews are available only for patents “described in section 3(n)(1)” of the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”). AIA § 6(f)(2)(A); *see Arkema Inc. v. Honeywell Int’l Inc.*, PGR2016-00011, Paper 13 at 15 (PTAB Sept. 2, 2016). These patents issue from applications “that contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date as defined in section 100(i) of title 35, United States Code, that is on or after”

¹ John E. Harris et al., *A Mouse Model of Vitiligo with Focused Epidermal Depigmentation Requires IFN- γ for Autoreactive CD8⁺ T-Cell Accumulation in the Skin*, J. Investigative Dermatology, Vol. 132 (2012), 1869–1876 (“Harris,” Ex. 1006).

² Luzhou Xing et al., *Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition*, Nature Medicine 20 (2014), 1043–1049 (“Xing,” Ex. 1007).

“the expiration of the 18-month period beginning on the date of the enactment of” the AIA. AIA § 3(n)(1). Accordingly, post-grant reviews are available only for patents that issue from applications that at one point contained at least one claim with an effective filing date of March 16, 2013, or later. *See also* 37 C.F.R. § 42.204(a) (requiring that “petitioner . . . certify that the patent for which review is sought is available for post-grant review”).

Petitioner asserts that the ’505 patent claims earliest priority to April 24, 2017. Accordingly, the ’505 patent issued from applications having a filing date of March 16, 2013 or later. Petitioner filed the request for post-grant review on December 22, 2022, which is within nine months of the grant of the ’505 patent on March 22, 2022. *See* Pet. 21; 35 U.S.C. § 321(c).

Patent Owner does not challenge the eligibility of the ’505 patent for post-grant review at this time. We determine that the ’505 patent is eligible for post-grant review.

B. Level of Ordinary Skill in the Art

In determining the level of ordinary skill in the art, various factors may be considered, including the “type of problems encountered in the art; prior art solutions to those problems; rapidity with which innovations are made; sophistication of the technology; and educational level of active workers in the field.” *In re GPAC, Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995) (quotation marks omitted). Furthermore, the prior art itself can reflect the appropriate level of ordinary skill in the art. *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

Petitioner contends that a person of ordinary skill in the art by April 24, 2017 “would have had an advanced degree (e.g., Ph.D., M.D.,

M.S., or equivalent), in a field related to medicine, immunology, molecular biology, cell biology, microbiology, pathology, biochemistry, peptide chemistry, or a related field.” Pet. 18 (citing Ex. 1002 ¶¶ 39–40; Ex. 1004 ¶¶ 31–32). Petitioner asserts that the person of ordinary skill would also have had “at least 3–5 years of experience in treating autoimmune diseases or researching cytokine signaling pathways relevant to treating autoimmune diseases.” *Id.*

At this stage of the proceeding, Patent Owner does not assert a different level of skill in the art at the time of the alleged invention and uses Petitioner’s proposed level of skill. Prelim. Resp. 16.

For the purposes of this Decision, we too adopt Petitioner’s level of ordinary skill in the art because it appears consistent with the problems addressed in the ’505 patent and the prior art of record.

C. Claim Construction

A claim “shall be construed 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). Under that standard, the “words of a claim ‘are generally given their ordinary and customary meaning.’” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc).

Both parties state that express claim construction is unnecessary at this stage of the proceeding and that all terms are to given their plain and ordinary meaning. Pet. 23; Prelim. Resp. 17. We agree.

Construction is needed only for those terms “that are in controversy, and only to the extent necessary to resolve the controversy.” *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200

F.3d 795, 803 (Fed. Cir. 1999)). Consequently, we need not construe any terms for purposes of institution.

D. Section 325(d)

Patent Owner raises several arguments as to why we should deny institution under 35 U.S.C § 325(d). Prelim. Resp. 44—54. The Board has discretion under 35 U.S.C. § 325(d) to reject a petition when the same or substantially the same prior art or arguments were presented previously in another proceeding before the Office. The relevant portion of that statute is reproduced below:

In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, 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.

35 U.S.C. § 325(d). In evaluating whether to deny institution on the basis of 35 U.S.C. § 325(d), the Board has considered certain non-exclusive factors: (a) the similarities and material differences between the asserted art and the prior art involved during examination; (b) the cumulative nature of the asserted art and the prior art evaluated during examination; (c) the extent to which the asserted art was evaluated during examination; (d) the extent of the overlap between the arguments made during examination and the manner in which a petitioner relies on the prior art or a patent owner distinguishes the prior art; (e) whether a petitioner has pointed out sufficiently how the Office erred in evaluating the asserted prior art; and (f) the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments. *See Becton Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017).

Factors (a), (b), and (d) relate to whether the art or arguments presented in the Petition are the same or substantially the same as those previously presented to the Office. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 10 (PTAB Feb. 13, 2020) (designated precedential Mar. 24, 2020) (“*Advanced Bionics*”). Factors (c), (e), and (f) “relate to whether the petitioner has demonstrated a material error by the Office” in its prior consideration of that art or arguments. *Id.* Under a two-part framework set forth in *Advanced Bionics*, we first determine whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office by considering factors (a), (b), and (d). *Id.* at 8, 10. If “either condition of first part of the framework is satisfied”—that is, if “the same or substantially the same art previously was presented to the Office” or “the same or substantially the same arguments previously were presented to the Office,” we then consider factors (c), (e), and (f) to determine whether Petitioner has demonstrated a material error by the Office. *Id.* at 8, 10.

1. 35 U.S.C. § 103 challenge based on Harris and Xing

Patent Owner first addresses § 325(d) with respect to the § 103 obviousness challenge. In its § 103 obviousness challenge, Petitioner contends that claims 1–5 would have been obvious over Harris and Xing. Pet. 64–74. With respect to this challenge, Patent Owner contends the Board should exercise its discretion to deny institution under 35 U.S.C. § 325(d) for at least two reasons. First, Harris was considered previously by the Office. Prelim. Resp. 44–45 (citing Ex. 1010, 79). Specifically, Harris was listed on an Information Disclosure Statement (“IDS”) submitted to the Office during the prosecution of the application leading to the ’505 patent.

