

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTAS PHARMACEUTICALS LTD.,
Petitioner,

v.

ATOSSA THERAPEUTICS, INC.,
Patent Owner.

PGR2023-00043
Patent 11,572,334 B2

Before SHERIDAN K. SNEDDEN, TINA E. HULSE, and
JAMIE T. WISZ, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

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

I. INTRODUCTION

Intas Pharmaceuticals Ltd. (“Petitioner”) filed a Petition requesting a post-grant review of claims 1–22 of U.S. Patent No. 11,572,334 B2 (Ex. 1001, “the ’334 patent”). Paper 1 (“Pet.”). Atossa Therapeutics, Inc. (“Patent Owner”) filed a Preliminary Response. Paper 7 (“Prelim. Resp.”). With our authorization, Petitioner filed a Reply to Patent Owner’s Preliminary Response. Paper 10 (“Reply”).

We have authority under 35 U.S.C. § 324(a), which provides that a post-grant review may not be instituted “unless . . . the information presented in the petition . . ., 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.” Upon considering the arguments and evidence presented by the parties, we determine Petitioner has demonstrated that it is more likely than not that at least one of the claims challenged in the Petition is unpatentable.

A. *Real Parties-in-Interest*

Petitioner identifies itself and Accord Healthcare, Inc. (a U.S. subsidiary of Petitioner) as the real parties-in-interest to this proceeding. Pet. 1. Petitioner also states that “[o]ther parties who may be interested in the outcome of this PGR include the National Cancer Institute/National Institutes of Health Clinical Center, Eli Lilly and Company, Pfizer Inc., Jina Pharmaceuticals Inc., Cheiljedang Corp., Alchem Laboratories Corporation, and Lambda Therapeutic Research Limited.” *Id.*

Patent Owner identifies itself as the real party-in-interest. Paper 5, 1.

B. *Related Proceedings*

Petitioner states that there are no current related matters. Pet. 1. Patent Owner states that the ’334 patent is not involved in any related

litigation matters, but identifies various patent applications from which the '334 patent claims the benefit. Paper 5, 1.

C. The '334 Patent

The '334 patent, entitled “Methods for Making and Using Endoxifen,” was issued on February 7, 2023, and claims the benefit of several continuation and provisional applications, the earliest of which was filed September 11, 2017. Ex. 1001, codes [54], [63], [64]. According to the Abstract, the '334 patent “provides industrially scalable methods of making (Z)-endoxifen or a salt thereof, crystalline forms of endoxif[e]n, and compositions comprising them,” as well as “methods for treating hormone-dependent breast and hormone-dependent reproductive tract disorders.” *Id.*, Abstract.

Endoxifen is the active metabolite of tamoxifen, a selective estrogen receptor modulator that is used to treat endocrine responsive breast cancer, i.e., hormone-dependent or hormone-sensitive breast cancer. *Id.* at 1:63–2:9. Endoxifen has two isomers, (E)-endoxifen and (Z)-endoxifen. According to the Specification, “[i]t is widely accepted that (Z)-endoxifen is the main active metabolite responsible for the clinical efficacy of tamoxifen.” *Id.* at 2:36–38. “Several cytochrome P450 (CYP) mutations have been proposed to cause reduced conversion of tamoxifen to its active metabolite, endoxifen, and reduce tamoxifen efficacy and increase resistance to the drug,” but “changes in the CYP genotype do not fully explain the tamoxifen resistance and the reduced endoxifen levels observed in some subjects.” *Id.* at 2:7–22. Accordingly, the Specification states that several alternatives to tamoxifen are being developed for treating breast cancer. *Id.* at 2:23–24.

The Specification states that although hydrochloride and citrate salts of endoxifen are known in the art and being evaluated for metastatic cancer,

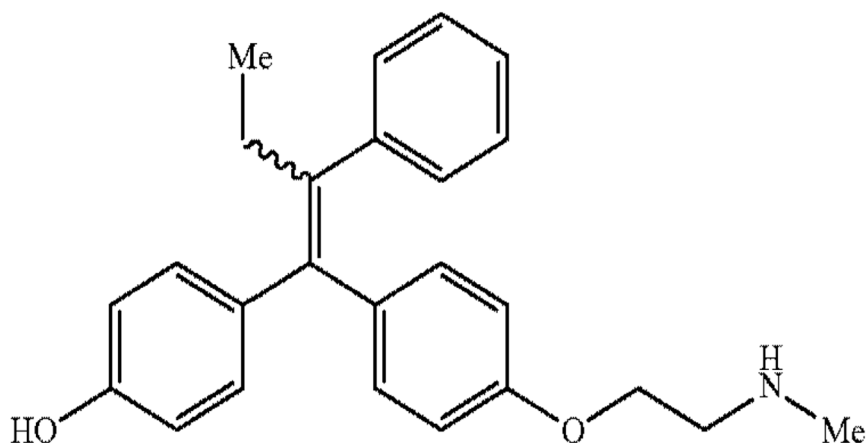
“there remains [an] unmet medical need for new compositions and methods for the treatment and/or prevention of hormone-dependent breast and reproductive tract (gynecologic) disorders.” *Id.* at 2:39–53.

D. Illustrative Claim

Petitioner challenges claims 1–22 of the '334 patent, of which claims 1 and 15 are independent. Claims 1 and 15 are illustrative and are reproduced below:

1. An oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):

Formula (III)

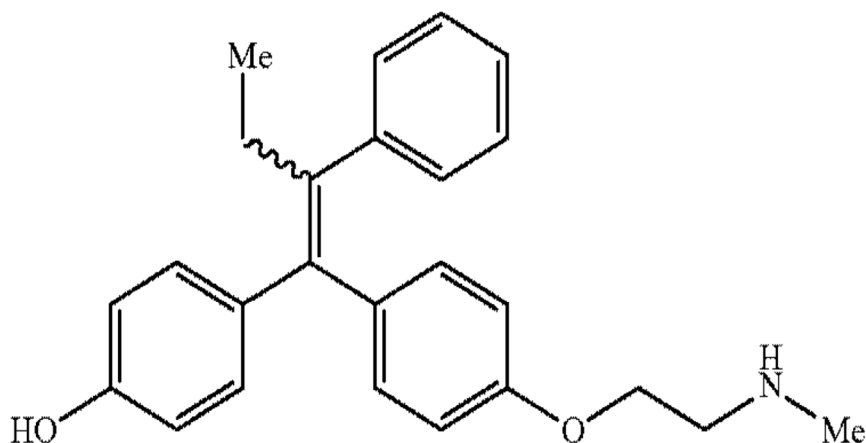


wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.

Ex. 1001, 98:13–30.

15. A method of delivering (Z)-endoxifen to a subject, the method comprising administering to the subject an oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):

Formula (III)



wherein at least 90% by weight of the compound of Formula (III)
is (Z)-endoxifen.

Id. at 99:7–26.¹

E. The Asserted Grounds of Unpatentability

Petitioner challenges claims 1–22 of the '334 patent based on the grounds set forth in the table below.

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1, 2, 4, 15, 20–22	102	Ahmad ²
1, 2, 4, 15, 20–22	103	Ahmad
5–8, 16, 17	103	Ahmad, Cole ³

¹ We note that the Petition fails to recite claim 15 correctly. *Compare* Pet. 7–8 with Ex. 1001, claim 15. We also note several obvious citation errors to Dr. Davies’s Declaration. *See, e.g.*, Pet. 29 (citing Ex. 1020 ¶ 54, which should apparently be Ex. 1020 ¶ 59); Pet. 30 (citing Ex. 1020 ¶ 59, which should apparently be Ex. 1020 ¶ 64). We caution Petitioner to check its citations carefully, as we decline to search the record to determine the proper support for Petitioner’s arguments.

