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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 IPR2017-02106
Patent 9,067,992 B2

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, 2, and 5–7 of U.S. Patent No. 9,067,992 B2 ("the '992 patent," Ex. 1001). Paper 1 ("Pet."). AbbVie Biotechnology Ltd. ("Patent Owner") filed a Preliminary Response. Paper 12 ("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, 2, and 5–7 (collectively, the "challenged claims") of the '992 patent.

II. BACKGROUND

A. Related Matters

The parties do not identify any litigation or other Office proceedings involving the '992 patent. *See* Pet. 3; Paper 6, 1. Petitioner identifies litigation involving one or more patents that are related to the '992 patent, captioned *AbbVie Inc. v. Amgen Inc.*, No. 1:16-00666-cv-MSG (D. Del. Aug. 4, 2016). Pet. 3.

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 '992 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.* at 4–5. Petitioner further notes that it filed concurrently with this proceeding a petition challenging U.S. Patent No. 9,090,689, "which claims priority to the same applications to which the '992 patent claims priority." *Id.* at 5.

Patent Owner further identifies a number of United States patent applications to which the '992 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 '992 patent. Paper 6, 1–2.

B. The '992 Patent

The '992 patent, titled "Use of TNFα Inhibitor for Treatment of Psoriatic Arthritis," issued on June 30, 2015. Ex. 1001, [45], [54]. The '992 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 20:60–21:1. 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 22:20–26. 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 22:26–29. The '992 patent identifies rheumatoid arthritis ("RA") and

psoriatic arthritis ("PsA") as "disorder[s] in which TNFα activity is detrimental. *Id.* at 3:4–11.

In one embodiment, the TNFα inhibitor is used to treat erosive polyarthritis associated with psoriatic arthritis ("PsA"). *Id.* at 24:20–24. PsA "refers to chronic inflammatory arthritis which is associated with psoriasis, a common chronic skin condition that causes red patches on the body." *Id.* at 24:45–47. "About 1 in 20 individuals with psoriasis will develop arthritis along with the skin condition, and in about 75% of cases, psoriasis precedes the arthritis." *Id.* at 24:47–50. PsA ranges from mild to severe arthritis and usually affects the fingers and the spine. *Id.* at 24:50–52.

The written description discloses methods for determining the efficacy of the TNFα inhibitor in treating PsA, which include "any assay which measures the degree of joint destruction, including joint space narrowing and/or joint erosion," such as radiography. *Id.* at 26:39–44. "Additional improvements in arthritic conditions, such as [RA and] PsA . . . may be determined by measuring the ACR response."[1]

The '992 patent exemplifies a study to determine the efficacy of adalimumab for treating erosive polyarthritis in patients with PsA. *Id.* at

[1] According to the '992 patent, the American College of Rheumatology ("ACR") responses—ACR20, ACR50, and ACR70—define improvement in RA and PsA and indicate the percentage of improvement (20%, 50%, or 70%) in seven disease activity measures. *Id.* at 26:54–57. Criteria include the percentage improvement in tender joint count and swollen joint count, as well as improvement of at least three of the following: (1) patient pain assessment, (2) patient global assessment, (3) physician global assessment, (4) patient self-assessed disability, or (5) laboratory measures of disease activity (i.e., erythrocyte sedimentation rate or C-reactive protein level). *Id.* at 26:57–63.

37:18–40:25. Patients with moderate to severely active PsA were randomized to receive either 40 mg adalimumab or placebo subcutaneously every other week for 24 weeks. *Id.* at 37:31–47. Patients who completed the 24-week trial were able to enroll in an open-label extension study, in which all patients received adalimumab every other week. *Id.* at 37:47–49. Patients failing to meet pre-specified criteria after 12 weeks of treatment with open-label therapy were eligible to receive 40 mg weekly. *Id.* at 37:49–51.

Radiographic assessments were performed during the blinded portion of the study at Weeks 0 and 24, and during the open-label portion at Week 48. *Id.* at 37:52–54. At Week 24, adalimumab-treated patients had significantly less progression of structural damage assessed by radiograph than patients treated with placebo. *Id.* at 38:54–57. The study results also indicated that the ACR20, ACR50, and ACR70 responses for the "adalimumab-treated patients at Week 24 were significantly better than placebo." *Id.* at 38:28–31, Table 1. The study results demonstrated that adalimumab "was effective in treating erosive polyarthritis and radiographic disease progression" in patients with PsA. *Id.* at 40:30–33.

