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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ INC.,
Petitioner,

v.

ABBVIE BIOTECHNOLOGY LTD.,
Patent Owner.

Case IPR2017-02105
Patent 9,090,689 B1

Before SUSAN L. C. MITCHELL, TINA E. HULSE, and MICHELLE N. ANKENBRAND, *Administrative Patent Judges*.

ANKENBRAND, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Sandoz Inc. ("Petitioner") requests an *inter partes* review of claims 1, 4, 7, 10, 13, 16, and 19 of U.S. Patent No. 9,090,689 B1 ("the '689 patent," Ex. 1001). Paper 1 ("Pet."). AbbVie Biotechnology Ltd. ("Patent Owner") filed a Preliminary Response. Paper 13 ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). We may not institute an *inter partes* review "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Applying that standard, and upon consideration of the information presented in the Petition and the Preliminary Response, we institute an *inter partes* review as to claims 1, 4, 7, 10, 13, 16, and 19 of the '689 patent.

II. BACKGROUND

A. Related Matters

The parties do not identify any litigation or other Office proceedings involving the '689 patent. *See* Pet. 2–3; Paper 6, 1. Petitioner identifies litigation involving one or more patents that are related to the '689 patent, captioned *AbbVie Inc. v. Amgen Inc.*, No. 1:16-cv-00666-MSG (D. Del. Aug. 4, 2016). Pet. 2.

Petitioner also identifies several *inter partes* review proceedings in which the Board previously found claims of certain of Patent Owner's patents unpatentable, but acknowledges that those patents and the '689 patent do not claim priority to any of the same applications. *Id.* at 3–4. Petitioner directs us to additional petitions that it previously filed requesting an *inter partes* review of certain other patents of Patent Owner: IPR2017-

01823 (challenging U.S. Patent No. 8,802,100), IPR2017-01824 (challenging U.S. Patent No. 9,512,216), and IPR2017-01987 (challenging U.S. Patent No. 8,911,737), IPR2017-01988 (challenging U.S. Patent No. 8,974,790). *Id.* Petitioner further notes that it filed concurrently with this proceeding a petition challenging U.S. Patent No. 9,067,992, "which claims priority to the same applications to which the '689 patent claims priority." *Id.* at 4.

Patent Owner further identifies a number of United States patent applications to which the '689 patent claims the benefit of priority, as well as a currently pending United States patent application that is a continuation of the application that matured into the '689 patent. Paper 6, 1–2.

B. The '689 Patent

The '689 patent, titled "Use of TNFα Inhibitor for Treatment of Psoriasis," issued on July 28, 2015. Ex. 1001, [45], [54]. The '689 patent is related to methods of treating disorders in which tumor necrosis factor alpha ("TNFα" or "TNF-α") activity is detrimental by administering the TNFα inhibitor adalimumab (also referred to as Humira or D2E7). *See id.* at 21:6–14. The written description defines the term "a disorder in which TNFα activity is detrimental" to "include diseases and other disorders in which the presence of TNFα in a subject suffering from the disorder has been shown to be or is suspected of being either responsible for the pathophysiology of the disorder or a factor that contributes to a worsening of the disorder." *Id.* at 22:35–41. In other words, "a disorder in which TNFα activity is detrimental is a disorder in which inhibition of TNFα activity is expected to alleviate the symptoms and/or progression of the disorder." *Id.* at 22:41–44.

In one embodiment, the TNFα inhibitor is used to treat skin and nail disorders in which TNFα activity is detrimental, such as psoriasis, including chronic plaque psoriasis. *Id.* at 25:38–46, 26:43–54. The written description explains that psoriasis is "a skin inflammation (irritation and redness) characterized by frequent episodes of redness, itching, and thick, dry silvery scales on the skin." *Id.* at 25:64–67. Psoriasis often is associated with other inflammatory disorders, including psoriatic arthritis ("PsA") and rheumatoid arthritis ("RA"). *Id.* at 24:61–63, 26:11–14.

The '689 patent exemplifies a study to determine the efficacy of a multiple-variable dose regimen of adalimumab for treating psoriasis. *Id.* at 40:25–42:31. Patients with a diagnosis of moderate to severe psoriasis were randomized into three groups—two treatment groups and one placebo group. *Id.* at 40:32–37. Patients in both treatment groups received an induction dose of 80 mg adalimumab at week 0. *Id.* at 40:38–39. Patients in the first treatment group subsequently received a treatment dose of 40 mg adalimumab at week 1, followed by 40 mg every other week (with placebo administered on alternate weeks), starting at week 3. *Id.* at 40:39–42. Patients in the second treatment group subsequently received an induction dose of 80 mg at week 1, followed by a treatment dose of 40 mg adalimumab weekly, starting at week 2. *Id.* at 40:42–46; *see also id.* at Table 5 (providing a more detailed description of the psoriasis study regimens).

The primary efficacy endpoint of the study was the percentage of patients achieving a clinical response, which was defined as at least a 75%

reduction in the Psoriasis Area and Severity Index ("PASI")[1] score at week 12. *Id.* at 41:7–10. Secondary efficacy measures included a Physician's Global Assessment ("PGA") of "clear" or "almost clear" at week 12. *Id.* at 41:11–23.[2] The study results showed that adalimumab administered for 12 weeks was effective in treating moderate to severe chronic plaque psoriasis. *Id.* at 42:23–31.

C. Illustrative Claim

Of the challenged claims, claims 1 and 7 are independent. Claim 1 is illustrative of the claimed subject matter and recites:

> 1. A method of administering adalimumab for treatment of moderate to severe chronic plaque psoriasis, comprising filling adalimumab into vessels and subcutaneously administering 40 mg of said adalimumab to a patient having moderate to severe chronic plaque psoriasis every other week.

Ex. 1001, 57:15–19. Claim 7 recites a "method of preparing adalimumab for treating moderate to severe chronic plaque psoriasis" that is similar to the method recited in claim 1. *Id.* at 57:30–35. Claims 4 and 10 depend from claims 1 and 7, respectively, and further require that the vessels are syringes.

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[1] According to the written description, the PASI "is a composite measure of the erythema, induration, desquamation and body surface area that is affected by psoriasis for a particular patient. . . . Scores range from 0 (clear) to 72 (maximum severity)." *Id.* at 27:64–28:3.

[2] The '689 patent explains that "PGA was determined according to a seven-point scale used to measure the severity of psoriasis at the time of the physician's evaluation," including the following: (1) severe = very marked plaque elevation, scaling, and/or erythema; (2) moderate to severe = marked plaque elevation, scaling, and/or erythema; (3) moderate = moderate plaque elevation, scaling, and/or erythema; (4) mild to moderate = intermediate between moderate and mild; (5) mild = slight plaque elevation, scaling, and/or erythema; (6) almost clear = intermediate between mild and clear; and (7) clear = no signs of psoriasis. *Id.* at 41:11–23.