Ex. 1010, 79. The IDS states “[a]ll references considered except where lined through” and this statement was initialed by the examiner. *Id.* Harris was not lined through. *Id.* Thus, Harris was “[p]reviously presented art” which “includes art made of record by the Examiner, and art provided by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Advanced Bionics*, Paper 6 at 7–8. Second, Xing is “no more relevant than, and cumulative to,” the references previously considered and overcome during prosecution. *See id.* at 45–48 (quoting *Gardner Denver, Inc. v. Utex Indus., Inc.*, IPR2020-00333, Paper 12, 8–14 (PTAB Aug. 5, 2020)).

Patent Owner specifically argues that Xing is less relevant than Pavlakis³ and cumulative of Harris-2015⁴ and Damsky⁵. *Id.* According to Patent Owner, Xing is less relevant than Pavlakis because Xing teaches administering an IL-15R antibody to treat alopecia rather than vitiligo. *See id.* at 45–47 (citing Pet. 76–77). Patent Owner asserts that the Examiner found that Pavlakis taught using IL-15 inhibitors to treat autoimmune disorders and “mentioned vitiligo” as one of those disorders. *Id.* at 45 (citing Ex. 1010, 14, 56–57). Patent Owner then argues that Pavlakis “failed to support obviousness because ‘there is zero evidence in Pavlakis that an inhibitor of IL-15 or the IL-15 receptor could actually be used to treat a subject who has a vitiligo lesion.’” *Id.* (quoting Ex. 1010, 14). In the

³ WO 2009/002562 A2, published Dec. 31, 2008. Ex. 1009 (“Pavlakis”).

⁴ John E. Harris et al., *Rapid skin repigmentation on oral ruxolitinib in a patient with coexistent vitiligo and alopecia areata (AA)*, 74(2) J. Am. Acad. Dermatol. 370–371 (2015) (“Harris-2015”).

⁵ William Damsky and Brett A. King, *JAK inhibitors in dermatology: The promise of a new drug class*, 76(4) J. Am. Acad. Dermatol. 736–744 (April 2017) (“Damsky”).

reasons for allowance, the Examiner stated that “[t]he prior art does not disclose a method which fits within the scope of . . . the instant claims nor does it disclose an obvious variant.” Ex. 1010, 15. Because Xing does not teach treating vitiligo, Patent Owner concludes that “Xing in no way overcomes Pavlakis’s deficiency and the Examiner’s bases for allowance.” Prelim. Resp. 45–46.

Patent Owner next contends that Xing is cumulative to Harris-2105 and Damsky, which were “cited by Patent Owner and considered by the Examiner during prosecution.” *Id.* at 47 (citing Ex. 1010, 79). According to Patent Owner, the references are cumulative to Xing because all three references teach treating alopecia. *See id.* at 46–48. For example, Patent Owner argues that Harris-2015 describes using ruxolitinib (a JAK inhibitor) to treat a patient having both vitiligo and alopecia areata, resulting in unsuccessful treatment of vitiligo. *See id.* at 47 (citing Ex. 2001, 1, Fig. 1). Likewise, Patent Owner asserts that Damsky “specifically discusses Xing and summarizes treatment strategies using JAK inhibitors for vitiligo separate from other dermatological diseases, including alopecia areata.” *Id.* at 47–48 (citing Ex. 1021, 2–3, 5, 7).

Petitioner contends that the Examiner never considered Xing “or any reference cumulative thereto.” Pet. 76. Petitioner argues instead that “Xing discloses the very things the Examiner believed were missing from the prior art.” *Id.* Specifically, Petitioner argues that Xing “provides new and non-cumulative evidence that a [person of ordinary skill in the art] had good reason and a reasonable expectation of success for treating CD8⁺ T cell-induced vitiligo lesions by using a mouse CD122 antibody to deplete the CD8⁺ T cells causing the depigmentation.” *Id.* at 77.

Petitioner further contends that there is material error because:

(1) “the record is not well-developed on the art and issue presented here,” and (2) “the petition presents new evidence in the form of highly-qualified expert testimony as well as new references demonstrating . . . that the same result achieved in the patent was obvious in view of the prior art.” *Id.* at 78–79.

Patent Owner’s argument is unpersuasive because the combination of Harris with Xing is not cumulative of Pavlakis, Harris-2015, and Damsky. Here the combination of Harris with Xing is argued in different ways compared to what was made to the Examiner. Additionally, we agree with Petitioner that Xing discloses information the Examiner indicated were absent from the prior art. *See* Ex. 1010, 14–15. For example, Xing teaches administering a therapeutically effective amount of an inhibitor of IL-15 or the IL-15 receptor is administered to the subject. *Compare id.* at 15, *with* Ex. 1007, 3. Xing also teaches that TM- β 1-mediated blockade of CD122 prevented disease development and progression and that inhibiting IFN- γ production downstream of IL-15 through topical administration of JAK inhibitors effectively eliminated existing lesions.

Thus, we do not find that the same or substantially the same arguments were presented previously to the Office, nor do we find that the same or substantially the same art was previously presented to the Office. Thus, the first part of the *Advanced Bionics* framework is not satisfied for Petitioner’s § 103 challenge, and we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of a trial proceeding on this challenge.

2. 35 U.S.C. § 112(a) enablement and written description

Patent Owner also contends the Board should exercise its discretion to deny institution under 35 U.S.C. § 325(d) in light of the § 112(a) enablement

and written description challenges. Prelim. Resp. 44–54. Specifically, Patent Owner argues that “Petitioner presents no evidence that the Examiner was unaware of the requirement to evaluate the application for compliance with the written description and enablement requirements.” Prelim. Resp. 50. Patent Owner further argues that “substantively, the Examiner *did not err* in not making Petitioner’s [§ 112] arguments,” which Patent Owner argues are “legally and factually baseless.” *Id.* at 50–51.