² Ahmad et al., US 9,333,190 B2, issued May 10, 2016 (Ex. 1003, “Ahmad”).

³ Cole, et al., *Enteric coated HPMC capsules designed to achieve intestinal targeting*, 231 INTL. J. PHARMACEUTICS 83–95 (2002) (Ex. 1008, “Cole”).

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
3	103	Ahmad, Benameur ⁴
9–13	103	Ahmad, Stegemann ⁵ , HPE ⁶
14, 18, 19	103	Ahmad, Ahmad 2010, ⁷ Ahmad 2012 ⁸

Petitioner also relies on the Declaration of Jason McConville, Ph.D. (Ex. 1020). Patent Owner relies on the Declaration of Stephen Graham Davies, D. Phil. (Ex. 2001).

II. ELIGIBILITY FOR POST-GRANT REVIEW

We must first determine whether the '334 patent is eligible for post-grant review. Section 6(d) of the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (Sept. 16, 2011) (“AIA”) sets forth the post-grant review provisions, which apply only to patents subject to the first-inventor-to-file provisions of the AIA. AIA § 6(f)(2)(A) (stating the provisions of Section 6(d) “shall apply only to patents described in section 3(n)(1)”). Post-grant reviews are only available for patents that issue from applications

⁴ Hassan Benameur, *Capsule Technology: Enteric capsule drug delivery technology – Achieving Protection Without Coating*, 15 DRUG DEVELOPMENT & DELIVERY 34–37 (June 2015) (Ex. 1010, “Benameur”).

⁵ Stegemann et al., *Hard gelatin capsules today – and tomorrow*, Capsugel Library 3–23 (2d ed., 2002) (Ex. 1011, “Stegemann”).

⁶ HANDBOOK OF PHARMACEUTICAL EXCIPIENTS (Raymond C. Rowe et al. eds., 5th ed. 2006) (Ex. 1012, “HPE”).

⁷ Ahmad et al., *Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability, and Systemic Bioavailability in Healthy Human Subjects*, 88 CLINICAL PHARMACOLOGY & THERAPEUTICS 814–17 (Dec. 2010) (Ex. 1006, “Ahmad 2010”).

⁸ Ahmad et al., *Endoxifen for breast cancer: Multiple-dose, dose-escalation study characterizing pharmacokinetics and safety in metastatic breast cancer patients*, 30 J. CLINICAL ONCOLOGY 3089 (2012 ASCO Annual Meeting Abstract) (May 20, 2012) (Ex. 1007, Ahmad 2012).

“that contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date . . . on or after” March 16, 2013. AIA § 3(n)(1). Moreover, “[a] petition for a post-grant review may only be filed not later than the date that is 9 months after the date of the grant of the patent or of the issuance of a reissue patent (as the case may be).” 35 U.S.C. § 321(c). Petitioner has the burden of demonstrating eligibility for post-grant review. *See Mylan Pharms. Inc. v. Yeda Res. & Dev. Co.*, PGR2016-00010, Paper 9 at 10 (PTAB Aug. 15, 2016).

The ’334 patent claims the benefit of several provisional applications, the earliest of which was filed September 11, 2017. Ex. 1001, code (60). For purposes of the Petition, Petitioner applies September 11, 2017, as the date of the invention (Pet. 5), which Patent Owner does not dispute. Thus, for purposes of this proceeding, the ’334 patent claims have an effective filing date after March 16, 2013.

Moreover, the ’334 patent issued on February 7, 2023, and the Petition was filed on August 18, 2023. Ex. 1001, code (45); Pet. 2. Thus, the Petition was filed less than nine months after the date the patent was granted.

We, therefore, determine that the challenged claims are eligible for post-grant review, and Patent Owner does not assert otherwise. *See generally* Prelim. Resp.

III. ANALYSIS OF GROUNDS

A. *Person of Ordinary Skill in the Art*

Petitioner asserts that a person of ordinary skill in the art (“POSA”) would be “someone with a Ph.D. in pharmaceutical sciences or a closely related field and experience in research related to pharmaceutical dosage

forms or someone with at least a Bachelor's or Master's degree in pharmaceutical sciences and three to five years of practical experience in formulating drugs.” Pet. 9 (citing Ex. 1020 ¶ 27).

Patent Owner argues that Petitioner's definition of a person of ordinary skill in the art “ignores the complex chemistry at the center of the '334 invention and should be rejected.” Prelim. Resp. 12. Patent Owner contends that a person of ordinary skill in the art would have had “a graduate degree in organic chemistry, medicinal chemistry, pharmaceutical chemistry, or a related field, and four to six years of experience in the synthesis, purification, and design of pharmaceutical compounds and derivatives thereof as of the date of the claimed inventions” and “would have worked with a team of professionals with training in related disciplines, such as pharmacology, pharmacokinetics, formulation, drug discovery and/or drug development as of the date of the claimed inventions.” *Id.* at 12–13 (citing Ex. 2001 ¶¶ 42–43).

Although Patent Owner's definition of a POSA includes an additional four to six years of experience, we do not discern a substantive difference between the parties' respective definitions for purposes of our analysis. Both definitions provide for a highly skilled POSA with experience in formulating drugs, and our Decision would be unchanged whether we applied Petitioner's definition or Patent Owner's.

Nevertheless, on this record, we adopt Patent Owner's definition as it is consistent with the level of ordinary skill in the art as reflected by the prior art in this proceeding. *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 for testimony is not shown” (*quoting Litton Indus. Prods., Inc. v. Solid*

State Sys. Corp., 755 F.2d 158, 163 (Fed. Cir. 1985))). To the extent the parties dispute the level of ordinary skill and its impact on the analysis of the challenged claims, we encourage the parties to address this issue further during trial.

Moreover, at this stage of the proceeding, we find that Dr. McConville and Dr. Davies are both qualified to opine from the perspective of a skilled artisan as both are persons of at least ordinary skill in the art, based on either party's definition. *See* Ex. 1020 ¶¶ 3–15; Ex. 2001 ¶¶ 4–11.

B. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claims in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 42.200(b) (2021). 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 “all terms should be given their plain and ordinary meaning,” but contends “[t]he term ‘enteric capsule’ in independent claim 1 means a capsule ‘with one or more enteric coating agent,’ or an intrinsically enteric capsule that does not need an additional coating to provide the enteric property.” Pet. 9–10 (citing Ex. 1020 ¶¶ 28–29).

Patent Owner states that it

agrees that the plain and ordinary meaning of “enteric capsule” is appropriate, but disagrees with the suggested definition, which omits the following passage from the specification: “to control or delay disintegration and absorption of the compositions comprising endoxifen or salts thereof in the gastrointestinal tract and thereby provide a sustained action over a longer period of time.”

Prelim Resp. 11 (citing Ex. 1001, 39:22–26).

Patent Owner contends “Petitioner’s proposed construction of ‘enteric capsule’ does not have any impact on its failure to meet its burden at this institution stage. Thus, the Board does not need to construe this or any other claim term in denying the Petition.” *Id.* at 11–12.

Because Petitioner’s construction—with Patent Owner’s addition—is consistent with the Specification, we apply that construction of “enteric capsule” in this proceeding. *See* Ex. 1001, 39:22–26.