Id. at 57:24–25, 40–41. Claim 13 depends from claim 7 and requires that "at least 5% of body surface area (BSA) of the patient is affected by psoriasis." *Id.* at 58:18–19. Claims 16 and 19 depend from claim 7 and recite that the patient "has both psoriasis and [PsA]." *Id.* at 58:24–25, 32–33. In addition, claim 16 requires that the patient "achieves at least a 75% reduction in [PASI] score at week 12 of the treatment," and claim 19 requires that the patient "achieves at least a [PGA] score of clear or almost clear at week 12 of the treatment." *Id.* at 58:25–27, 33–35.

D. The Asserted Grounds of Unpatentability

Petitioner asserts claims 1, 4, 7, 10, 13, 16, and 19 of the '689 patent are unpatentable based on the following grounds:

References	Asserted Priority Date	Statutory Basis	Claims Challenged
Keystone,[3] Lorenz,[4] and Chaudhari[5]	July 18, 2003	§ 103	1, 4, 7, 10, 13, 16, 19
Keystone, Mease 2000,[6] and Chaudhari	July 19, 2002	§ 103	1, 4, 7, 10, 13, 16, 19

Petitioner supports the Petition with the testimony of Simon Helfgott, M.D. (Ex. 1002) and R. Todd Plott, M.D. (Ex. 1012).

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[3] E Keystone et al., *The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (the Armada Trial),* 60 (Suppl. 1) ANN. RHEUM. DIS. A481 (2001) (Ex. 1003).

[4] Hanns-Martin Lorenz & Joachim R Kalden, *Supplement Review Perspectives for TNF-α-targeting therapies*, 4 (Suppl. 3) ARTHRITIS RES. S17–S24 (2002) (Ex. 1028).

[5] U Chaudhari et al., *Efficacy & safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial*, 357 LANCET 1842–47 (2001) (Ex. 1036).

[6] Philip J Mease et al., *Etanercept in the treatment of psoriatic arthritis & psoriasis: a randomised trial,* 356 LANCET 385–390 (2000) (Ex. 1017).

III. ANALYSIS

We organize our analysis into five sections. First, we discuss briefly the effective filing date of the '689 patent. Second, we address the level of ordinary skill in the art. Third, we turn to claim construction. Fourth, we provide an overview of the asserted references. Fifth, taking account of the information presented, we consider whether the grounds asserted in the Petition meet the threshold showing for instituting an *inter partes* review based on obviousness.

A. Effective Filing Date of the '689 Patent

The application that issued as the '689 patent, Application No. 14/681,704 ("the '704 application") "claims priority" to United States provisional application No. 60/681,645, which was filed on May 16, 2005. Ex. 1001, 1:6–7. The "Related U.S. Application Data" section of the '689 patent states that the '704 application is related to a number of continuation and continuation-in-part applications, with the earliest-filed application having a filing date of July 18, 2003. Ex. 1001 [63]. The '689 patent also sets forth several United States provisional applications that are identified as related, including provisional application No. 60/455,777, filed on March 18, 2003; provisional application No. 60/417,490, filed on October 10, 2002; provisional application No. 60/411,081, filed on September 16, 2002; and provisional application No. 60/397,275, filed on July 19, 2002. *Id.* [60].

For purposes of this proceeding, Petitioner contends that the effective filing date of the challenged claims is July 18, 2003. Pet. 6, 9. In so doing, Petitioner contends that the '689 patent is not entitled to the priority date of any of the provisional applications "because none of them disclose[s] the '40 mg' adalimumab administered 'every other week' dosing regimen" that

every claim of the '689 patent requires. *Id.* at 7–8. Thus, argues Petitioner, the provisional applications fail to provide the written description support under 35 U.S.C. § 112 that is required for a claim of priority. *Id.* at 8.

Notwithstanding those arguments, however, Petitioner asserts a ground of obviousness based on the earliest provisional application filing date of July 19, 2002. *See, e.g.*, *id.* at 9 (asserting that the challenged claims are unpatentable as obvious over Keystone, Mease 2000, and Chaudhari based on an assumed priority date of July 19, 2002). Petitioner also asserts a ground of obviousness based on an assumed priority date of July 18, 2003. *See, e.g.*, *id.*

For purposes of the Preliminary Response, Patent Owner does not dispute Petitioner's alternative use of July 18, 2003 or July 19, 2002 as the effective filing dates for the challenged claims. Prelim. Resp. 15.

Given that Patent Owner does not dispute Petitioner's alternative use of effective filing dates, we decline to provide a preliminary determination of the effective filing date of the challenged claims at this stage of the proceeding. Rather, for purposes of this Decision, we accept Petitioner's asserted effective filing dates for each ground, and we consider whether Petitioner's grounds based on the alternative effective filing dates meet the threshold showing for instituting an *inter partes* review based on obviousness. As explained below, we find that Petitioner demonstrates a reasonable likelihood of prevailing on its asserted grounds, whether based on the assumed priority date of July 18, 2003 or July 19, 2002. *See infra* § III.E. Because the record is not fully developed at this stage of the proceeding, we invite the parties to address the effective filing date that

applies to the challenged claims in Patent Owner's Response and Petitioner's Reply.

B. Level of Ordinary Skill in the Art

We consider the asserted grounds of unpatentability in view of the understanding of a person of ordinary skill in the art. Petitioner contends that, as of either July 16, 2002 or July 18, 2003, a person of ordinary skill in the art would have had an M.D. and at least three years of post-residency experience treating patients for psoriasis, PsA and/or RA, including with TNF-α inhibitors, and would have been "familiar with dosing regimens for TNF-α inhibitors that had been reported in the literature." Pet. 14 (citing Ex. 1002 ¶ 26; Ex. 1012 ¶ 26). Petitioner asserts that Dr. Helfgott and Dr. Plott have been treating patients with psoriasis and PsA, including with TNFα inhibitors, for over twenty years, "are qualified to provide opinions as to what a [person of ordinary skill in the art] would have understood, known, or concluded based on the prior art," and are competent to testify in this proceeding. *Id.* at 11 (citing Ex. 1012 ¶¶ 3–13, 25–27; Ex. 1002 ¶¶ 3–15, 25–27).

Patent Owner disputes that Dr. Helfgott is a person of ordinary skill in the art. Prelim. Resp. 14–15. In particular, Patent Owner asserts that the claims of the '689 patent are directed "to treating moderate-to-severe chronic plaque psoriasis, which predominantly manifests on the skin and thus would typically have been treated by a dermatologist." *Id.* at 14 (citing Ex. 1008, 30, 33, 46, 49; Ex. 2007, 36). Patent Owner further asserts that Petitioner fails to support expanding the definition of a person of ordinary skill in the art to a person with training in RA—a separate condition from the claimed condition. *Id.* at 14. According to Patent Owner, we should

give Dr. Helfgott's testimony "little weight" because he is a rheumatologist, not a dermatologist. *Id.* at 15 (citing *Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1257 (Fed. Cir. 2007)).