Petitioner contends that “[t]he Examiner never issued any rejection under 35 U.S.C. § 112, and never provided any analysis of whether the specification provides written description and enablement support for the claims.” Pet. 75–76. Specifically, Petitioner contends that the Examiner did not evaluate or discuss the different forms for inhibiting IL-15 or IL-15R. *See id.* at 76. Petitioner contends that there is material error because the Petition “presents new evidence in the form of highly-qualified expert testimony as well as new references demonstrating the specification is not commensurate with the scope of the claims.” *Id.* at 78–79.

Petitioner is correct that during the prosecution of the ’505 patent, the Examiner did not issue a rejection under 35 U.S.C. § 112, did not articulate any analysis of whether the specification provides written description and enablement support for the claims, and certainly did not do so in the context of Petitioner’s newly asserted arguments and evidence. *See* Pet. 75–76. Therefore, the same or substantially the same arguments presented in the Petition could not have been presented previously to the Office. We, thus, determine that the first part of the *Advanced Bionics* framework is not satisfied for Petitioner’s enablement and written description challenges, and we need not proceed with our analysis. Even if we were to consider the second part of the *Advanced Bionics* framework, we nonetheless would find

that Petitioner has demonstrated the Office erred with regards to the challenged claims because, based on the current record, the claims should have been rejected for lack of enablement and written description, as detailed below. Accordingly, we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of a trial proceeding.

IV. ANALYSIS

A. Alleged Lack of Written Description

Petitioner argues claims 1–5 are unpatentable for lack of written description “because the specification fails to reasonably convey to a POSA that the applicant invented the broad invention that is claimed.” Pet. 23–48. Patent Owner disagrees. Prelim. Resp. 17–30. For the reasons discussed below, we find Petitioner has shown that at least one of the challenged claims is more likely than not unpatentable for lack of written description.

1. Legal Principles

35 U.S.C. § 112(a) requires that a patent’s specification “contain a written description of the invention . . . in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). This provision ensures that as of the filing date “the inventor actually invented the invention claimed” (*id.* at 1350–51) and “the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor’s contribution to the field of art as described in the patent specification” (*id.* at 1353–54). The specification therefore must demonstrate conception and at least constructive reduction to practice of “the complete and final invention with all its limitations.” *Id.* at 1353. A specification that merely renders the invention obvious does not satisfy the written description requirement. *Id.* The determination “requires

an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Id.* at 1351.

The level of detail required to satisfy the written description requirement “varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology.” *Id.*; *see also Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (what is required “varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence”). In the case of a claim to a genus, the Federal Circuit has held that “a sufficient description of the genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can ‘visualize or recognize’ the members of the genus.” *Ariad*, 598 F.3d at 1350. “[F]unctional claim language can meet the written description requirement when the art has established a correlation between structure and function.” *Id.*

2. *Petitioner’s position*

Petitioner asserts that “[t]he ’505 patent claims lack written description support because they are overly broad and functionally defined and because the specification fails to disclose a representative number of species commensurate with the scope of the claim.” Pet. 24. Petitioner argues that claim 1 is overly broad because it “encompasses *any method* of treating *any subject* who has a vitiligo lesion, if that method comprises (a) identifying a subject in need of treatment; and (b) administering to the subject a therapeutically effective amount of *any inhibitor* of IL-15 or the IL-15 receptor.” *Id.* at 25. Petitioner further asserts the ’505 patent “claims the use of any small molecule, antibody, peptide, or nucleic acid targeting

IL-15 or the IL-15 receptor, among other inhibitors, for treating vitiligo.”
Id. (citing Ex. 1001, claim 2, 2:6–8).

Petitioner argues that as compared to the broad functional limitations recited by the claims, the specification provides only one working example, “limited to using a specific, Fc-diminished rat/mouse chimeric antibody called ChMBC7 to target mouse CD122 (IL-2R β /IL-15R β), one half of the mouse $\beta\gamma$ receptor complex that conveys both IL-2 and IL-15 signaling.” *Id.* at 26 (citing Ex. 1002 ¶¶ 37, 66, 69, 71–72, 76, 86). Petitioner argues that “[b]ased only on its experiments using ChMBC7 to deplete the CD8+ T cells in a CD8+ T cell-induced lesion mice model, the ’505 patent would preempt the use of a very broad genus of inhibition pathways to treat vitiligo in any subject, including humans.” *Id.* (citing Ex. 1002 ¶ 85; Ex. 1004 ¶¶ 24–27, 42–45). Petitioner concludes that “the ’505 patent merely draws ‘a fence around the outer limits of a purported genus’ of treating vitiligo by administering any inhibitor of either IL-15 or the IL-15 receptor.” *Id.* at 28 (citing *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (en banc)).

3. Patent Owner’s position

Patent Owner responds that Petitioner mischaracterizes the claims as directed to a genus of chemical compounds and fails “to account for the specification’s extensive disclosure and information known in the art.” Prelim. Resp. 17–18.

First, Patent Owner argues that the claims “are directed to *novel methods* of treating vitiligo entailing identifying subjects and administering IL-15 inhibitors or IL-15R inhibitors to treat the subject’s vitiligo,” not a “vast genus of chemical compounds” as Petitioner asserts. *Id.* at 19 (citing Pet. 24; Ex. 1001, claim 1, 33:1–33:45; Ex. 1010, 15). Patent Owner

distinguishes the “present method-of-treatment claims” from claims directed to a genus of compounds. *See id.* at 19–21 (citing *Merck Sharp & Dohme Corp. v. Genentech, Inc.*, PGR2021-00036 (“Merck PGR”), Paper 10 at 20 (PTAB July 24, 2021) (denying institution and relying on *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629 (E.D. Tex. 2017) (“UroPep”), *aff’d*, 739 F. Appx 643 (Fed. Cir. 2018))”). Patent Owner argues that “the proper written description inquiry is, therefore, whether the specification describes the novel method of treatment, not whether it describes an ‘existing class of chemical compounds.’” *Id.* at 26 (citing *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006)).