We also note that Patent Owner appears to construe the claim phrase “the compound of Formula (III) is (Z)-endoxifen” to be limited to the free base form of (Z)-endoxifen. *See, e.g.*, Prelim. Resp. 2 (“The ’334 patent claims enteric coated capsule formulations containing at least 90% (Z)-endoxifen *free base*, methods of delivering such formulations to a patient resulting in specific pharmacokinetic parameters, and methods of treating hormone-dependent breast and reproductive tract disorders.”) (emphasis added). The Specification, however, expressly states “‘a compound’, such as compounds of . . . Formula (III) . . . include the polymorphic salt, free base, co-crystal, and solvate forms of the formulas and/or compounds disclosed herein.” Ex. 1001, 12:48–52; *see also id.* at 12:52–59 (stating “‘compounds of Formula (III)’ . . . include . . . the free base of the compounds of Formula (III), and/or the gluconate salts as described herein”).

To the extent there is any dispute as to the scope of “the compound of Formula (III) is (Z)-endoxifen” in the claims, the parties should address that construction at trial. For purposes of this Decision, we adopt the express definition set forth in the Specification. That is, we construe “the compound of Formula (III) is (Z)-endoxifen” to include the polymorphic salt, free base, co-crystal and solvate forms of (Z)-endoxifen. *See* Ex. 1001, 12:48–59.

We determine it is unnecessary to expressly construe any other claim terms for purposes of this 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. Ground 1: Alleged Anticipation by Ahmad

In Ground 1, Petitioner asserts claims 1, 2, 4, 15, and 20–22 of the ’334 patent are anticipated by Ahmad. Pet. 28–35. Patent Owner opposes. Prelim. Resp. 30–40.

Having considered the evidence and argument presented by the parties, we determine Petitioner has shown it is more likely than not that the challenged claims are anticipated by Ahmad.

1. Ahmad (Ex. 1003)

Ahmad is a U.S. patent entitled “Endoxifen Compositions and Methods,” which issued on May 10, 2016. Ex. 1003, codes (54), (45). Ahmad describes “compositions containing endoxifen, formulations and liposomes of endoxifen, methods of preparation of such agents and formulations, and use of such agents and formulations for the treatment of breast cancer and other diseases susceptible to endoxifen.” Ex. 1003, Abstract. Ahmad explains that “[r]ecently, endoxifen has been shown to be anti-estrogenic in breast cancer cells and to be more potent than Tamoxifen,” which is a widely-used, anti-estrogenic drug prescribed for long-term, low-dose therapy of breast cancer. *Id.* at 1:64–66; *see also id.* at 1:36–39.

Ahmad describes methods of preparing a composition containing a therapeutically active amount of endoxifen in its free base or salt form. *Id.* at 2:21–26. Ahmad explains that the endoxifen can be crystallized and/or

chromatographically treated to produce a purified preparation that contains predominantly E-isomer, predominantly Z-isomer, or a mixture of E- and Z-isomers of endoxifen. *Id.* at 3:55–61, 11:17–23 (“The separation of E- and Z-isomers of endoxifen in the present invention can be done, e.g., by crystallization, or purification by liquid chromatography (LC), or high pressure liquid column chromatography (HPLC).”). In some embodiments, the composition comprises a tablet or a filled capsule that optionally comprises an enteric coating material. *Id.* at 3:62–4:44.

Ahmad states that “[o]ne object of the present invention is to provide E-endoxifen or Z-endoxifen with at least 80% purity, such as at least 90% pure or at least 95% pure or at least 98% pure or at least 99% pure or at least 100% pure.” *Id.* at 12:14–17.

2. *Analysis*

Anticipation requires that “each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citation omitted). “To establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.’” *Id.* (citation omitted). Moreover, to anticipate, a prior art reference must “disclose[] within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim.” *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008). The reference must also be enabling, which requires that the reference “teach a skilled artisan—at the time of filing—to make or carry out what it discloses in relation to the claimed invention without undue experimentation.” *In re Morsa*, 803 F.3d

1374, 1377 (Fed. Cir. 2015) (citing *In re Antor Media Corp.*, 689 F.3d 1282, 1289–90 (Fed. Cir. 2012)). The reference, however, “need not enable the claim in its entirety, but instead the reference need only enable a single embodiment of the claim.” *Id.*

a) Independent Claims 1 and 15

Regarding claim 1, Petitioner asserts that Ahmad discloses each limitation of the claim. Pet. 28–32 (citing Ex. 1020 ¶¶ 58–68). For example, Petitioner asserts that Ahmad discloses “the endoxifen composition . . . of Formula (III)” as Ahmad “depicts the same chemical structure” (albeit depicted slightly differently). *Id.* at 28–29 (citing Ex. 1003, cover, Fig. 1). Petitioner also asserts that Ahmad discloses “at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen” because Ahmad teaches that “[o]ne object of the present invention is to provide E-endoxifen or Z-endoxifen with at least 80% purity, such as at least 90% pure.” *Id.* at 29–30 (citing Ex. 1003, 12:14–17, 2:24–40, 3:55–61; Ex. 1020 ¶¶ 62–64). Ahmad further teaches that the purification can be accomplished using crystallization or chromatography. *Id.* at 30 (citing Ex. 1003, 11:17–23). To the extent Patent Owner argues the 90% limitation is not enabled, Petitioner asserts that forming such pure formulations was known in the art, as taught by Liu⁹ and Song.¹⁰ *Id.* at 30 (citing Ex. 1004 ¶ 76; Ex. 1005 ¶¶ 92–94, 97–98). Finally, Petitioner asserts that Ahmad discloses “encapsulated in an enteric capsule” because Ahmad teaches that its formulations may be

⁹ Liu et al., WO 2017/070651 A1, published Apr. 27, 2017 (Ex. 1004, “Liu”). Liu teaches a process for preparing (Z)-endoxifen “with isomeric purity of 99% (HPLC analysis).” Ex. 1004 ¶ 76.

¹⁰ Song et al., WO 2012/050263 A1, published Apr. 19, 2012 (Ex. 1005, “Song”). Song teaches a method of “Z-form endoxifen of at least 99% purity.” Ex. 1005, Abstract.

“encapsulated in enteric-coated capsules to protect it from acids in the stomach.” *Id.* at 30 (citing Ex. 1003, 18:19–21; Ex. 1020 ¶¶ 65–66).

Regarding claim 15, Petitioner asserts that claim 15 is anticipated by Ahmad for the same reasons as claim 1, because “[w]hile claim 15 is independent, it recites a ‘method of delivering (Z)-endoxifen to a subject, the method comprising administering to the subject’ a formulation that is identical to the oral formulation of claim 1.” Pet. 33 (citing Ex. 1020 ¶ 75; Ex. 1003, 18:1–7 (disclosing administering orally)).