C. Illustrative Claims

Of the challenged claims, claims 1 and 2 are independent. Claims 1 and 2 are illustrative of the claimed subject matter and recite:

> 1. A method of treatment of moderate to severe active psoriatic arthritis in adult patients, wherein each said patient has ≥ 3 swollen and ≥ 3 tender joints prior to the treatment and has failed NSAID[2] therapy, comprising subcutaneously administering to each said patient 40 mg of adalimumab every

[2] The term NSAID is short-hand for nonsteroidal anti-inflammatory drug. Ex. 1001, 3:17–18.

> other week, wherein 23% of said patients achieve 70% reduction in American College of Rheumatology (ACR) score at week 24 of the treatment.

Ex. 1001, 55:18–25.

> 2. A method for reducing or inhibiting symptoms in a patient with psoriatic arthritis, comprising subcutaneously administering to said patient 40 mg of adalimumab every other week.

Id. at 55:26–29. Claim 5 depends from claim 2 and recites that the patient "achieves at least a 50% reduction in ACR score at week 24 of the treatment." *Id.* at 56:19–21. Claim 6 depends from claim 5 and recites that the patient "achieves at least a 70% reduction in ACR score at week 24 of the treatment." *Id.* at 56:22–24. Claim 7 depends from claim 2 and recites that the "symptoms are progression of structural damage assessed by radiograph." *Id.* at 56:25–26.

D. The Asserted Grounds of Unpatentability

Petitioner asserts claims 1, 2, and 5–7 of the '992 patent are unpatentable based on the following grounds:

Reference(s)	Asserted Priority Date	Statutory Basis	Claim(s) Challenged
Mease 2004[3]	May 16, 2006	§ 102	1, 5, 6

[3] Philip J. Mease et al., *Adalimumab Therapy in Patients with Psoriatic Arthritis: 24-Week Results of a Phase III Study*, 50 ARTHRITIS & RHEUMATISM 4097 (2004) (Ex. 1056).

Reference(s)	Asserted Priority Date	Statutory Basis	Claim(s) Challenged
Keystone,[4] Lorenz,[5] and Mease 2000[6]	July 18, 2003	§ 103	1, 2, 5–7
Keystone, Mease 2000, and Dechant 2000[7]	July 19, 2002	§ 103	1, 2, 5, 6
Keystone, Mease 2000, Dechant 2000, and Rau[8]	July 19, 2002	§ 103	7

Petitioner supports the Petition with the testimony of Simon Helfgott, M.D. (Ex. 1002).

III. ANALYSIS

We organize our analysis into six sections. First, we discuss briefly the effective filing date of the '992 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 anticipation ground asserted in the Petition meets the threshold showing for instituting an *inter partes*

[4] 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).
[5] Hanns-Martin Lorenz & Joachim R Kalden, *Supplement Review Perspectives for TNF-α-targeting therapies*, 4 (Suppl. 3) ARTHRITIS RES. S17–S24 (2002) (Ex. 1028).
[6] Philip J Mease et al., *Etanercept in the treatment of psoriatic arthritis & psoriasis: a randomised trial*, 356 LANCET 385–390 (2000) (Ex. 1017).
[7] Claudia Dechant et al., *One Year Outcome of Patients with Severe Psoriatic Arthritis Treated with Infliximab*, 43 (Suppl.) ARTHRITIS & RHEUMATISM S102 (2000) (Ex. 1029).
[8] R. Rau et al., *Experience with D2E7*, 25 RHEUMATOLOGY TODAY 83–88 (2000) (Ex. 1021).

review. Sixth, taking account of the information presented, we consider whether the obviousness grounds asserted in the Petition meet the threshold showing for instituting an *inter partes* review.

A. Effective Filing Date of the '992 Patent

The application that issued as the '992 patent, Application No. 14/563,056 ("the '056 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 '992 patent states that the '056 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 '992 patent also claims priority to 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. Ex. 1031, 10 (Corrected Application Data Sheet).

Petitioner asserts that the applicant added new matter to the specification of the '056 application at different times, and the challenged claims, therefore, are entitled to different effective filing dates. Pet. 6. For purposes of this proceeding, Petitioner asserts the following effective filing dates for the challenged claims:

> claims 1, 5, and 6: May 16, 2006—the date Petitioner alleges that the ACR response criteria was first added to the disclosure and to the claims pursuant to continuation-in-part application No. 11/435,844;
>
> claim 2: July 18, 2003—the date Petitioner alleges that the claimed 40 mg adalimumab every other week dosing regimen

> was first added to the disclosure through application No. 10/622,932; and
>
> claim 7: May 16, 2005—the date Petitioner alleges that the recited reduction/inhibition of progression of structural damage assessed by radiograph was first filed with provisional application No. 60/681,645.