Second, Patent Owner argues that the specification provides “extensive support for the claimed method.” *Id.* at 21–23. Patent Owner argues that the working examples describes “using an accepted mouse model demonstrating effective vitiligo treatment by inhibiting the IL-15 pathway.” *Id.* at 21 (citing Ex. 1001, 33:1–34:45; Fig. 6C, 8C, 8D). Patent Owner contends that “Petitioner endorses the reliability of the vitiligo mouse model” by relying on Harris in its obviousness arguments. *Id.* at 22 (citing Pet. 65–67, 68–69; *Grünenthal GmbH v. Antecip Bioventures II LLC*, PGR2019-00026, Paper 24, 43–44 (PTAB July 28, 2020)). Patent Owner further argues that the specification connects the mouse model to human disease and formulating dose ranges for human use. *Id.* at 22–23 (Ex. 1001, 5:40–45, 23:43–45).

Third, Patent Owner argues that the specification discloses IL-15 inhibitors and IL-15R inhibitors known in the art. *See id.* at 23–26. Specifically, Patent Owner argues that “the specification describes at least *nine* classes and 20 individual IL-15 inhibitors or IL-15R inhibitors that

would inhibit the same pathway shown by the *in vivo* working example to effectively treat vitiligo.” *Id.* (citing Ex. 1001, 7:34–8:37; Ex. 1002 ¶ 29). Patent Owner further argues that Petitioner’s exhibits disclose alternative inhibitors of IL-15 and IL-15R, including anti-IL-15 and anti-CD122 antibodies. *Id.* at 25 (citing Ex. 1018, 3; Ex. 1011, Abstract; Ex. 1012, 1).

4. Analysis

We understand Patent Owner’s argument to be that given the nature of the claims, the proper inquiry under the written description requirement (1) should be whether the disclosure in the specification shows that the inventors possessed the recited method of administering a therapeutically effective amount of an IL-15 or IL-15 receptor inhibitor to treat vitiligo lesions, and (2) does not turn on whether the patentees were in possession of the entire genus of IL-15 or IL-15 receptor inhibitors. *See* Prelim. Resp. 17–18.

We do not agree. The present case is similar to *University of Rochester v G.D. Searle & Co., Inc.*, 358 F.3d 916, 925–926 (Fed. Cir. 2004) where the patentee argued that holdings in precedential case law was limited to composition of matter claims, whereas the disputed claim was directed to a method. The CAFC held that argument to be “a semantic distinction without a difference.” *Univ. of Rochester*, 249 F.Supp.2d at 228. The Court held that “[r]egardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.” *Id.*

Here, the specification only provides a single working example using an Fc-diminished ChMBC7 mouse antibody to the beta subunit of the IL-15 receptor (i.e., IL-15R β) and a recitation of 20 individual inhibitors known in the prior art. *See* Ex. 1001, 7:34–8:37, 33:1–34:45. Patent Owner argues that this disclosure of a “large variety and number of species that ‘might be used to achieve’ vitiligo treatment is significantly more than what has been found sufficient” in other cases to support written description of a claimed method. *See* Prelim. Resp. 24 (citing *Ajinomoto Co. v. Int’l Trade Comm’n*, 932 F.3d 1342, 1359 (Fed. Cir. 2017); *UroPep*, 276 F. Supp. 3d at 649.). Patent Owner’s argument is unpersuasive for at least two reasons.

First, satisfaction of the written description standard is fact-intensive and is determined on a case-by-case basis; the Federal Circuit has declined to “set out any bright-line rules governing, for example, the number of species that must be disclosed to describe a genus claim.” *Ariad Pharm.*, 598 F.3d at 1351. Therefore, what may be satisfactory in one case may be insufficient in another case depending on the specific facts of each case, the language of the claims, and the complexity of the technology at issue.

Second, the ’505 patent fails to explain why the Fc-diminished ChMBC7 antibody would be representative of the different inhibitors recited in the specification (*see* Ex. 1001, 7:34–8:37), and never explains whether and why the enumerated molecules would be representative of all other compounds that can inhibit IL-15 or the IL-15 receptor. The specification also fails to explain adequately what structural features of small molecules, peptides, antibodies, or nucleic acids are necessary or sufficient to perform the claimed method. Nor is there evidence presented in the current record that such information was generally known in art.

We also note Patent Owner’s reliance on the Merck PGR’s holding and its underlying citation to the UroPep case. *Id.* But these cases are distinguishable because in those cases there was evidence that there were well-known classes of compounds known to perform the function recited in the claim methods that either the Petitioner failed to address (Merck PGR) or that presented a material issue of fact for resolution by the fact finder (UroPep). *See Merck*, PGR2021-00036, Paper 10 at 20; *Erfindergemeinschaft UroPep GbR*, 2016 WL 6138124, 15 (E.D. Tex. Oct. 21, 2016). Such facts are not presented on the current record.

In sum, based on the current record, Petitioner has shown that it is more likely than not that the ’505 patent does not provide sufficient description of the compounds that can be used to carry out the claimed methods—an essential element of every claim.

B. Alleged Lack of Enablement

Petitioner argues claims 1–5 are unpatentable for lack of enablement because the ’505 patent does not disclose how to make and use the full scope of treating vitiligo by inhibiting IL-15 or IL-15R across the genus claimed subjects. Pet. 48–63. Patent Owner disagrees. Prelim. Resp. 30–38. For the reasons discussed below, we find Petitioner has shown that at least one of the challenged claims is more likely than not unpatentable for lack of enablement.