In its Preliminary Response, Patent Owner does not assert that Ahmad fails to disclose each limitation of claim 1. Rather, Patent Owner argues that Ahmad does not anticipate claims 1 and 15 because it fails to enable a POSA to make 90% pure (Z)-endoxifen. *See* Prelim. Resp. 32 (citing Ex. 2001 ¶¶ 98–108). Specifically, Patent Owner asserts that Ahmad fails to teach how to separate the (E)- and (Z)-isomers to generate 90% pure (Z)-endoxifen. *Id.* at 33. Patent Owner argues that Ahmad merely recites “generic lists of solvents, acids, fractional crystallization, and column chromatography conditions.” *Id.* (citing Ex. 1003, 11:24–12:13). Moreover, Patent Owner asserts that a POSA following the synthesis examples in Ahmad “would most likely generate a roughly 1:1 ratio of (E):(Z) isomers, or a 50% pure (Z)-endoxifen mixture.” *Id.* at 34 (citing Ex. 1003 ¶¶ 109–111). Patent Owner also argues that the file history of Ahmad suggests that the inventors never “made a formulation comprising 90% (Z)-endoxifen of any form, let alone 90% (Z)-endoxifen free base, as contemplated by the ’334 patent.” *Id.* at 36–37 (citing Ex. 2010, 54, 96–98). Finally, Patent Owner asserts that Petitioner’s reliance on Liu and Song to support Petitioner’s argument that forming 90% pure (Z)-endoxifen was known in the art is misplaced. *Id.* at 37. Patent Owner argues that neither reference

describes synthetic pathways suitable for use as pharmaceutical formulations, neither describes the same synthetic pathway as the '334 patent or Ahmad, and neither describes the stability profile of the resulting endoxifen. *Id.* at 38. Patent Owner concludes that the “Petition provides no explanation for how a POSA could use either synthetic method described in the disclosure of [Ahmad] to create an oral formulation comprising 90% pure (Z)-endoxifen.” *Id.*

In its Reply, Petitioner notes that Ahmad is presumed enabling and asserts that Patent Owner’s attempt to rebut the presumption of enablement should be addressed at trial. Prelim. Reply 3–4 (citing *10x Genomics, Inc. v. Bio-Rad Lab ’ys, Inc.*, IPR2020-00089, 2020 WL 20206695, at *15 (PTAB Apr. 27, 2020); *Apple Inc. v. Corephotonics, Ltd.*, 861 Fed. App’x 443, 449 (Fed. Cir. 2021)). Petitioner also notes that, although it had no burden to do so, it provided additional evidence of enablement, stating that “forming [90% pure (Z)-endoxifen] formulations was known in the art as taught by e.g., Liu and Song.” *Id.* at 5 (citation omitted). Petitioner states that it will make clear at trial that Patent Owner’s arguments regarding Liu “relate to limitations not present in the claimed invention (e.g. stability), and thus cannot rebut the presumption of enablement.” *Id.*

On this record at this stage of the proceeding, we find that Petitioner has shown it is more likely than not that Ahmad discloses each limitation of claims 1 and 15 for the reasons stated in the Petition, which we adopt for purposes of this Decision. *See* Pet. 28–33; Ex. 1003, Abstract, Fig. 1, 4:41–44, 7:43–48, 11:17–23, 12:14–17, 18:1–6; Ex. 1020 ¶¶ 57–68, 75.

Although we acknowledge Patent Owner’s argument that Ahmad does not enable claims 1 and 15, we agree with Petitioner that it does not have the burden to show Ahmad enables the claims in the Petition. As the Federal

Circuit reminds us, “[i]t is well-established that prior art patents . . . are presumed enabling.” *Apple*, 861 Fed. App’x 443, 449 (Fed. Cir. 2021) (citing *Impax Lab’ys, Inc. v. Aventis Pharm., Inc.*, 545 F.3d 1312, 1316 (Fed. Cir. 2008)). Moreover, *Apple* instructs us that a petitioner need not provide evidence in its petition to show a prior art patent is enabling as part of its burden to prove anticipation. *Id.* (finding Board erred in shifting the burden to petitioner to provide evidence in its petition to show prior art patent publication was enabling); *see also id.* at 450 (“[R]egardless of the forum, prior art patents and publications enjoy a presumption of enablement, and the patentee/applicant has the burden to prove nonenablement for such prior art.”). Thus, because enablement is a highly fact-intensive issue, without Petitioner’s arguments and evidence in response (including the cross-examination of Patent Owner’s expert), we decline to prematurely address Patent Owner’s enablement arguments in this Decision.¹¹

Accordingly, in light of the presumption that Ahmad is enabled and that Petitioner was not required to preemptively rebut that presumption in the Petition, we find we will be able to better evaluate Patent Owner’s enablement argument—and Petitioner’s response, once filed—after the record has been fully developed at trial.

b) Claims 2, 4, and 20–22

Claims 2, 4, and 20–22 depend from claim 1 or claim 15, either directly or indirectly. Petitioner asserts that Ahmad discloses each

¹¹ We note that Patent Owner and Dr. Davies’s argument appears to be premised on limiting the claims to the free base form of (Z)-endoxifen. *See* Ex. 2001 ¶¶ 36–37 (“[Ahmad] does not disclose or teach a POSA how to make an oral formulation comprising at least 90% (Z)-endoxifen free base.”). As explained above, we construe the term more broadly, consistent with the express definition in the Specification. *See supra* Section III.B.

additional limitation of those claims. *See* Pet. 32–35. Patent Owner argues that the dependent claims are not anticipated because independent claims 1 and 15 are not enabled by Ahmad. Prelim. Resp. 39–40.

We find Petitioner has shown sufficiently that Ahmad discloses the additional limitations of the claims for the reasons stated in the Petition, which we adopt for purposes of this Decision. *See* Pet. 32–35; Ex. 1003, 2:2–5, 5:33–36, 18:22–24, 18:47–52, 18:54–60, 28:37–38; Ex. 1020 ¶¶ 72–74, 76–80. For the same reasons stated above, we find Patent Owner’s enablement argument is better evaluated once the record has been fully developed at trial.

Accordingly, having considered the arguments and evidence presented by the parties at this stage of the proceeding, we find Petitioner has shown that it is more likely than not that claims 1, 2, 4, 15, and 20–22 are anticipated by Ahmad.

D. Ground 2: Alleged Obviousness over Ahmad

Petitioner asserts that if claims 1, 2, 4, 15, and 20–22 of the ’334 patent are not anticipated by Ahmad, they would have been obvious in view of Ahmad’s teachings. Pet. 36–41. Patent Owner opposes. Prelim. Resp. 40–48.

Having considered the evidence and argument presented by the parties, we determine Petitioner has shown it is more likely than not that the challenged claims would have been obvious over Ahmad.¹²

¹² We note that we address Patent Owner’s evidence of secondary considerations as to Petitioner’s obviousness Grounds 2–6 in Section III.F. below.

A 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 that subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness when presented. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In analyzing the obviousness of a combination of prior art elements, it can be important to identify a reason that would have prompted one of skill in the art “to combine . . . known elements in the fashion claimed by the patent at issue.” *KSR*, 550 U.S. at 418. A precise teaching directed to the specific subject matter of a challenged claim is not necessary to establish obviousness. *Id.* Rather, “any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420. Accordingly, Petitioner must show that “a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (quotations and citations omitted).

As explained above, we find Petitioner has shown sufficiently that Ahmad anticipates each of the challenged claims and, therefore, teaches each of the claim limitations. *See supra* Section III.C.2. Nevertheless, for

claims 1 and 15, to the extent an endoxifen composition comprising at least 90% (Z)-endoxifen is not disclosed by Ahmad, Petitioner asserts that a POSA would have been motivated to use 90% (Z)-endoxifen in that formulation because it was known that the (Z)-form was more active at estrogen receptors. Pet. 37 (citing Ex. 1020 ¶ 62; Ex. 1004 ¶ 4). Petitioner further argues that a POSA would have been motivated to use an enteric capsule because it was known that endoxifen could degrade in the acidic stomach and was typically provided with an enteric coating. *Id.* (citing Ex. 1020 ¶ 65; Ex. 1006; Ex. 1014; Ex. 1018, 253; Ex. 1029, 1353). According to Petitioner, a POSA would have had a reasonable expectation of success in arriving at the claimed invention because “both forming (Z)-endoxifen and enteric capsules were well known in the art.” *Id.* (citing Ex. 1020 ¶ 68).