Id. at 6–7. Petitioner further contends that the '992 patent is not entitled to the priority date of any of the provisional applications filed before July 18, 2003 "because none [of them] disclose[s] the '40 mg' adalimumab administered 'every other week' PsA dosing regimen" that every claim of the '992 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 claims 1, 2, 5, and 6 are unpatentable as obvious over Keystone, Mease 2000, and Dechant 2000, and claim 7 is unpatentable as obvious over those same references and Rau based on an assumed priority date of July 19, 2002). Petitioner also asserts an alternative challenge to claims 1, 2, 5, 6, and 7 based on an assumed priority date of July 18, 2003. *See, e.g.*, *id.* And Petitioner asserts that claims 1, 5, and 6 are anticipated by Mease 2004 based on an assumed priority date of May 16, 2006. *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. 16. Patent Owner does not address substantively Petitioner's argument that claim 7 is entitled to an effective filing date of May 16, 2005, or that claims 1, 5, and 6

are entitled to an effective filing date of May 16, 2006, but reserves its right to dispute later Petitioner's asserted effective filing dates. *Id.* at 16–17, 49 n.12.

Given that Patent Owner does not dispute Petitioner's alternative use of July 19, 2002 and July 28, 2003 effective filing dates and, further, does not address substantively the effective filing dates of claims 1, 5, 6, and 7, 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 three alternative effective filing dates meet the threshold showing for instituting an *inter partes* review based on anticipation and 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 May 16, 2006, July 18, 2003, or July 19, 2002. *See infra* §§ III.E.–III.F. 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 each of 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 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 PsA and 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 ¶ 25). Petitioner asserts that Dr. Helfgott is an expert in rheumatology and treating PsA, is qualified to provide opinions as to what a person of ordinary skill in the art "would have understood and concluded from the prior art," and is competent to testify in this proceeding. *Id.* at 10 (citing Ex. 1002 ¶¶ 3–15, 24–26).

Patent Owner does not contest that a person of ordinary skill in the art would have the skill set of a physician treating PsA patients or the level of experience that Petitioner asserts the ordinarily skilled artisan would have possessed. Prelim. Resp. 16. Patent Owner, however, 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.* According to Patent Owner, RA experience should be excluded from the definition of a person of ordinary skill in the art. *Id.*

We find Patent Owner's arguments unpersuasive at this stage of the proceeding. First, we note that although the claims of the '992 patent are directed to treating PsA, the '992 patent generally describes disorders in which TNFα activity is detrimental, including PsA and RA, as well as methods of treating those disorders with TNFα inhibitors, including adalimumab. Ex. 1001, 3:5–11, 22:20–26:38. The '992 patent also discloses clinical outcome measures that are the same for both disorders, e.g., ACR outcomes. *Id.* at 26:52–63.

Second, the prior art of record indicates that physicians investigating anti-TNFα therapy for treating PsA 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).

Accordingly, at this stage of the proceeding, we do not exclude RA experience from the level of ordinary skill in the art. We further find, for purposes of this decision, that the prior art itself is sufficient to demonstrate the level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that the prior art, itself, can reflect the appropriate level of ordinary skill in art).

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).

1. Claim 1 and 2 Preambles and "moderate to severe active [PsA]"

Petitioner proposes three phrases for construction: (1) the preamble of claim 1, which recites a "method of treatment of moderate to severe active [PsA]"; (2) the preamble of claim 2, which recites a "method for reducing or inhibiting symptoms in a patient with [PsA]"; and (3) "moderate to severe active [PsA]." Pet. 14–15. In particular, Petitioner argues that the preambles of claims 1 and 2 are statements of intended use and, therefore,

are non-limiting. *Id.* at 14 (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 should be construed, the term "treatment" in the claim 1 preamble "should be given its [broadest reasonable interpretation] of 'reducing the signs and symptoms and/or progression' of 'moderate to severe active [PsA].'" *Id.* Petitioner further contends that we should give the claim 2 preamble "its plain and ordinary meaning of reducing or inhibiting symptoms of PsA without requiring any specific level of therapeutic effect." *Id.* at 14–15 (citing Ex. 1001, 11:20–23, 22:26–29; Ex. 1002 ¶¶ 28–30).

Petitioner also argues that the written description of the '992 patent defines the term "moderate to severe active" PsA to mean that a patient has ≥ 3 swollen and ≥ 3 tender joints, a common definition with which a person of ordinary skill in the art would have been familiar. *Id.* at 15 (citing Ex. 1001, 37:31–33; Ex. 1002 ¶¶ 22, 30).