1. Legal Principles

A patent’s specification must describe the invention and “the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.” 35 U.S.C. § 112(a). If a patent claims an entire class of processes, machines,

manufactures, or compositions of matter, the patent's specification must enable a person skilled in the art to make and use the entire class. *Amgen v. Sanofi*, No. 21-757, 598 U.S. [REDACTED] (May 18, 2023) (citing *Holland Furniture Co. v. Perkins Glue Co.*, 277 U. S. 245 (1928)). Specifically, the specification must enable the full scope of the invention without undue experimentation. *Wyeth and Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (The enablement requirement asks whether “the specification teach[es] those in the art to make and use the invention without undue experimentation.”). This is true even for method claims that are directed to a new use of an existing class of compounds. *Wyeth*, 720 F.3d at 1385.

A claim is not enabled where the specification discloses only a starting point for further iterative research in an unpredictable and poorly understood field. *Wyeth*, 720 F.3d at 1386; *Enzo Life Sciences v. Roche Molecular Sys.*, 928 F.3d 1340, 1345-46 (Fed. Cir. 2019) (where claims require both a particular structure and functionality, no enablement where specification fails to teach which of the many embodiments of the broad claims would exhibit that required functionality of being both hybridizable and detectable upon hybridization). In analyzing undue experimentation, we consider factors such as: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Wands*, 858 F.2d at 737.

2. *Petitioner's position*

Petitioner applies the *Wands* factors to argue that the specification does not enable a person skilled in the art to make and use the claimed invention. *See* Pet. 53–63. First, Petitioner addresses the nature of the invention and state of the art. *Id.* at 53–54. Petitioner asserts that “[t]he claims involve a complex invention of treating the autoimmune disease vitiligo across a broad genus of subjects . . . using inhibitors of complex and biologically unpredictable cytokine signaling pathways.” *Id.* (citing Ex. 1002 ¶ 84; Ex. 1004 ¶ 59).

Second, Petitioner addresses the breadth of the claims. *Id.* at 54–58. Petitioner asserts that “claims are extremely broad at least with respect to the (1) multiple genera of inhibitory pathways; (2) multiple genera of structures used for each those inhibitory pathways; and (3) the broad and disparate genus of subjects implicated. *Id.* at 54–55 (citing Ex. 1002 ¶¶ 33, 85–87, 93; Ex. 1004 ¶¶ 35–36, 57). For example, Petitioner asserts that the claims recite the use of any inhibitor of IL-15 or the IL-15 receptor, including its various subunits. *Id.* at 55. Petitioner asserts that “each of these four subgenera of inhibition is itself very broad, and inhibiting one subunit in a particular manner is not representative of the effects of inhibiting the other subunits or of inhibiting the same subunit in a different manner.” *Id.* (citing Ex. 1002 ¶ 86). Petitioner further asserts that the “claimed scope also is very broad because it encompasses using not only the few known compounds that are invoked (but never administered) in the specification, but also any other compounds that meet the claims’ functional requirements.” *Id.* at 56–57 (citing Ex. 1002 ¶¶ 31–33, 87).

Third, Petitioner addresses the amount of guidance and working examples in the specification. *Id.* at 59–61. Petitioner asserts that the

specification provides “sparse guidance” and a single example. *Id.* at 59 (citing Ex. 1002 ¶¶ 35, 62; Ex. 1004 ¶¶ 24–25, 33–34). Petitioner asserts that the single example discloses inhibiting CD122 (IL-2R/IL-15R β) with the ChMBC7 antibody, but does not disclose the sequence or structure of ChMBC7 nor the species of CD122 inhibition (IL-15 or IL-2). *Id.* at 59–60 (citing Ex. 1002 ¶¶ 37, 72, 89).

Fourth, Petitioner addresses the quantity of experimentation and the unpredictability of the art. *Id.* at 61–63. Petitioner asserts that “the only way to determine whether other forms of inhibition claimed by the ’505 patent would achieve the desired result even in the mouse would be to individually test them” through an iterative, trial-and-error process. *Id.* at 61 (citing Ex. 1002 ¶¶ 79–81, 90–92). Furthermore, Petitioner asserts that “the number of compounds implicated by the claims is so large that it is truly incalculable.” *Id.* at 62 (citing Ex. 1002 ¶¶ 83–87).

3. *Patent Owner’s position*

Patent Owner responds that the claims are directed to a new method of using of an existing class of compounds; a method that is enabled by the specification. Prelim. Resp. 30. Patent Owner argues that “Petitioner fails to establish that undue experimentation would be required to practice this method in view of the patent’s disclosures and a POSA’s knowledge.” *Id.* at 31 (citing *Bayer Healthcare LLC v. Baxalta Inc.*, 989 F.3d 964, 982 (Fed. Cir. 2021)). Patent Owner argues that the enablement inquiry should focus “on how much direction the patent provides for and whether it provides working examples supporting the *method of treatment*.” *Id.* (citing *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997); *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App’x 917, 922–23 (Fed. Cir. 2011)).

Patent Owner asserts that the specification is not limited to one working example, but instead includes “*six* working examples and **52** figures with data based on *in vivo* testing and human skin biopsies.” *Id.* at 33. Patent Owner asserts that “[t]he data demonstrates, among other things, that human vitiligo patients possess antigen-specific T_h17 cells that express IL-15R β /CD122, and IL-15 signaling can be targeted for effective vitiligo treatment.” *Id.* (citing Ex. 1001, Fig. 6C, 8B). Moreover, Patent Owner asserts that the Harris mouse model “described in the specification was considered representative of human vitiligo.” *Id.* at 34 (citing Ex. 1006, 6; Ex. 1001 5:40–45). Finally, Patent Owner argues that “neither Petitioner nor its declarants identified *any* IL-15 inhibitor or IL-15R inhibitor that would not treat vitiligo or any subject having vitiligo that could not be so treated.” *Id.* at 35 (citing *Alcon Rsch. Ltd. v. Barr Lab ’ys, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984)).