We find Patent Owner's arguments unpersuasive at this stage of the proceeding. First, we note that although the claims of the '689 patent are directed to treating moderate to severe chronic plaque psoriasis, the '689 patent discloses that psoriasis often is associated with other inflammatory disorders, including RA. Ex. 1001, 26:11–13. Similarly, the '689 patent generally describes disorders in which TNFα activity is detrimental, including psoriasis and RA, as well as methods of treating those disorders with TNFα inhibitors, including adalimumab. *See id.* at 21:6–14, 22:35–28:22.

Second, the prior art of record indicates that physicians investigating anti-TNFα therapy for treating psoriasis also would have reviewed how the same therapy had been used to treat RA. *See, e.g.*, Ex. 1017, 385 (studying efficacy of etanercept in patients with PsA and psoriasis after etanercept had "shown efficacy" in treating RA); Ex. 1028, S17–S19 (physicians from the Institute for Clinical Immunology and Rheumatology, Department of Medicine, University of Erlangen-Nuremberg reviewing the use of anti-TNFα agents for treating patients with, *inter alia*, RA and psoriasis); *see also Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that the prior art, itself, can reflect the appropriate level of ordinary skill in art).

Third, Dr. Helfgott need not be a person of ordinary skill in the art, but rather, must be "qualified in the pertinent art." *Sundance Inc. v. Demonte Fabricating Ltd.*, 550 F.3d 1356, 1363–64 (Fed. Cir. 2008).

Nevertheless, Dr. Helfgott testifies that, by July 19, 2002, he had been treating patients with RA, *psoriasis*, and PsA for over 20 years. Ex. 1002 ¶ 14. Thus, contrary to Patent Owner's arguments, Dr. Helfgott has experience treating patients with psoriasis. We, therefore, find that Dr. Helfgott is qualified to opine from the perspective of a person of ordinary skill in the art at the time of the invention. Ex. 1002 ¶¶ 3–15 (statement of qualifications), App'x A (curriculum vitae).

C. Claim Construction

The Board interprets claims in an unexpired patent using the "broadest reasonable construction in light of the specification of the patent." 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, claim terms are given their ordinary and customary meaning in view of the specification, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner proposes two phrases for construction: (1) the preamble of claim 1, which recites a "method of administering adalimumab for treatment of moderate to severe chronic plaque psoriasis"; and (2) the preamble of claim 7, which recites a "method of preparing adalimumab for treating moderate to severe chronic plaque psoriasis." Pet. 15–16. Petitioner argues that the preambles are statements of intended use and, therefore, are non-limiting. *Id.* at 15 (citing *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003)). Alternatively, Petitioner contends if the Board concludes that the preambles are limiting

and should be construed, the terms "treatment" or "treating" in the preambles "should be given [their] broadest reasonable interpretation of 'reducing the signs and symptoms of moderate to severe chronic plaque psoriasis,' without requiring any specific level of therapeutic effect." *Id.*

At this stage of the proceeding, Patent Owner does not contest Petitioner's proposed construction of "treatment" or "treating." Prelim. Resp. 15. Patent Owner also does not provide any argument responding to Petitioner's position that the preambles are not limiting, but reserves the right to do so should we institute a trial. *See id.* at 15–16. After having considered the parties' arguments and evidence, we decline to determine whether the preamble phrases are limiting at this stage of the proceeding, because we need not do so to resolve the parties' dispute. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("we need only construe terms 'that are in controversy, and only 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)). We further find that no other clam term requires express construction for the purposes of this decision.

D. Asserted References

Before turning to Petitioner's asserted grounds, we provide an overview of the asserted references.

1. Keystone (Ex. 1003)

Keystone describes the results of a dose-ranging study to investigate the clinical efficacy and safety of adalimumab, administered subcutaneously in combination with methotrexate, to RA patients. Ex. 1003, A481. Patients in the study were randomized to receive placebo or adalimumab at 20, 40, or

80 mg every other week. *Id.* The investigators conclude that "adalimumab (D2E7), in addition to [methotrexate] in patients with longstanding RA is significantly better than placebo when given every other week subcutaneously." *Id.*

2. Lorenz (Ex. 1028)

Lorenz discloses that experimental data has suggested the "central role" of TNFα in initiating and/or perpetuating inflammatory processes in RA and other chronic inflammatory diseases, noting that such data "has been clearly verified by the overwhelming success of TNF-α-targeted therapies." Ex. 1028, S17. Lorenz continues that "a lot of enthusiasm has been put into the development of further strategies aimed at blocking TNF-α with new and innovative drugs. . . . Furthermore, new indications for TNF-α-targeted treatment are forthcoming." *Id.* Such developments "may include additional clinical trials with the established agents, or clinical studies with new TNF-α-targeting immunobiologicals, such as the human D2E7 antibody [i.e., adalimumab]." *Id.* at S18.

Lorenz further describes studies directed to new indications for TNFα-targeting therapies, including for patients with psoriasis and PsA. *Id.* at S18–S19. According to Lorenz, psoriasis is reported in 1–3% of adults in the United States, with PsA occurring in approximately 6–20% of psoriasis patients. *Id.* at S18. PsA patients have increased amounts of TNFα in T lymphocytes and macrophages, as well as elevated TNFα levels in synovial fluid, tissue, and skin lesions, "with TNF-α levels correlating with disease activity." *Id.* "As a logical consequence, studies with TNF-α-blocking biologicals were initiated[,]" including five studies evaluating whether

infliximab or etanercept were effective at treating psoriasis and PsA. *Id.* at S18–S19.

In the first study with infliximab, nine patients (eight of whom had psoriasis at baseline) received 5 mg/kg of infliximab at weeks 0, 2, and 6. *Id.* at S18. Baseline PASI scores "were significantly improved" after twelve weeks and "clinical improvements in all PsA and psoriasis disease manifestations were maintained over a follow-up period of 1 year." *Id.*

In a second infliximab study, ten patients received 5 mg/kg infliximab at weeks 0, 2, and 6. *Id.* The authors concluded that "infliximab treatment was efficacious and safe in PsA and psoriasis." *Id.* With respect to psoriasis, "mean PASI scores were reduced by 71% at week 10" and six patients "experienced nearly complete clearing of erythematous psoriasis plaques" after ten weeks of infliximab therapy. *Id.* at S18–S19.