For dependent claims 2, 4, and 20–22, Petitioner asserts that each limitation of those claims is taught by Ahmad and that those claims would have been obvious over Ahmad in view of the knowledge in the art, as demonstrated, for example, by “the Endoxifen Art.”¹³ *Id.* at 37–41 (citing Ex. 1020 ¶¶ 72–74, 76–82).

Patent Owner argues in response that because Ahmad is a single obviousness reference, Ahmad must enable the portions of its disclosure being relied upon. Prelim. Resp. 40–41 (citing *Raytheon Techs. Corp. v. GE*, 993 F.3d 1374, 1381 (Fed. Cir. 2021)). As such, Patent Owner argues

¹³ In Section VII of the Petition entitled “Summary of the prior art,” Petitioner includes a subsection B entitled “Endoxifen Art.” *See* Pet. 10–16. The references discussed in the “Endoxifen Art” subsection include Liu (Ex. 1004), Song (Ex. 1005), Ahmad 2010 (Ex. 1006), and Ahmad 2012 (Ex. 1007).

that the Petition “fails to explain how a POSA would use [Ahmad] to get to the 90% (Z)-endoxifen required by independent claims 1 and 15.” *Id.* at 42. Patent Owner further asserts that the Petition fails to explain how or why a POSA would be motivated to modify Ahmad to get to 90% (Z)-endoxifen, even if Liu and Song were considered to be background art. *Id.* at 45–48.

At this stage of the proceeding, we are persuaded that Petitioner has shown sufficiently that Ahmad teaches each limitation of claims 1, 2, 4, 15, and 20–22 and that a POSA would have had a reason to use 90% (Z)-endoxifen as taught by Ahmad with a reasonable expectation of success because it was known to be more active at estrogen receptors and forming 90% pure (Z)-endoxifen was known in the art, as evidenced at least by Liu. *See* Pet. 37 (citing Ex. 1020 ¶¶ 62, 68); *see also* Ex. 1020 ¶ 54. As for Patent Owner’s argument that Ahmad is not enabled and its related argument that the Petition fails to explain how to modify Ahmad to achieve the recited purity, we find those issues are better evaluated once the record has been fully developed at trial for the same reasons stated with respect to Ground 1. *See supra* Section III.C.

E. Grounds 3–6: Remaining Obviousness Grounds over Ahmad

Petitioner asserts that claims 5–8, 16, and 17 are unpatentable as obvious over Ahmad in view of Cole (Ground 3) (*id.* at 41–46), claim 3 is unpatentable as obvious over Ahmad in view of Benameur (Ground 4) (*id.* at 46–48), claims 9–13 are unpatentable as obvious over Ahmad in view of Stegemann and/or the HPE (Ground 5) (*id.* at 49–54), and claims 14, 18, and 19 are unpatentable as obvious over Ahmad in view of Ahmad 2010 and Ahmad 2012 (Ground 6) (*id.* at 54–57). Patent Owner opposes. Prelim. Resp. 48–57.

Having considered the evidence and argument presented by the parties, we determine Petitioner has shown it is more likely than not that the challenged claims are unpatentable as obvious over the cited art in Grounds 3–5 and claim 14 of Ground 6, but not claims 18 and 19 of Ground 6.

We incorporate here our findings and discussion of Ahmad.

1. Cole (Ex. 1008)

Cole is an article entitled, “Enteric coated HPMC capsules designed to achieve intestinal targeting,” which appears to have been published in the International Journal of Pharmaceutics in 2002.¹⁴ Ex. 1008, 83. Cole describes manufacturing experiments in which hydroxypropyl methylcellulose (HPMC) capsules containing paracetamol are coated with enteric polymers Eudragit® L 30 D-55 and Eudragit® FS 30 D, “which are designed to achieve enteric properties and colonic release, respectively.” *Id.* According to Cole, “[e]nteric coated products are designed to remain intact in the stomach and then to release the active substance in the upper intestine.” *Id.* Cole explains that “site specific delivery into the upper intestine has been achieved for many years by the use of pH-sensitive coatings.” *Id.* at 84. Cole reports that capsules coated with Eudragit® L 30 D-55 disintegrated relatively rapidly within the small intestine and capsules coated with Eudragit® FS 30 D disintegrated further down the GI tract, towards the distal small intestine and proximal colon. *Id.* at 93.

¹⁴ Patent Owner asserts that Petitioner has failed to prove that Cole qualifies as a printed publication. Prelim. Resp. 28–30. At this stage of the proceeding, we find Cole—which is a journal article with a publication date—has sufficient indicia of publication on its face for purposes of institution. *See Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 17 (PTAB Dec. 20, 2019) (precedential).

2. *Benameur (Ex. 1010)*

Benameur is an article entitled, “Enteric Capsule Drug Delivery Technology – Achieving Protection Without Coating,” which appears to have been published in the journal *Drug Development & Delivery* in June 2015.¹⁵ Ex. 1010, 34. Benameur describes the use of enteric capsule drug delivery technology (ECDDT), which “was developed to provide oral delivery with full enteric protection and rapid release in the upper gastrointestinal (GI) tract without the use of coatings.” *Id.* According to Benameur, “[t]he major hurdle in oral delivery of many sensitive molecules, such as nucleotides, peptides, live biopharmaceutical products, and vaccines, is protecting the active entity from acidic and enzymatic degradation in the GI tract.” *Id.* at 35. ECDDT can be used for oral delivery of such sensitive molecules to provide full enteric protection and rapid release in the upper GI tract without coating and is a new, faster, and easier means for oral delivery of labile entities, such as peptides, nucleotides, live biopharmaceutical products, and vaccines. *Id.* at 35, 37.

3. *Stegemann (Ex. 1011)*

Stegemann is an article entitled, “Hard gelatin capsules today – and tomorrow,” which appears to have been published in 2002 in *Capsugel Library*.¹⁶ Ex. 1011, 2. Stegemann provides an overview of hard gelatin

¹⁵ Patent Owner asserts that Petitioner has failed to prove that Benameur qualifies as a printed publication. Prelim. Resp. 28–30. At this stage of the proceeding, we find Benameur—which is a journal article with a publication date—has sufficient indicia of publication on its face for purposes of institution. *See Hulu*, IPR2018-01039, Paper 29 at 17.

¹⁶ Patent Owner asserts that Petitioner has failed to prove that Stegemann qualifies as a printed publication. Prelim. Resp. 28–30. At this stage of the proceeding, we find Stegemann—which is an article with a publication

capsules used as a dosage form, including their usage, manufacture, and compatibility with various drug substances. *See generally id.* Stegemann explains that “[t]he capsule is one of the oldest dosage forms in pharmaceutical history, known to the ancient Egyptians,” with the first patent for a gelatin capsule granted in 1834. *Id.* at 3. Stegemann reports that “[h]ard gelatin capsules are a modern dosage form for medicinal use” and are “increasingly being chosen for new medicines in solid oral dosage form.” *Id.* at 3–4. According to Stegemann, there are many benefits to using gelatin capsules, including increased control of GI transit time, enhanced bioavailability, and the ability to develop oral dosage forms of drug actives with low melting points, low doses, and instability when exposed to oxygen, light, or humidity. *Id.* at 14, 18–19, 21.