4. Analysis

Claims 1 and 3–5 of the ’505 patent recite methods for treating vitiligo using the entire class of IL-15 inhibitors or the entire class of IL-15 receptor inhibitors. *See* Ex. 1001, 44:12–26. Claim 2 is slightly narrower and limits the inhibitors of claim 1 to “a small molecule inhibitor, an antibody, a peptide inhibitor, or an inhibitory nucleic acid targeting IL-15 or the IL-15 receptor.” *Id.* at 44:18–20. The enablement of such broad “genus claims” was addressed recently by the Supreme Court in *Amgen v. Sanofi*, No. 21-757, 598 U.S. at [REDACTED] (May 18, 2023).

In the *Amgen* case, the patentee purported treating patients with high LDL cholesterol using antibodies that inhibit PCSK9—a naturally occurring protein that binds to and degrades LDL receptors responsible for extracting

LDL cholesterol from the blood stream. *Id.* at 4. The patents claimed an “the entire genus” of antibodies that (1) “bind to specific amino acid residues on PCSK9,” and (2) “block PCSK9 from binding to [LDL receptors].” *Id.* at 5. The patent specifications described the relevant antibody by its unique amino acid sequence and specifically identified the amino acid sequences of 26 antibodies that perform the two claimed functions. *Id.* The specification also described two methods for making other antibodies that performed the claimed binding and blocking function. *Id.* at 5–6.

The Court found that patentee’s specifications enabled the 26 exemplary antibodies identified by their amino acid sequences. *Id.* at 15. But found that the patent failed to enable the broader scope of the claims beyond those specifically disclosed exemplary antibodies. *Id.*

The facts of the present case are similar to the *Amgen* case. Here, Patent Owner attempts to claim an entire class of treatment based on the function of two classes of inhibitors: inhibitors of IL-15 and inhibitors of the IL-15 receptor. As the Supreme Court in the *Amgen* case stated “the more a party claims, the broader the monopoly it demands, the more it must enable.” *Id.* at 16. Patent Owner explains that the ’505 patent encompasses a “large variety and number of species that ‘might be used to achieve’ vitiligo treatment. Prelim. Resp. 25. In fact, the ’505 patent lists such divergent inhibitors as antibodies, benzoic acid derivatives, and small molecules such as cis-imidazoline analogs and trifluoroacetate. *See* Ex. 1001, 7:34–8:37.

Yet, unlike in *Amgen*, neither the claims nor the specification, provide any structural requirement for the claimed inhibitor. Nor does the ’505 patent explain how these inhibitors are related structurally so that such

inhibitors could be identified at an operational level. Specifically, the specification here does not provide (1) the sequence or structure that corresponds to the exemplary inhibitor, (2) a purported binding site on the exemplary inhibitor that would correspond to other inhibitors that fall within the scope of the claims, or (3) how the exemplary inhibitor binding to/blocking of IL-15 receptor is representative of the binding/blocking by the 20 inhibitors listed in the specification. *See* Ex. 1001, 7:34–8:37.

Moreover, the '505 patent discloses that the beta subunit “is a shared receptor for both IL-2 and IL-15.” *Id.* at 6:3–4. The specification, however, does not explain how the disclosed antibody targets only the IL-15 receptor signaling pathway or why the invention is limited to only IL-15 and IL-15 receptor and not IL-2.

Additionally, unlike *Amgen* where the specification provided at least two purported methods for making the claimed antibodies, the '505 patent does not provide a single disclosure on how to make a claimed inhibitor. Patent Owner attempts to avoid the “how to make” requirement by stating that the claims are directed towards a method of treatment and providing one example of treatment in the specification. *See* Ex. 1001, 33:1–34:45. Yet, the claims specifically recite “an inhibitor of IL-15 or the IL-15 receptor.” *See id.* at 44:15–16. The specification’s listing of nine classes and 20 individual compounds that could be used as an inhibitor of IL-15 or the IL-15 receptor (with references where information about each inhibitor may be located) is unsatisfactory because these references do not appear to be incorporated by reference, nor does these references fully explain how to make each inhibitor of IL-15 or the IL-15 receptor. *See* Ex. 1001, 7:34–8:4. In order to satisfy the enablement requirement, Patent Owner must describe with particularity how to make and use such an inhibitor. *Amgen*, at 13. But

it fails to do so. Accordingly, we find Petitioner has shown that it is more likely than not that claims 1–5 are unpatentable for lack of enablement.

C. Alleged Obviousness of Claims 1–5 in view of Harris and Xing

Petitioner argues claims 1–5 are unpatentable as obvious over Harris and Xing. Pet. 64–74. Patent Owner disagrees. Prelim. Resp. 38–43. For the reasons discussed below, we find Petitioner has not shown that at least one of the challenged claims is more likely than not unpatentable as obvious in view of Harris and Xing.

1. Harris (Ex. 1006)

Harris discloses “an adoptive transfer mouse model of vitiligo using melanocyte-specific CD8⁺ T cells, which recapitulates the human condition by inducing epidermal depigmentation while sparing the hair.” Ex. 1006, 1869. Harris discloses that previous observations support “a direct role for cytotoxic T lymphocytes in melanocyte destruction in human vitiligo.” *Id.*

In view of the mouse model, Harris discloses that “depigmentation requires IFN- γ , which induces the local accumulation of melanocyte-specific CD8⁺ T cells within the skin.” *Id.* at 1870. Moreover, “[t]he ability of antibody-mediated neutralization of IFN- γ to prevent CD8⁺ T-cell accumulation in the skin as well as depigmentation in this model suggests a therapeutic potential for this approach.” *Id.*

2. Xing (Ex. 1007)

Xing discloses that cytotoxic CD8⁺ T cells are implicated in alopecia areata (“AA”), a common autoimmune disease that damages the hair follicles resulting in hair loss. Ex. 1006, 1. Xing uses a mouse model to test the etiology of AA. For example, Xing discloses that transferring cytotoxic CD8⁺ T cells from AA mice to healthy recipients induced AA in the health recipients. *Id.* at 2. As to the underlying cytokines involved in

AA, Xing “detected a marked upregulation of [IL-15 and its chaperone receptor IL-15R α] in AA hair follicles in both human and mouse AA and found IL-15R β expressed in infiltrating CD8⁺ T cells in humans.” *Id.* at 2–3.