In a third study designed to investigate the efficacy of infliximab in psoriasis patients, thirty patients were randomized to receive placebo, 5 mg/kg infliximab, or 10 mg/kg infliximab. *Id.* at S19. Nine out of eleven patients treated with 5 mg/kg infliximab and ten out of eleven patients treated with 10 mg/kg infliximab "achieved good, excellent, or clear ratings on PGA [physician's global assessment]," compared to only two out of ten patients receiving placebo. *Id.* Further, "[a] significantly higher proportion of patients treated with infliximab obtained a 75% improvement in PASI scores compared with placebo." *Id.*

In a first study evaluating etanercept, eight out of ten PsA patients experienced improvement in PGA scores after twelve months of treatment with 25 mg etanercept administered twice weekly. *Id.* at S18. All four patients in the trial with active psoriasis "had significant improvement in

their psoriatic skin lesions, including complete resolution in three patients." *Id.*

In a second etanercept study, 87% of patients receiving etanercept, 25 mg twice weekly via subcutaneous injection, achieved PsA response criteria, compared with 23% of patients receiving placebo. *Id.* at S19. "Of 19 patients in each treatment group with active psoriasis, the median improvement in PASI scores was significantly higher in etanercept-treated patients than in placebo-treated patients," with 26% of psoriasis patients treated with etanercept achieving a 75% improvement, compared with no patients treated with placebo achieving improvement. *Id.* In an extension of that study, "etanercept continued to effectively reduce clinical signs and symptoms of PsA and psoriasis for up to 36 weeks." *Id.*

Lorenz explains that the results of the studies "suggest that TNF-α plays a pivotal role in the pathogenesis of PsA and psoriasis. In addition, anti-TNF-α therapy offers patients with PsA and psoriasis a new therapeutic option for the control of their disease." *Id.*

3. Mease 2000 (Ex. 1017)[7]

Mease 2000 describes a clinical trial involving treating PsA and psoriasis patients with etanercept. *See generally* Ex. 1017. Mease 2000 explains that etanercept "functions by inhibiting [TNFα], a proinflammatory cytokine that is involved in many inflammatory disorders," including PsA and psoriasis. *Id.* at 385. Mease 2000 discloses that TNFα inhibition with etanercept "has previously been shown to diminish the activity in [RA]" and

[7] Mease 2000 is one of the etanercept studies that Lorenz discloses and describes. Ex. 1028, S19.

that the study "was undertaken to assess the benefit of etanercept" in treating PsA and psoriasis. *Id.*

The study assessed the efficacy and safety of etanercept, with 60 patients randomized to receive either placebo or etanercept at a dose of 25 mg administered twice weekly via subcutaneous injection for twelve weeks. *Id.* at 385–386. The median duration of psoriasis was 18 years for all patients and 20 years for the 38 patients with evaluable psoriasis (≥ 3% of body surface area involvement). *Id.* at 387, 388. Psoriasis efficacy endpoints included improvement in the PASI score and improvement in prospectively-identified individual target lesions (assessed for plaque elevation, scaling and erythema). *Id.* at 385–386. The primary endpoint with respect to efficacy in psoriasis was the proportion of patients achieving a 75% improvement in PASI score from baseline to twelve weeks. *Id.* at 386–387.

The trial determined that etanercept was effective in improving the skin lesions of the psoriasis patients, with 26% of patients in the etanercept group achieving a 75% improvement in PASI at 12 weeks, compared with no patients in the placebo group. *Id.* at 388. Mease 2000 concludes that the trial results indicate that blocking TNFα in both PsA and psoriasis "offers patients with [PsA] and psoriasis a new therapeutic option for control of their disease." *Id.* at 385; *see id.* at 389.

4. Chaudhari (Ex. 1036)[8]

Chaudhari explains that psoriasis affects 1–3% of the United States and European population and about 25% of patients have moderate to severe

[8] Chaudhari is one of the infliximab studies that Lorenz discloses and describes. Ex. 1028, S19.

disease. Ex. 1036, 1842. The treatments available for moderate to severe psoriasis "are either incompletely effective in some patients or are associated with serious toxic effects. There is therefore a need for highly efficacious treatments that are safe to use in a long-term regimen." *Id.*

Chaudhari discloses that TNFα plays a potential role in both of the major pathological lesions in psoriasis. *Id.* "Consequently, blockade of TNF-α activity should, in theory, reduce inflammation and keratinocyte proliferation and differentiation abnormalities in psoriasis." *Id.* The scientific rationale for blocking TNFα in psoriasis and the authors' anecdotal experience with infliximab in psoriatic patients led to the trial of infliximab in patients with moderate to severe psoriasis. *Id.* at 1843.

The study assessed the safety and efficacy of infliximab, with 33 patients having moderate to severe plaque psoriasis (involving at least 5% of the body surface area) randomized to receive either placebo or infliximab dosed at 5 or 10 mg/kg at weeks 0, 2, and 6. *Id.* at 1843. The primary efficacy endpoint was the PGA at week 10, with a positive response defined as attaining a good (50–74% clearing with moderate improvement), excellent (75–99% clearing with striking improvement), or clear (100% clearing) rating. *Id.* A secondary endpoint was the PASI, with a positive response defined as at least 75% improvement from the baseline PASI score. *Id.*

Chaudhari discloses that patients who received infliximab experienced a higher degree of clinical benefit, with 82% of responders achieving an excellent or clear rating on the PGA and at least 75% improvement in PASI score from baseline. "There did not seem to be any clinically important difference between the infliximab 5 and 10 mg/kg doses with regard to

efficacy. Infliximab was well tolerated by all study participants." *Id.* at 1845; *see id.* at 1844 (setting forth study results in greater detail). Chaudhari concludes that the study results "suggest that TNF-α has a pivotal role in the pathogenesis of psoriasis." *Id.* at 1842. Chaudhari also concludes that although "the precise pathways" infliximab blocks in psoriasis patients "remain to be established," "some combination of inflammatory downregulation mechanisms seen in infliximab-treated patients with [RA] . . . also contributes to the benefit seen in the treatment of psoriasis with infliximab." *Id.* at 1846.

E. Asserted Obviousness over the Combination of Keystone, Lorenz, and Chaudhari or Keystone, Mease 2000, and Chaudhari

Petitioner asserts that claims 1, 4, 7, 10, 13, 16, and 19 of the '689 patent are unpatentable under 35 U.S.C. § 103(a) because the subject matter of those claims would have been obvious over the combination of: (1) Keystone, Lorenz, and Chaudhari; or (2) Keystone, Mease 2000, and Chaudhari. Pet. 27–64. Petitioner's arguments for both grounds are substantively similar, except that Petitioner replaces the teachings of Lorenz with the teachings of Mease 2000 "in the event that [Patent Owner] obtains the benefit of the July 19, 2002 filing date." *Id.* at 50. Patent Owner opposes, addressing both asserted grounds together. Prelim. Resp. 16–46. Accordingly, we address both grounds together. Having considered the arguments and evidence before us, for the reasons set forth below, we find that Petitioner establishes a reasonable likelihood of prevailing on its asserted grounds.

1. Whether Certain Background References Qualify as Prior Art

As a preliminary matter, Patent Owner asserts that Petitioner fails to show that certain background references qualify as prior art printed

publications. Prelim. Resp. 43–46 (referring to Ex. 1006; Ex. 1026; Ex. 1034; Ex. 1049). Patent Owner contends that "[e]ven for [] alleged 'background references,' Petitioner still must meet its burden of making a threshold showing that each alleged prior art reference was available as a printed publication." *Id.* at 43 (citing *Coal. for Affordable Drugs IV LLC v. Pharmacyclics, Inc.*, Case IPR2015-01076, Paper 33, 5–6 (PTAB Oct. 19, 2015) ("*Pharmacyclics*")).