4. *The HPE (Ex. 1012)*

The HPE is the Handbook of Pharmaceutical Excipients and “is an internationally acclaimed reference work recognized as one of the most authoritative and comprehensive sources of information on excipients used in pharmaceutical formulation.” Ex. 1012, 8.¹⁷ The HPE provides information on the uses, chemical and physical properties, licensing, and safety of excipients. *Id.*

5. *Ahmad 2010 (Ex. 1006)*

Ahmad 2010 is an article entitled, “Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability, and Systemic Bioavailability in Healthy Human Subjects,” that appears to have been

date—has sufficient indicia of publication on its face for purposes of institution. *See Hulu*, IPR2018-01039, Paper 29 at 17.

¹⁷ We cite to the page number of the exhibit rather than the page number of the HPE.

published in the journal *Clinical Pharmacology & Therapeutics* in December 2010.¹⁸ Ex. 1006, 814.

According to Ahmad 2010, endoxifen is an active metabolite of tamoxifen, which is a drug used in the treatment of breast cancer and is extensively metabolized by cytochrome P450 (CYP) enzymes into its active metabolites. *Id.* Certain genetic polymorphisms and drugs that interfere with cytochrome P450 2D6 (CYP2D6) inhibit metabolism of tamoxifen and render it less effective in treating breast cancer. *Id.* Ahmad 2010's authors sought to substitute endoxifen for tamoxifen and administered single escalating oral doses of endoxifen to humans to evaluate the safety, tolerability, and pharmacokinetics (PK) of the drug. *Id.* at 814, 816. Ahmad 2010 reports that "single oral doses of endoxifen are safe and well tolerated and have sufficient bioavailability to reach systemically effective levels in human subjects." *Id.* at 814. Ahmad 2010 states that "multiple daily endoxifen doses of 2.0–4.0 mg will result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who are administered tamoxifen at 20 mg/day" and "a dose of 4 mg of endoxifen should be appropriate for breast cancer prevention and therapy." *Id.* at 816.

6. *Ahmad 2012 (Ex. 1007)*

Ahmad 2012 is a printout from the Journal of Clinical Oncology's web page of an abstract allegedly from the 2012 ASCO Annual Meeting entitled "Endoxifen for breast cancer: Multiple-dose, dose-escalation study

¹⁸ Patent Owner asserts that Petitioner has failed to prove that Ahmad 2010 qualifies as a printed publication. Prelim. Resp. 28–30. At this stage of the proceeding, we find Ahmad 2010—which is a journal article with a publication date—has sufficient indicia of publication on its face for purposes of institution. *See Hulu*, IPR2018-01039, Paper 29 at 17.

characterizing pharmacokinetics and safety in metastatic breast cancer patients.” Ex. 1007, 1.¹⁹ Ahmad 2012 states it was “[p]ublished online May 20, 2012.”²⁰

Ahmad 2012 reports that preclinical studies show that single oral doses of endoxifen tested up to 4 mg are safe, well tolerated, and bioavailable in humans. *Id.* Ahmad 2012 discusses results of a multiple-dose escalating study conducted in three cohorts, each of which included six patients, for a total of 18 metastatic breast cancer patients. *Id.* In the study, “Endoxifen at 3 dose levels (2, 4, or 8 mg) was given once daily for 28 days” and was found to be safe up to 8 mg. *Id.* at 1–2. Ahmad 2012 finds that “[m]ultiple daily endoxifen doses of 4.0–8.0 mg resulted in endoxifen exposures that would be sufficient for effective therapy.” *Id.* at 2.

7. Analysis

Petitioner asserts that the combination of the cited references discloses each limitation of the challenged claims and that a POSA would have been motivated to combine the references to reach the claimed invention with a reasonable expectation of success. Pet. 41–57 (citing Ex. 1020 ¶¶ 85–127). Patent Owner opposes. Prelim. Resp. 48–59. We have considered the parties’ respective arguments and evidence and find Petitioner has shown sufficiently that the challenged claims of Grounds 3–5 and claim 14 of

¹⁹ We cite to the page number of the exhibit rather than the page number of Ahmad 2012.

²⁰ Patent Owner asserts that Petitioner has failed to prove that Ahmad 2012 qualifies as a printed publication. Prelim. Resp. 27–28. At this stage of the proceeding, we find Ahmad 2012—which is a printout of an abstract that states it was “published online on May 20, 2012”—has sufficient indicia of publication on its face for purposes of institution. *See Hulu*, IPR2018-01039, Paper 29 at 17.

Ground 6 would have been obvious over the cited art, but not claims 18 and 19 of Ground 6.

For example, regarding Ground 3 over Ahmad and Cole, Petitioner asserts that a POSA would understand Cole teaches the dissolution profiles recited in claims 5–8, 16, and 17. Pet. 41–46 (citing Ex. 1020 ¶¶ 85–97). Petitioner further asserts that a POSA would have been motivated to combine Ahmad’s formulation with Cole’s enteric coating to ensure that the endoxifen was released in the small intestine where it could be absorbed into the body and not released in the stomach where it may be degraded by acid, as taught by Ahmad. *Id.* Patent Owner asserts that because Cole is incorporated by reference into the Specification, Petitioner “engages in impermissible hindsight analysis when combining [Cole] and [Ahmad] to arrive at the enteric coating limitation of the dependent claims.” Prelim. Resp. 49 (citing Ex. 1001, 86:55–61). We are not persuaded. As Petitioner notes, Ahmad teaches that the purpose of the enteric coating is to prevent release of the drug in the stomach. Pet. 41 (citing Ex. 1003, 18:19–21). And Cole teaches the use of a particular commercially available enteric coating with certain dissolution profiles. *See* Ex. 1008 at 84–85, 89. Thus, at this stage of the proceeding, we are persuaded that Petitioner has shown sufficiently that a POSA would have been motivated to combine Ahmad’s formulation with Cole’s enteric coating to achieve the claimed dissolution profiles with a reasonable expectation of success.

Regarding Ground 4 over Ahmad and Benameur, Petitioner asserts that “[i]t would have been a routine and obvious modification of Ahmad to instead use an uncoated enteric capsule, as had been developed in the art by e.g., Capsugel.” Pet. 46 (citing Ex. 1020 ¶ 98). Patent Owner contends Petitioner’s argument is “untethered from any relevant facts” as there is no

teaching in Ahmad that (Z)-endoxifen would benefit from the uncoated enteric capsules described in Benameur. Prelim. Resp. 51–52. We disagree. Petitioner identifies the benefits of uncoated capsules that Benameur describes, including “eliminating the preparation and application steps used for enteric coating,” and asserts that a POSA would have been motivated to use an uncoated capsule “to obtain the benefits Benameur highlights, the ability to produce drug without exposing it to the heating necessary for a coating process or to eliminate the need for process development of an enteric coating step, and as a routine design choice.” Pet. 47–48 (citing Ex. 1010, 34; Ex. 1020 ¶¶ 99–102). Because a POSA is “a person of ordinary creativity, not an automaton,” we find Petitioner has shown sufficiently that a POSA would have had a reason to combine Ahmad and Benameur to obtain the benefits described in Benameur. *See KSR*, 550 U.S. at 421. Thus, we are not persuaded that Petitioner relies on impermissible hindsight to reconstruct the claimed invention, as Patent Owner asserts.