Xing discloses using an AA graft model to test targeted therapies. *Id.* at 4. Of the tested therapies, Xing discloses that systemically administered IL-15RB blocking antibodies “prevented AA in grafted mice [and] blocked the accumulation of CD8⁺NKG2D⁺ T cells in the skin.” *Id.* at 4, Fig. 2g–2i. “For anti-IL-15-R β experiments, i.p. injections of rat isotype control IgG or anti-IL-15R β antibody (Biolegend, clone TM- β 1) (200 μ g in 100 μ l PBS) were administered two times weekly for 12 weeks.” *Id.* at 8. Xing reports that neither IL-2 nor IL-15R β 1 “blocking antibodies given alone were able to reverse established AA.” *Id.* at 4.

Xing further discloses treating AA by administering JAK inhibitors “which signal downstream of a wide range of cell surface receptors.” *Id.* at 4–5. For example, both systemically and topically administering JAK inhibitors resulted in hair regrowth in AA mice. *Id.* at 6.

3. *Legal Principles*

A patent claim is unpatentable as obvious under 35 U.S.C. § 103(a) if “the differences between” the claimed subject matter and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a); *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The legal conclusion of obviousness is resolved on the basis of underlying factual determinations, including: (1) “the scope and content of the prior art,” (2) “differences between the prior art and the claims at issue,” (3) “the level of ordinary skill in the pertinent

art,” and (4) any “secondary considerations,” or objective indicia, of nonobviousness. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17–18 (1966). These underlying factual determinations “must be considered by the trier of fact” in an obviousness analysis. *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998).

“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). The reason for this is that “[w]hile the Supreme Court made clear that a mechanical application of the teaching-suggestion-motivation test, requiring an explicit teaching in the prior art, is inappropriate, ‘[w]e must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention.’” *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1343, 1368 (Fed. Cir. 2012) (quoting *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008)); *see also* *KSR*, 550 U.S. at 421 (“A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.”); *Graham*, 383 U.S. at 36 (warning against a “temptation to read into the prior art the teachings of the invention in issue” and instructing courts to “‘guard against slipping into use of hindsight’” (citation omitted)). Thus, “[c]are must be taken to avoid hindsight reconstruction by using ‘the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.’” *Grain Processing Corp. v. Am.-*

Maize Prods. Co., 840 F.2d 902, 907 (Fed. Cir. 1988) (quoting *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012 (Fed. Cir. 1983)).

4. *Analysis of Independent Claim 1*

Petitioner contends that Harris teaches the same mouse model used in the '505 patent, wherein the mouse is a subject who has a vitiligo lesion and needs treatment. Pet. 70–71 (citing Ex. 1001 ¶¶ 107–108). Petitioner contends that Xing teaches administering a therapeutically effective amount of an inhibitor of the IL-15 receptor to a subject to treat autoimmune skin lesions mediated by CD8⁺ T cells. *Id.* at 70 (citing Ex. 1007, 1, 4, 8, Fig. 2h, 2i). Specifically, Petitioner contends that Xing teaches administering an anti-IL-15R β (CD122) antibody (TM- β 1) that “reduces the number of autoreactive CD8⁺ T cells in the skin to nearly undetectable levels.” *Id.* According to Petitioner, Xing uses a comparable amount of antibody “to that used in the '505 patent (200 μ g, 2x weekly vs. 100 μ g 3x weekly),” and Xing describes a “reduction in the population of autoreactive CD8⁺ T cells [that] is comparable (if not more dramatic) than that disclosed in the '505 patent with its mouse CD122 antibody ChMBC7.” *Id.* at 70–71 (citing Ex. 1007, 8; Ex. 1001, 29:22–23, 33:26–35, Fig. 6D). Petitioner asserts that “a POSA would have expected TM- β 1 administration as described by Xing to achieve similar reductions in depigmentation as provided in the '505 patent with ChMBC7.” *Id.* at 71 (citing Ex. 1002 ¶ 109).

Patent Owner contends that Xing does not teach successful treatment with an anti-IL-15R antibody. *See* Prelim. Resp. 42–43. Patent Owner argues that, instead, “Xing reports that the mouse CD122 antibody ‘TM- β 1’ (anti-IL-15R β) (on which Petitioner relies for purported obviousness (Pet. 64–74)) was *not* “able to reverse established AA.” *Id.* at 43 (citing Ex. 1007, 4). Recalling that JAK is downstream from IL-15, Patent Owner

further argues that Xing's durable treatment with JAK inhibitors was reported by Harris-2016⁶ to not provide durable repigmentation and hair regrowth in a subject with concurrent vitiligo and AA during treatment with oral ruxolitinib. *Id.* at 43 (citing Ex. 1032, 1; Ex. 1004 ¶ 46).

Patent Owner further argues that Petitioner "fails to address objective evidence of nonobviousness reported in the specification, asserted by Patent Owner during prosecution, and relied upon by the Examiner in allowing the '505 patent." *Id.* at 38–39. Specifically, Patent Owner contends that "*the inventors of the present application surprisingly discovered that treatment with an IL-15R β blocking antibody effectively depleted autoreactive T_h1, inhibited their function, and resulted in durable reversal of disease in mice.*" *Id.* at 40–41 (citing Ex. 1010, 38).