Contrary to Patent Owner's argument, however, the *Pharmacyclics* decision does not address whether a petitioner must show that background references were available as prior art printed publications. *See Pharmacyclics*, Paper 33, 5–6. Rather, the decision addresses whether a petitioner made a sufficient threshold showing under 35 U.S.C. § 311(b) that the references in its *asserted grounds* were "prior art consisting of patents or printed publications" where the petitioner "relie[d] on a copy of a webpage to challenge the claims of the [] patent." *Id.* at 5.

Nevertheless, Patent Owner raises a factual issue regarding Petitioner's background references. For purposes of this decision, we find that Petitioner establishes a reasonable likelihood of prevailing without reference to the background references that Patent Owner contends fail to qualify as prior art printed publications,[9] or Petitioner's arguments and expert testimony regarding such references. We invite the parties to address in Patent Owner's Response and Petitioner's Reply whether a petitioner

[9] Notably, Patent Owner relies on one of those background references—the Enbrel Label (Ex. 1006)—to support its argument that Petitioner fails to make a sufficient showing with regard to its challenges to claims 16 and 19. Prelim. Resp. 38–39 (citing Ex. 1006, 11–12 as reflecting that a PASI 75 score is a difficult target to achieve).

must show that background references demonstrating the knowledge and perspective of the person of ordinary skill in the art qualify as prior art printed publications. We encourage the parties to address the issue in view of Federal Rule of Evidence 703, which provides that "[a]n expert may base an opinion on facts or data in the case that the expert has been made aware of" and that "[i]f experts in the particular field would reasonably rely on those kinds of facts or data in forming an opinion on the subject, they need not be admissible for the opinion to be admitted."

2. Claims 1 and 7

For both asserted grounds, Petitioner argues that the "only difference" between Keystone and the dosing regimen recited in claims 1 and 7 is that the claimed dosing regimen recites treating "moderate to severe chronic plaque psoriasis" instead of treating RA. Pet. 41; *see id.* at 50 (citing Ex. 1003, A481). Petitioner further contends that either Lorenz or Mease 2000, in combination with Chaudhari, disclose or suggest that 40 mg of adalimumab administered subcutaneously every other week would effectively treat moderate to severe psoriasis. *Id.* at 41–43, 50–51 (referring to Petition §§ VI.C.5–V.I.C.6 and citing Ex. 1002 ¶ 46; Ex. 1012 ¶ 63; Ex. 1017, 385, 389; Ex. 1028, S18–S19; Ex. 1036, 1842–46). Petitioner points to, *inter alia*: (1) Lorenz's prediction that adalimumab could be used to treat inflammatory diseases such as RA, PsA, and psoriasis (*id.* at 41); (2) Lorenz's discussion of the clinical trial successes using TNFα inhibitors infliximab and etanercept to treat psoriasis, including moderate to severe chronic plaque psoriasis (*id.*); (3) Chaudhari's disclosures that the TNFα inhibitor infliximab was effective in treating patients with moderate to severe plaque psoriasis (*id.* at 40, 50–51); and (4) Mease 2000's teaching

that the TNFα inhibitor etanercept was effective in treating patients with psoriasis (*id.* at 50–51). *See also id.* at 57–60 (claim charts).

At this stage of the proceeding, Patent Owner does not contest Petitioner's arguments or evidence that the asserted references collectively teach or suggest each limitation of claims 1 and 7. We find, on the current record, that Petitioner shows sufficiently that Keystone, Lorenz, and Chaudhari, or Keystone, Mease 2000, and Chaudhari disclose each limitation of those claims.

The nub of the parties' dispute at this stage of the proceeding centers on whether Petitioner shows sufficiently that one of ordinary skill in the art: (a) would have had a reasonable expectation of success in using adalimumab to treat moderate to severe chronic plaque psoriasis; and (b) a reason to use, or a reasonable expectation of success in using, 40 mg adalimumab administered every other week to treat moderate to severe chronic plaque psoriasis. We address both of those issues below.

a. Reasonable expectation of success in using adalimumab to treat moderate to severe chronic plaque psoriasis

With respect to a reasonable expectation of success in using adalimumab to treat moderate to severe chronic plaque psoriasis, Petitioner asserts that the prior art taught that adalimumab was a prime candidate to treat moderate to severe chronic plaque psoriasis. Pet. 30, 41. Specifically, Petitioner points to Lorenz's disclosure of adalimumab (D2E7) as one of the new TNFα inhibitors for treating chronic inflammatory diseases mediated by TNFα. *Id.* at 30 (citing Ex. 1028, S17–18). Petitioner also argues that Lorenz "restated the known relationship between TNF-α and [psoriasis] and PsA: 'TNF-α plays a pivotal role in the pathogenesis of PsA and psoriasis.'" *Id.* (citing Ex. 1028, S19). Petitioner further relies on Lorenz's conclusion

that "anti-TNF-α therapy offers patients with PsA and psoriasis a new therapeutic option for the control of their disease" and Lorenz's statements identifying adalimumab, infliximab, and etanercept as anti-TNFα therapies available to treat chronic inflammatory disorders. *Id.* at 30–31 (citing Ex. 1028, S17–S19). Based on such disclosures, Petitioner contends that "a [person of ordinary skill in the art] reading Lorenz would clearly understand that adalimumab was an obvious therapeutic agent for the treatment of PsA and [psoriasis]." *Id.* at 41 (citing Ex. 1002 ¶ 46; Ex. 1012 ¶ 63).

For its asserted ground relying on Mease 2000 instead of Lorenz, Petitioner argues that a person of ordinary skill in the art would have known that adalimumab "was a prime candidate for treating [psoriasis]" based on "(1) Keystone's description of adalimumab's success in treating RA"; and "(2) the teachings of Mease 2000 and Chaudhari that the TNF-α inhibitors etanercept and infliximab were successful in treating RA, [psoriasis], and PsA." *Id.* at 51 (citing Ex. 1002 ¶ 121; Ex. 1012 ¶ 95); *see also id.* at 50 (describing the disclosures of Mease 2000 and Chaudhari).

Patent Owner responds that the asserted art fails to disclose that adalimumab would treat moderate to severe chronic plaque psoriasis. *Id.* at 17–20. Patent Owner notes that Keystone—the only asserted reference disclosing an adalimumab dosing regimen—is not directed to treating moderate to severe psoriasis (or any form of psoriasis), but rather, to treating RA. *Id.* at 17. Patent Owner further asserts that "Keystone also does not disclose or suggest how adalimumab's distribution to the affected tissue of [RA] (a joint disease) would be predictive of the distribution of adalimumab to the affected tissues of moderate-to-severe-chronic plaque psoriasis (a skin disease)." *Id.* Patent Owner makes similar arguments about distribution in

skin affected by moderate to severe chronic plaque psoriasis with respect to Chaudhari's, Lorenz's, and Mease 2000's disclosures of clinical trials in which patients received infliximab and/or etanercept to treat psoriasis. *Id.* at 17–20. Patent Owner also asserts that Petitioner fails to address any pharmacokinetic differences between adalimumab, infliximab, and etanercept. *Id.* at 19.