Regarding Ground 5 over Ahmad, Stegemann, and/or HPE, Petitioner asserts that claims 9–13 recite “various common excipients for use in capsules” that were “well-known as disclosed in Stegemann and the HPE” and therefore obvious to combine with Ahmad. Pet. 49–54 (citing Ex. 1020 ¶¶ 104–118). Patent Owner argues that the Petitioner’s motivation to combine the references and explanation of the reasonable expectation of success are conclusory. Prelim. Resp. 53. Patent Owner asserts that “[e]specially in dealing with an unstable compound such as (Z)-endoxifen, a POSA would need more of a motivation to combine than just a listing of certain excipients in the index of a textbook.” *Id.* As Patent Owner notes, the dependent claims recite fillers, disintegrants, and lubricants. *Id.* at 52–53. Petitioner asserts that these limitations are “common pharmaceutical

excipient[s],” the use of which “was a routine and common practice in the formulation arts.” Pet. 49–54 (citing Ex. 1020 ¶¶ 104–118). At this stage of the proceeding, we find Petitioner has shown sufficiently that a POSA would have been motivated to use each recited excipient “for its normal use” with a reasonable expectation of success, given they were commonly used in the art and appear to be no more than “the predictable use of prior art elements according to their established functions.” *See KSR*, 550 U.S. at 417.

Regarding Ground 6, Petitioner asserts that Ahmad 2010 and 2012 teach administering 4 to 8 mg doses of endoxifen, which teaches the broad dosage limitation of “from 0.01 mg to 200 mg” in claim 14. Pet. 54–55 (citing Ex. 1020 ¶¶ 120–121). Petitioner notes that although Ahmad 2010 and 2012 do not disclose whether the endoxifen is (E), (Z), or a mix of isoforms, a POSA would have understood that “the (Z) form is more active and thus preferred, and would understand to use highly pure (Z) form” and that “the formulations of Ahmad should include from 0.01 mg to 200 mg (Z)-endoxifen per enteric capsule.” *Id.* at 55 (citing Ex. 1020 ¶¶ 120–121). Patent Owner disagrees, arguing that a POSA would understand that dosage information regarding an unknown form of endoxifen “may not be immediately applicable to a 90% pure (Z)-endoxifen formulation.” Prelim. Resp. 54 (citing Ex. 2001 ¶¶ 150–154). We acknowledge Patent Owner’s argument, but we find Petitioner has shown sufficiently at this stage of the proceeding that a POSA reading Ahmad 2010 and 2012 would have found it obvious to use (Z)-endoxifen within the broad range of 0.01 mg to 200 mg per enteric capsule, because (Z)-endoxifen is the more active form of endoxifen and the references teach that 4 mg doses of endoxifen were safe and effective. Pet. 54 (citing Ex. 1006, 816; Ex. 1007, 1–2; Ex. 1020 ¶ 121).

For the pharmacokinetic properties recited in claims 18 and 19, however, Petitioner asserts that the limitations would have been “the inherent result” of dosing the formulations of Ahmad within the dosing ranges taught by Ahmad 2010 and Ahmad 2012, relying on the results provided by Ahmad 2010. *Id.* at 55–57. As Patent Owner notes, inherent obviousness is present “only when the limitation at issue is the ‘*natural result*’ of the combination of prior art elements.” Prelim. Resp. 55 (quoting *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014)). Petitioner acknowledges, however, that Ahmad 2010 and Ahmad 2012 are both silent as to whether the endoxifen is (E), (Z), or a mix. Pet. 55. We, therefore, agree with Patent Owner that Petitioner has not shown sufficiently that “different isomers or different formulations would have similar pharmacokinetic profiles.” Prelim. Resp. 55 (citing Ex. 2001 ¶¶ 150–154). In other words, Petitioner has not explained sufficiently why a POSA would understand the recited pharmacokinetic profiles of the 90% pure (Z)-endoxifen of the claims would be the “natural result” of the use of Ahmad 2010’s unknown mixture of endoxifen. *See Par Pharm.*, 773 F.3d at 1195. Thus, at this stage of the proceeding, we find Petitioner has not shown that it is more likely than not that the combination of Ahmad, Ahmad 2010, and Ahmad 2012 would have rendered claims 18 and 19 obvious.

F. Secondary Considerations

Patent Owner argues that, for Grounds 2–6, Petitioner ignores the unexpected results and long felt need of the claimed invention. Prelim. Resp. 57. Patent Owner asserts that the Board has held that “petitions may be denied if they do not address known secondary considerations.” *Id.* (citing *Stryker Corp. v. KFx Med., LLC*, IPR2019-00817, Paper 10 at 28–29 (PTAB Sept. 16, 2019) (collecting cases)). The *Stryker* decision, however,

makes clear that the “known secondary considerations” are those that have been previously presented in other proceedings or during prosecution. *See Stryker*, IPR2019-00817, Paper 10 at 29 (citing cases denying institution for failure to address secondary considerations presented during an ITC proceeding, during original prosecution, and during reexamination). At this stage of the proceeding, Patent Owner does not assert that its evidence of unexpected results or long-felt need has previously been considered in another proceeding. Thus, *Stryker* is inapposite.

Patent Owner argues “the claimed methods of synthesizing endoxifen and purifying (Z)-endoxifen resulted in isomerically purified (Z)-endoxifen compositions with unexpected stability as compared to the hydrochloride salt.” Prelim. Resp. 58 (citing Ex. 2001 ¶ 157). Patent Owner further argues that the superior bioavailability of the oral formulations were unexpected compared to tamoxifen citrate oral formulation and endoxifen citrate oral formulation. *Id.* Finally, Patent Owner asserts that the ’334 patent addressed an unmet medical need for new compositions and methods for the prevention and treatment of hormone-dependent breast and reproductive tract disorders. *Id.* at 59 (citing Ex. 1001, 2:50–54).

At this stage of the proceeding, Petitioner has not yet had an opportunity to respond to Patent Owner’s arguments and evidence of secondary considerations. Thus, although we have considered Patent Owner’s evidence of secondary considerations, we find the record is insufficiently developed to find that Patent Owner’s evidence of unexpected results and long felt need when considered together with the prior art outweighs Petitioner’s obviousness challenge.

G. Conclusion as to Grounds 1–6

Having considered the parties’ respective arguments and evidence, we conclude that Petitioner has shown it is more likely than not that claims 1–17 and 20–22 are unpatentable over the cited references, but not claims 18 and 19.

IV. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 325(d)

Alternatively, Patent Owner urges us to exercise our discretion to deny institution under 35 U.S.C. § 325(d). Prelim. Resp. 13–24. For the reasons discussed below, we decline to do so.

A. Legal Standards

Under § 325(d), we have discretion to deny a petition that presents the same or substantially the same prior art or arguments as previously presented to the Office. *See* 35 U.S.C. § 325(d).

In performing an analysis under § 325(d), the Board uses a two-part framework:

- (1) We consider whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and
- (2) If either condition of the first part of the framework is satisfied, we consider whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential).

To help us evaluate the *Advanced Bionics* framework, we consider a number of non-exclusive factors, as set forth in our decision in *Becton, Dickinson and Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at

17–18 (PTAB Dec. 15, 2017) (precedential) (“the *Becton, Dickinson* factors”):

- (a) the similarities and material differences between the asserted art and the prior art involved during examination;
- (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
- (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
- (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
- (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
- (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

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

According to *Advanced Bionics*, *Becton, Dickinson* factors (a), (b), and (d) relate to whether the same or substantially the same art or arguments previously were presented to the Office, and factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office.

Advanced Bionics, IPR2019-01469, Paper 6 at 9–11.

On this record, we are not persuaded that we should exercise our discretion to deny institution under § 325(d) in this proceeding. As explained further below, we focus our analysis on arguments regarding Grounds 1 and 2 because they are dispositive of this issue.