Based on the express disclosure of Harris and Xing, we agree with Petitioner that Harris and Xing each appear to describe individual limitations of the challenged claims. Specifically, Harris discloses a mouse model with vitiligo lesions. *See* Ex. 1006. Xing, on the other hand, teaches administering antibodies to IFN- γ , IL-2, and IL-15R β to a mouse model with alopecia areata. *See* Ex. 1007, Abstract. Additionally, based on the current record, there is insufficient evidence regarding Patent Owner's objective indicia of obviousness. Therefore, any analysis of such objective indicia will benefit from a complete record that we invite the parties to develop.

Additionally, due to the incomplete record at this stage of the proceeding, we invite the parties to further develop its arguments as to whether (1) the disclosure in Xing as discussed by Patent Owner impacts the

⁶ John E. Harris et al., 74(2) J. Am. Acad. Dermatol. 370–371. Ex. 1032 ("Harris-2016").

enablement of the '505 patent and (2) the claims encompass transient and/or sustained treatment given that the claims themselves do not recite durability of treatment. Nonetheless, as explained below, based on the current record Petitioner fails to demonstrate that a person of ordinary skill in the art would have had reason to combine the disparate teachings of these two references to arrive at the claimed invention without the benefit of hindsight analysis.

5. Reasons to Combine the Teachings of Harris and Xing

Petitioner contends it would have been obvious to a person of ordinary skill in the art to combine the teachings of Harris with that of Xing for several reasons. *See* Pet. 64–69. First, Petitioner asserts that both Harris and Xing describe mouse models for autoimmune diseases resulting in lesions that depend on CD8⁺ T cells. *Id.* at 64–65 (citing Ex. 1002 ¶¶ 99, 103–106; Ex. 1004 ¶¶ 33–36). Petitioner argues that both Harris and Xing describe treating autoimmune disease by “depleting those same CD8⁺ cytotoxic T cells.” *See id.* at 65 (Ex. 1002 ¶¶ 95–97). Petitioner then argues that “because Harris expressly suggests that preventing autoreactive CD8⁺ T cell accumulation in the skin has therapeutic potential for treating vitiligo,” a “POSA would have had good reason to administer Xing’s CD122 [IL-15Rβ] antibody (i.e., TM-β1) in Harris’s mouse model of vitiligo.” *Id.* at 67 (citing Ex. 1002 ¶ 99).

Second, Petitioner asserts that “POSA would have been motivated to treat the mice lesions with TM-β1 to reduce the autoreactive CD8⁺ Trm cells in the skin that cause the melanocyte destruction in the mouse model, thereby reducing effector T cell-mediated lesions.” *Id.* at 68. Petitioner argues that “[a]ccordingly, a POSA had good reason to apply Xing’s mouse CD122 antibody to the epidermis of the vitiligo skin lesions in Harris’s mouse model, by subcutaneous injection, at a therapeutically effective dose

as determined through routine dose ranging studies.” *Id.* (citing Ex. 1002 ¶¶ 101–102). Finally, Petitioner asserts that “applying Xing’s antibody to Harris’s mouse model is further supported by prior art (e.g., Cheuk)⁷ teaching that [Trm cells] are activated by IL-15 in vitiligo, that JAK/STAT inhibition downstream of CD122 reversed vitiligo lesions.” *Id.* at 69 (citing Ex. 1027, 297).

At this stage of the proceeding, we are not persuaded by Petitioner’s arguments. Rather, we find Petitioner’s reasons to combine the references constitute impermissible hindsight reconstruction where the inventor’s own disclosure, rather than the prior art, supplies the rationale to combine the references. Although Petitioner articulates a reason why a person of ordinary skill in the art would combine Harris and Xing, this purported reasoning does not appear to comport with the disclosure of Xing itself.

Xing postulates that IFN- γ produced by CD8 T cells leads to the collapse of immune privilege in hair follicles and induces additional production of IL-15 creating a feed-forward loop that promotes type I cellular autoimmunity. *See* Ex. 1007, 6. Petitioner’s rationale does not account for the increased IL-15 production or the cellular autoimmunity and how that would affect an ordinarily skilled artisan’s decision to use TM- β 1 to reduce the autoreactive CD8⁺ Trm cells in the skin. Rather, Petitioner’s challenge appears to be based on a mosaic of prior art disclosures cobbled together using the teachings of the ’505 patent, which is the very definition of impermissible hindsight analysis. *See KSR Intern. Co. v. Teleflex Inc.*, 55 U.S. 398, 421 (2007) (“A factfinder should be aware, of course, of the

⁷ Stanley Cheuk et al., *CD49a Expression Defines Tissue-Resident CD8⁺ T Cells Poised for Cytotoxic Function in Human Skin*, 46 *Immunity* 287–300. Ex. 1027 (“Cheuk”).

distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.”); *see also In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) (citing *In re Gorman*, 933 F.2d 982, 987 (Fed. Cir. 1991) (“It is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.”)).

V. CONCLUSION

Based on the arguments in the Petition and the Preliminary Response, and the evidence of record, we determine that Petitioner has sufficiently demonstrated that the ’505 patent is eligible for post-grant review. Additionally, we determine that Petitioner has demonstrated, on the current record, that it is more likely than not that at least one claim of the ’505 patent is unpatentable. Thus, we institute a post-grant review of all challenged claims on all the challenges presented.

Our factual findings, conclusions of law, and determinations at this stage of the proceeding are preliminary, and based on the evidentiary record developed thus far. At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim. Our final decision will be based on the record as fully developed during trial.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324, a post-grant review is hereby instituted as to all challenged claims 1–5 of U.S. Patent No. 11,278,505 on all the challenges asserted in the Petition; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 324(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial, the trial commencing on the entry date of this Decision.

PGR2023-00014
Patent 11,278,505 B2

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