We are not persuaded, on the current record, that Petitioner's failure to address the distribution, activity, or pharmacokinetics of the different TNFα inhibitors negates a showing of reasonable expectation of success in using adalimumab to treat moderate to severe chronic plaque psoriasis. Although Patent Owner appears to argue that such information would have been important to the ordinarily skilled artisan in predicting whether adalimumab would be successful in treating moderate to severe psoriasis, Patent Owner does not direct us to evidence in the current record to support such an argument.

Rather, as Petitioner argues and Drs. Helfgott and Plott testify, the current record indicates that a person of ordinary skill in the art: (1) knew that TNFα was implicated in the pathogenesis of chronic inflammatory diseases, including RA and psoriasis (Pet. 27–28; Ex. 1002 ¶¶ 59–64; Ex. 1012 ¶ 40); (2) were using TNFα inhibitors, such as infliximab and etanercept, to treat RA and to treat psoriasis based on the known role of TNFα in those conditions (Pet. 29–30; Ex. 1002 ¶¶ 65–71; Ex. 1012 ¶ 41); and (3) would have predicted success in using adalimumab—one of the handful of TNFα inhibitors already known to treat RA—in treating moderate to severe chronic plaque psoriasis based on the successes of infliximab and etanercept in treating both RA and psoriasis (Pet. 30; Ex. 1002 ¶¶ 73, 75–76;

Ex. 1012 ¶¶ 62–63, 65–66). For example, Chaudhari discloses that "TNFα is pivotal in the pathogenesis of psoriasis," describes a study finding that infliximab was effective in treating patients with moderate to severe chronic plaque psoriasis, and explains that "some combination of inflammatory downregulation mechanisms seen in infliximab-treated patients with [RA] . . . also contribute[] to the benefit seen in the treatment of psoriasis with infliximab." Ex. 1036, 1846. Further, Mease 2000 teaches that TNFα inhibition with etanercept "has previously been shown to diminish the activity of [RA]" and finds similar diminished activity when patients with psoriasis received the same doses of etanercept. Ex. 1017, 385, 389. Similarly, Lorenz provides a review of clinical studies (including the studies that Chaudhari and Mease 2000 describe) in which infliximab and etanercept—already known to be effective in treating RA—were shown to be effective in treating psoriasis and suggests that other known TNFα inhibitors, such as adalimumab, would provide encouraging results in similar studies. Ex. 1028, S17–19.

Patent Owner next argues that Lorenz and Mease 2000 do not disclose treating moderate to severe chronic plaque psoriasis with any TNFα inhibitor. Prelim. Resp. 20–24. In that regard, Patent Owner contends that "Lorenz and Mease 2000 disclose using etanercept or infliximab to treat PsA patients with just 'psoriasis,' and neither Petitioner nor its declarants establish that this disclosure of 'psoriasis' teaches or suggests the claimed moderate-to-severe chronic plaque psoriasis." *Id.* at 20–21. Patent Owner further contends that "Petitioner cannot establish a reasonable expectation of success by focusing on references that are not directed to the 'highly desired goal' of treating moderate-to-severe chronic plaque arthritis." *Id.* at 21

(citations omitted). Patent Owner makes similar arguments regarding several of Petitioner's background references. *See id.* at 24–27.

Such arguments are part of a larger assertion Patent Owner makes regarding the limitation "moderate to severe chronic plaque psoriasis." Specifically, Patent Owner argues that "by failing to construe 'moderate-to-severe chronic plaque psoriasis,' Petitioner has provided no framework for analyzing [references that] non-specifically refer to treating patients with 'psoriasis'" and has "fail[ed] to establish any reasonable expectation of success for treating moderate-to-severe chronic plaque psoriasis based on these references." Prelim. Resp. 15–16.

At this stage of the proceeding, we do not find Petitioner's failure to set forth an express claim construction for the limitation "moderate to severe chronic plaque psoriasis" to be fatal to the asserted grounds. Petitioner asserts generally that the limitations of the challenged claims "should . . . be given their broadest reasonable interpretation." Pet. 15. As Patent Owner explains, Dr. Helfgott and Dr. Plott testify that the '689 patent explains that patients with "moderate to severe chronic plaque psoriasis" have "marked plaque elevation, scaling, and/or erythema." Ex. 1002 ¶ 22; *see id.* ¶ 29; Ex. 1012 ¶ 19. Dr. Plott further testifies that "when practitioners refer to 'psoriasis' in isolation, they generally mean plaque psoriasis," and that the term "psoriasis" generally includes moderate to severe chronic plaque psoriasis. Ex. 1012 ¶ 30 n.3; *see id.* ¶ 31. And Dr. Helfgott testifies—consistent with Dr. Plott's testimony—that the term "psoriasis" "refers to chronic plaque psoriasis, including moderate to severe chronic plaque psoriasis." Ex. 1002 ¶ 30 n.4. This testimony, which is uncontested on the present record, indicates that a person of ordinary skill in the art would have

understood references in the prior art to patients with "psoriasis" to include patients with moderate to severe chronic plaque psoriasis.

Further, despite acknowledging that Chaudhari refers to treating patients with moderate to severe chronic plaque psoriasis, Patent Owner's argument fails to account for that disclosure. Prelim. Resp. 22; *see id.* at 28 (recognizing that Chaudhari is directed to treating moderate to severe chronic plaque psoriasis). In other words, Patent Owner appears to attack Lorenz and Mease 2000 individually, which is not persuasive because "the test for obviousness is what the combined teachings of the references would have suggested to those having ordinary skill in the art." *In re Mouttet*, 686 F.3d 1322, 1333 (Fed. Cir. 2012) (citing *In re Keller*, 642 F.2d 413, 425 (CCPA 1981)).

Given the foregoing, and based on the current record, we find that Petitioner establishes sufficiently that a person of ordinary skill in the art would have had a reasonable expectation of success in using adalimumab to treat moderate to severe chronic plaque psoriasis.

b. Reason to treat moderate to severe chronic plaque psoriasis with the claimed dosing regimen with a reasonable expectation of success

Petitioner asserts that a person of ordinary skill in the art would have had a reason to use the known 40 mg every other week adalimumab dosing regimen to treat moderate to severe chronic plaque psoriasis given: (1) TNFα's role in the pathogenesis of both RA and psoriasis; (2) the use of TNFα inhibitors infliximab and etanercept to treat both RA and psoriasis with the same doses and dosing regimens; and (3) adalimumab's known potential for treating psoriasis. Pet. 2, 31–35, 43–46 (citing Ex. 1002 ¶¶ 59–72, 98–102, 122; Ex. 1004, 6; Ex. 1005, 1554; Ex. 1012 ¶¶ 76–78, 95–96; Ex. 1017, 385–389; Ex. 1027, 1085; Ex. 1033, 587–589; Ex. 1036, 1843–45;