B. Analysis

1. Step 1: whether the same or substantially the same art previously was presented to the Office

We first consider whether the same or substantially the same art previously was presented to the Office. *Advanced Bionics*, Paper 6 at 8. “Previously presented art includes . . . art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Id.* at 7–8.

Grounds 1 and 2 both rely solely on Ahmad, which was submitted in an IDS, considered by the Examiner, and is on the face of the patent. Prelim. Resp. 15; Ex. 1002, 346 (item no. 027); Ex. 1001, code (56). Thus, there is no dispute that Ahmad previously was presented to the Office. *See* Prelim. Resp. 15; Pet. 24.

2. Step 2: whether the petitioner has demonstrated that the Office erred

We next consider whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of the challenged claims. *Advanced Bionics*, Paper 6 and 8. The Examiner of the ’334 patent application allowed the claims without entering any rejections on December 21, 2022. Ex. 1002, 383. Thus, the Examiner did not discuss any references during prosecution of the ’334 patent. In the Reasons for Allowance, the Examiner simply stated that he “has conducted a thorough search of the appropriate electronic data bases for the claimed subject matter and did not discover any reference which anticipates that claimed subject matter or would form a basis for concluding that the claimed subject matter would have been obvious.” *Id.* at 388.

Petitioner asserts that the Examiner erred in not substantively considering Ahmad, particularly given that Ahmad teaches each limitation of the independent claims. *See* Pet. 26–27. As such, Petitioner argues that the “strong evidence of unpatentability (as well as supporting expert testimony) warrants reconsideration, and demonstrates that the Office erred in not considering the cited references and combinations.” *Id.* at 27.

Patent Owner disagrees, arguing that there is no evidence that the Examiner did not substantively consider the references. Prelim. Resp. 22. As support, Patent Owner cites the IDS where the Examiner stated that “[a]ll references [were] considered except where lined through.” *Id.* (citing, e.g., Ex. 1002, 346). Patent Owner cites *Biocon Pharma Ltd. v. Novartis Pharmaceuticals Corp.*, IPR2020-01263, Paper 12 at 9 (PTAB Feb. 16, 2021), arguing that the Board has exercised its discretion under § 325(d) “under similar circumstances.” Prelim. Resp. 22–23. But there, the panel followed *Advanced Bionics* Step 1 in finding the reference was previously presented because it was considered by the Examiner in an IDS with the same statement that “all references considered except where lined through.” *Biocon*, IPR2020-01263, Paper 12 at 9 (citing *Advanced Bionics*, Paper 6 at 7–8). When considering Step 2 of *Advanced Bionics*, the panel then substantively considered the reference and found Petitioner had failed to show that the reference taught the feature that the Examiner allegedly overlooked. *See id.* at 13–17. Accordingly, the panel found both Steps of *Advanced Bionics* were satisfied and exercised its discretion and denied institution. *Id.* at 18.

As explained above, unlike in *Biocon*, we find Petitioner has shown sufficiently—on this record—that Ahmad discloses or renders obvious each limitation of claims 1, 2, 4, 15, and 20–22 (i.e., Grounds 1 and 2). *See supra*

Section III.C and D. We, therefore, find that Petitioner has sufficiently shown that the Examiner erred in his consideration of Ahmad.

Patent Owner also argues that Petitioner disregards the prosecution history of the parent patent, US 11,261,151 B2 (Ex. 2003, “the ’151 patent”), noting that the ’151 patent “overcame obviousness rejections over [Liu]” and “the Examiner considered [Ahmad].” Prelim. Resp. 23. But the applicant for the ’151 patent overcame the obviousness rejection over Liu by canceling the claim, and the Examiner in the ’151 patent considered Ahmad in an IDS, but did not substantively address it. Ex. 2004, 24. Thus, we are not persuaded that the prosecution history of the ’151 patent is probative as to whether the Office erred in allowing the ’334 patent claims.

C. Conclusion

Having considered the parties’ respective arguments and evidence with respect to Grounds 1 and 2 challenging claims 1, 2, 4, 15, and 20–22, we decline to exercise our discretion to deny institution under 35 U.S.C. § 325(d). Moreover, as explained above, we find Petitioner has sufficiently shown on this record that it is more likely than not that claims 1, 2, 4, 15, and 20–22 are unpatentable over Ahmad. *See supra* Section III.C and D.

In light of our findings with respect to Grounds 1 and 2, we need not address Patent Owner’s contentions that we should exercise our discretion to deny institution of Grounds 3–6. That is because, under the Supreme Court’s decision in *SAS Institute, Inc. v. Iancu*, 138 S. Ct. 1348 (2018), if we institute trial on one ground, we are compelled to proceed with this post-grant review on all grounds raised in the Petition. *See* Guidance on the impact of *SAS* on AIA trial proceedings, *available at* <https://www.uspto.gov/patents/ptab/trials/guidance-impact-sas-aia-trial> (“If the PTAB institutes a trial, the PTAB will institute on all challenges raised

in the petition.”). Also, because we find that Petitioner has demonstrated error in the Examiner’s consideration of Ahmad for Grounds 1 and 2, we would not find that § 325(d) is sufficiently implicated such that the entire petition should be denied.²¹ In other words, under these circumstances, even if we found Patent Owner’s arguments regarding Grounds 3–6 persuasive, we would still institute trial on those Grounds. We, therefore, find Patent Owner’s request to exercise our discretion to deny institution of Grounds 3–6 to be moot.

V. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 324(a)

Patent Owner urges us to exercise our discretion to deny institution under 35 U.S.C. § 324(a) because Petitioner has failed to establish that several of its non-patent references are printed publications that qualify as prior art. Prelim. Resp. 24–30.

We note that Patent Owner does not argue that we should exercise our discretion under § 324(a) for Grounds 1 and 2 over the Ahmad patent. Thus, for the same reasons explained above with respect to § 325(d), we are compelled to proceed with this post-grant review on all grounds raised in the Petition, because we find Petitioner has shown it is more likely than not that the claims challenged in Grounds 1 and 2 are unpatentable. *See* Guidance on the impact of *SAS* on AIA trial proceedings. Thus, we find Patent Owner’s § 324(a) arguments to be moot.

Nevertheless, as noted above, we find at this stage of the proceeding that certain of the objected-to exhibits have sufficient indicia of publication on their face for purposes of institution. *See Hulu*, IPR2018-01039, Paper

²¹ *See SAS* Q&As, D1 (June 5, 2018) (available at https://www.uspto.gov/sites/default/files/documents/sas_qas_20180605.pdf).

29 at 17. If the issue of public availability remains in dispute, the parties are invited to address it further during trial.

VI. CONCLUSION

For the foregoing reasons, we determine that Petitioner has shown that it is more likely than not that at least one of the challenged claims of the '334 patent is unpatentable. Accordingly, we institute a post-grant review of claims 1–22 of the '334 patent.

Our determination in this Decision is not a final determination on the patentability of the challenged claims 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 in the context of an *inter partes* review 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)).

VII. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a), a post-grant review of claims 1–22 of the '334 Patent is *instituted* with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 324(c) and 37 C.F.R. § 42.4(b), post-grant review of the '334 Patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

PGR2023-00043
Patent 11,572,334 B2

PETITIONER:

Alejandro Menchaca
Ben Mahon
MCANDREWS, HELD & MALLOY, LTD.
amenchaca@mcandrews-ip.com
bmahon@mcandrews-ip.com

PATENT OWNER:

Melissa Harwood
Michael Sitzman
DLA PIPER LLP (US)
melissa.harwood@us.dlapiper.com
michael.sitzman@us.dlapiper.com