Ex. 1037, 429, 432; Ex. 1040, 2206, 2208; Ex. 1050, 128). Petitioner further contends that the numerous prior art references demonstrating the successful treatment of psoriasis with the same infliximab and etanercept doses that had been used to treat RA would have provided the ordinarily skilled artisan with a reasonable expectation of success in treating moderate to severe chronic plaque psoriasis with the claimed dosing regimen. *Id.* at 44–46; *see id.* at 27–35, 39.[10]

Patent Owner responds that Petitioner fails to support its rationale or reasonable expectation of success in using "the approved" RA dose of 40 mg adalimumab every-other-week to treat moderate to severe chronic plaque psoriasis because Petitioner's "asserted and cited references taught using *higher* doses than approved for [RA] to treat moderate-to-severe chronic plaque psoriasis." Prelim. Resp. 27. In that regard, Patent Owner contends that, contrary to Petitioner's argument, patients in Chaudhari's study received infliximab doses of 5 mg/kg or 10 mg/kg, "which are *66% to 233% higher* than the infliximab dose approved to treat [RA] (3 mg/kg)." *Id.* at 28 (citing Ex. 1036, 1842; Ex. 1027, 1087). Thus, argues Patent Owner, to the extent that one of ordinary skill in the art would have considered infliximab's dosing regimen for RA and psoriasis as predictive of adalimumab's dosing, Chaudhari would have led a person of ordinary skill in the art to test a higher dose for treating psoriasis. *Id.* at 28–29. Patent

[10] Petitioner also points to small molecule drugs that Petitioner contends were used to treat both RA and psoriasis at the same or similar doses and dosing regimens to support a reasonable expectation of success. Pet. 35–37. We agree with Patent Owner, however, that such evidence is less relevant on the current record because those drugs are not biologic TNFα inhibitors. *See* Prelim. Resp. 36.

Owner further argues that Chaudhari's use of the higher infliximab dose to treat psoriasis as compared to RA also does not support any reasonable expectation of success in using the same dose of adalimumab to treat both diseases. *Id.* at 29. Similarly, Patent Owner argues that Petitioner's background references also disclose using higher doses to treat moderate to severe chronic plaque psoriasis than approved to treat RA. *Id.* at 34–35.

Patent Owner's arguments appear to assume that the Food and Drug Administration ("FDA") approved dose is the only dosing information that would have been relevant to an ordinarily skilled artisan. An obviousness inquiry, however, is not limited to what has gained or could gain FDA approval. *Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1326 (Fed. Cir. 2017). Indeed, a reason to use a particular dosing regimen "may be found in many different places and forms; it cannot be limited to those reasons the FDA sees fit to consider in approving drug applications." *Id.* (quoting *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013)).

Here, Petitioner shows sufficiently on the current record that a person of ordinary skill in the art would have had a reason to use the same dose of adalimumab to treat both RA and moderate to severe chronic plaque psoriasis based on the prior art's disclosure of using the same or similar doses and dosing regimens to effectively treat both disorders. *See* Pet. 31–35, 42–43. For example, Petitioner directs us to the 2001 Remicade Package Insert,[11] which discloses a dosing regimen of 3 mg/kg infliximab administered at weeks 0, 2, and 6, then every 4 or 8 weeks thereafter in

[11] PHYSICIANS' DESK REFERENCE, Remicade entry, 1085–1088 (55th ed. 2001) (Ex. 1027).

combination with methotrexate to treat RA. Pet. 31, 34 (both citing Ex. 1027, 1087). Petitioner and its experts also point to a 2002 study by Marzo-Ortega,[12] which was designed to assess whether infliximab was effective in treating psoriasis at the same dose that was effective in treating RA, i.e., the 3 mg/kg dose (administered in combination with methotrexate) that the Remicade Package Insert discloses. Pet. 32, 33 (citing Ex. 1004, 6[13]); *see also* Ex. 1002 ¶¶ 79–82 (Dr. Helfgott's testimony regarding the prior art use of 3 mg/kg infliximab to treat RA and psoriasis); Ex. 1012 ¶¶ 43–47 (Dr. Plott's testimony regarding the prior art use of 3 mg/kg infliximab to treat RA and psoriasis). Marzo-Ortega determined that 3 mg/kg infliximab was effective at treating psoriasis, and explained that the reduced infliximab dose "also has considerable cost-saving implications." Ex. 1004, 6.

Petitioner also relies on studies showing that other doses of infliximab were effective in treating both RA and psoriasis. Pet. 31, 35. Petitioner points to additional data from the study disclosed in the Remicade Package Insert showing that 10 mg/kg of infliximab administered at weeks 0, 2, and 6, then every 4 or 8 weeks thereafter in combination with methotrexate was effective at treating RA. Pet. 31, 35; *see* Ex. 1002 ¶ 88; Ex. 1027, 1087 (Fig. 1). And Petitioner directs us to Chaudhari, which discloses that 10 mg/kg of infliximab administered at weeks 0, 2, and 6 successfully treated psoriasis. Pet. 31, 35; *see, e.g.*, Ex. 1036, 1842 ("patients receiving

[12] H Marzo-Ortega et al., *Infliximab is Effective in the Treatment of Resistant Psoriatic Arthritis & Skin Psoriasis: a Clinical and MRI Study*, 41 (Suppl. 1) RHEUMATOLOGY OP11 (2002) (Ex. 1004).
[13] We refer to the page numbers that Petitioner added to the exhibit instead of the exhibit's original page numbers.

the anti-TNF-α agent infliximab as monotherapy experienced a high degree of clinical benefit . . . in the treatment of moderate to severe plaque psoriasis"); *see also* Ex. 1002 ¶¶ 83–88 (testimony regarding additional prior art studies using 5 or 10 mg/kg infliximab to treat RA and psoriasis).

Petitioner further relies on Mease 2000, which investigated whether a dosing regimen of etanercept that was effective at treating RA, i.e., 25 mg, administered twice weekly, was also effective at treating psoriasis. Pet. 33–34. Mease 2000 determined that "[e]tanercept was also effective in improving the skin lesions of psoriasis in the trial," with 26% of patients in the etanercept group achieving a 75% improvement in PASI at 12 weeks, compared with no patients in the placebo group. Ex. 1017, 386, 388; *see* Ex. 1002 ¶¶ 91, 93; Ex. 1012 ¶¶ 55, 57.

Patent Owner argues that the differences between RA and psoriasis would have suggested using higher doses of drug to treat moderate to severe chronic plaque psoriasis than were used to treat RA. Prelim. Resp. 31–33. Patent Owner's arguments in that regard may have potential merit but, on the current record, the conclusions Patent Owner draws from the prior art disclosures regarding sites affected by RA as compared to psoriasis and the differing TNFα burdens associated with the two disorders rest only on attorney argument, which has little probative value. *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997).

At this stage of the proceeding and based on the current record, we find that Petitioner establishes sufficiently that a person of ordinary skill in the art would have had a reason to treat moderate to severe chronic plaque psoriasis with 40 mg adalimumab administered every other week and a reasonable expectation of success in treating the psoriasis with that dosing

regimen. Accordingly, Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the subject matter of claims 1 and 7 would have been obvious over the combination of Keystone, Lorenz, and Chaudhari or Keystone, Mease 2000, and Chaudhari.

3. Claims 4, 10, and 13

Petitioner asserts that the subject matter of dependent claims 4, 10, and 13 would have been obvious over the combined teachings of Keystone, Lorenz, and Chaudhari, or Keystone, Mease 2000, and Chaudhari. Pet. 46–47, 49 (citing Ex. 1002 ¶¶ 104, 125; Ex. 1003, A481; Ex. 1036, 1843); *see also id.* at 60–61 (claim charts). At this stage of the proceeding, Patent Owner does not address separately Petitioner's arguments directed to claims 4, 10, and 13. Having considered Petitioner's arguments, and based on our review of the present record, we are persuaded that Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the subject matter of those claims would have been obvious over Keystone, Lorenz, and Chaudhari, or Keystone, Mease 2000, and Chaudhari.

4. Claims 16 and 19

Claims 16 and 19 depend from claim 7 and additionally require that the "patient has both psoriasis and psoriatic arthritis." Claims 16 and 19 also recite clinical endpoints or efficacy requirements; namely, that the patient "achieves at least a 75% reduction in [PASI] score at week 12 of the treatment" (claim 16) or that the patient "achieves at least a [PGA] score of clear or almost clear at week 12 of the treatment" (claim 19). Petitioner asserts that the subject matter of dependent claims 16 and 19 would have been obvious over the combined teachings of Keystone, Lorenz, and

Chaudhari, or Keystone, Mease 2000, and Chaudhari. Pet. 47–49, 61–64 (claim charts).

With respect to the requirement that the patient has both psoriasis and PsA, Petitioner asserts that a person of ordinary skill in the art would have reasonably expected the claimed dosing regimen to treat patients with psoriasis, including the subset of psoriasis patients having PsA "for all of the same reasons that a [person of ordinary skill in the art] would reasonably expect a TNF-α inhibitor that treats RA to treat [moderate to severe chronic plaque psoriasis] using the same dose and dosing regimen." *Id.* at 47. Citing Lorenz, Petitioner further argues that treating psoriasis patients with the claimed method would inherently treat the percentage of psoriasis patients, i.e., 6–20%, that also have PsA. *Id.* (citing Ex. 1028, S18). Petitioner also points to Lorenz's disclosure of the Mease 2000 study and its finding that etanercept treated psoriasis in patients with PsA. *Id.* at 47–48 (citing Ex. 1028, S19; Ex. 1017).

At this stage of the proceeding, Patent Owner does not separately contest Petitioner's showing with regard to the claim 16 and claim 19 requirement that the patient have both psoriasis and PsA. Having considered Petitioner's arguments, and based on our review of the present record, we are persuaded that Petitioner shows sufficiently that the prior art discloses that limitation of claims 16 and 19, and that a person of ordinary skill in the art would have had a reasonable expectation of treating psoriasis and PsA with the claimed dosing regimen. *See supra* § III.E.2.

With respect to the clinical endpoints or efficacy requirements, Petitioner asserts that both are the obvious result of anti-TNFα therapy, citing Chaudhari's reported PASI and PGA scores for patients receiving

infliximab to treat psoriasis as support. *Id.* at 48 (citing Ex. 1036, 1844). Petitioner also directs us to Dr. Helfgott's and Dr. Plott's testimony that the recited clinical endpoints "are the obvious result of successful TNF-α blockade and adalimumab, like infliximab, was known in the prior art to successfully block TNF-α at the claimed dosing regimen of 40 mg [every other week]." *Id.* at 48 (citing Ex. 1002 ¶¶ 112–113, 133–134; Ex. 1012 ¶¶ 85–87, 103–105). Petitioner further asserts that the '689 patent explains that the recited endpoints are the inherent result of administering the claimed dosing regimen to psoriasis patients, because the results are achieved without the need for additional steps. *Id.* at 48–49 (citing Ex. 1001, 41:11–42:30).

Patent Owner responds that Petitioner fails to establish a reasonable likelihood that claims 16 and 19 are unpatentable under either theory. Prelim. Resp. 37. As to Petitioner's arguments regarding Chaudhari, Patent Owner repeats the argument that Chaudhari's study used higher doses of infliximab as compared to the approved dose for RA. *Id.* at 37 (citing *id.* § VIII.B.1; Ex. 1036, 4). At this stage of the proceeding, and on the current record, we find that Petitioner shows sufficiently that the clinical endpoints claims 16 and 19 require would have been obvious based on Chaudhari's disclosure for the same reasons set forth above in § III.E.2.b.

Regarding Petitioner's inherency theory, Patent Owner asserts that "Petitioner fails to establish, however, that the efficacy limitations are *necessarily present* at week 12, and thus fails to prove inherency." Prelim. Resp. 39. As support, Patent Owner points to Dr. Helfgott's and Dr. Plott's testimony that some portion of treated patients achieve the recited clinical endpoints. *Id.* (citing Ex. 1002 ¶¶ 113, 134; Ex. 1012 ¶¶ 86, 104). We find

that Patent Owner's arguments in this regard implicate claim interpretation with respect to the recited clinical endpoints, which the parties do not address in the Petition or Preliminary Response. That is, Patent Owner appears to argue that claims 16 and 19 require every patient receiving the claimed dosing regimen to achieve the recited clinical endpoints, whereas Petitioner appears to argue that the claims require nothing more than administering the claimed dosing regimen or, if the claims require more, they do not require every patient to achieve the recited clinical endpoints. *See id.* at 39; Pet. 48–49, 63 (pointing to the '689 patent's disclosure that 49% of patients receiving 40 mg of adalimumab every other week achieved a PGA score of "clear or almost clear" (Ex. 1001, 42:5–8)). We find that the parties' dispute is best resolved during trial based upon review of the entire record, and we invite Patent Owner and Petitioner to further address the issue in Patent Owner's Response and Petitioner's Reply. Accordingly, on the present record, Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the subject matter of claims 16 and 19 would have been obvious over the combination of Keystone, Lorenz, and Chaudhari, or Keystone, Mease 2000, and Chaudhari.

IV. CONCLUSION

Taking account of the information presented in the Petition and the Preliminary Response, and the evidence of record, we determine that Petitioner establishes a reasonable likelihood that it will prevail in showing that claims 1, 4, 7, 10, 13, 16, and 19 of the '689 patent are unpatentable. Our findings and conclusions are not final and may change after considering the full record developed during trial.

V. ORDER

It is hereby

ORDERED that the Petition is granted and an *inter partes* review is instituted as to:

Claims 1, 4, 7, 10, 13, 16, and 19 under 35 U.S.C. § 103 over the combination of Keystone, Lorenz, and Chaudhari; and

Claims 1, 4, 7, 10, 13, 16, and 19 under 35 U.S.C. § 103 over the combination of Keystone, Mease 2000, and Chaudhari; and

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

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