At this stage of the proceeding, Patent Owner does not contest Petitioner's proposed construction of "moderate to severe active [PsA]". Prelim. Resp. 17. Patent Owner, however, disputes Petitioner's assertion that the preambles of claims 1 and 2 are not limiting. *Id.* at 18. Specifically, Patent Owner argues that both preambles provide antecedent basis for the claims "because they are the only parts of the challenged independent claims that recite [PsA]." *Id.* Moreover, Patent Owner argues that claims 1 and 2 "each refer to the patient recited in the preamble with the phrase 'said patient,' and dependent claim 7 further limits claim 2 with reference to 'said symptoms.'" *Id.*

After having considered the parties' arguments and evidence, we decline to construe the term "moderate to severe [PsA]" because this phrase does not require construction for us to resolve the parties' dispute. Also, we do not need to determine whether the preamble phrases are limiting at this stage of the proceeding 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)).

2. Outcome Limitations of Claims 1, 5, 6, and 7

Patent Owner proposes that we construe the outcome limitations recited in the wherein clauses of claims 1, 5, 6, and 7. Prelim. Resp. 19–20. Claims 1, 5, and 6 recite that a patient achieves or a population of patients achieve an ACR50 or ACR70 score at week 24 of the treatment. Ex. 1001, 55:18–29, 56:18–26. Claim 7 recites a method of reducing or inhibiting symptoms of PsA, "wherein [the] symptoms are progression of structural damage assessed by radiograph." *Id.* at 56:25–26. Patent Owner argues that each limitation is a substantive limitation. Prelim. Resp. 19–20. For claims 1, 5, and 6, Patent Owner contends that the outcome limitations require a certain treatment duration, i.e., 24-weeks. *Id.* Patent Owner further contends that the outcome limitations of claims 1, 5, 6, and 7 introduce heightened efficacy requirements. *Id.* at 19.

Petitioner argues that the outcome limitations recited in claims 1, 5, and 6 are "merely statements of intended results that cannot impart patentability." Pet. 48. Alternatively, Petitioner contends that even if the outcome limitations are entitled to patentable weight, they are the natural

consequence of the method of treatment recited in claims 1, 5, and 6. *Id.* Likewise, Petitioner asserts that the reduction or inhibition of "progression of structural damage" recited in the claim 7 "wherein" clause is inherent in practicing the claimed method. *Id.* at 50–51.

At this stage of the proceeding, and based on the current record, we agree with Patent Owner that the outcome limitations recited in the "wherein" clauses are substantive limitations of the claims that are entitled to patentable weight. We recognize that the Federal Circuit has declined to give weight to phrases in "whereby" clauses of method claims that simply express an intended result of a positively recited process step. *See, e.g.*, *Minton v. Nat'l Ass'n of Sec. Dealers, Inc.*, 336 F.3d 1373, 1381 (Fed. Cir. 2003) (holding that the district court was correct in not giving weight to the phrase "traded efficiently" because the term "efficiently" was a laudatory term characterizing the result of a process step). The inquiry in that regard, however, is fact-specific and determined on a case-by-case basis. Here, the outcome limitations of the "wherein" clauses appear to provide a means for assessing the efficacy of the treatment recited in the claims, which the written description discloses as important to the invention. *See, e.g.*, Ex. 1001, 4:55–5:8, 26:43–51. Thus, we determine at this preliminary stage of the proceeding that the outcome limitations of claims 1, 5, 6, and 7 are entitled to patentable weight, but we invite the parties to address this issue further in Patent Owner's Response and Petitioner's Reply.[9]

[9] We address Petitioner's arguments that the outcome limitations are inherent in practicing the claimed methods below in § III.F.

D. Asserted References

Before turning to Petitioner's asserted grounds, we provide an overview of the asserted references. First, however, we address a preliminary argument Patent Owner raises with respect to whether Rau is prior art to the '992 patent.

1. Whether Rau is Prior Art

Patent Owner contends that Petitioner does not establish sufficiently that Rau is prior art because Exhibit 1021 "is an English language translation [of Rau] prepared in *2015*, and is therefore *not* prior art to the '992 patent." Prelim. Resp. 46–47 (citing Ex. 1021, 11). As a result, Patent Owner argues we should deny "Ground 3" because it is not based on a prior art printed publication. *Id.* at 47. Patent Owner further argues that "even if Petitioner intended to rely on the 2000 date of the original German version of [Rau], it failed to include a copy of that document with the Petition, thereby failing to meet the statutory requirement under 35 U.S.C. § 312(a)(3)(A)." *Id.* We disagree.

First, Petitioner's asserted ground that includes Rau as a reference relies on Rau only for arguments regarding claim 7, even though the asserted ground also challenges claims 1, 5, and 6. Thus, Patent Owner's argument that we should deny the ground in its entirety based on Petitioner's alleged failure to show that Rau is a prior art printed publication is not persuasive.

Second, we find that Exhibit 1021 bears indicia sufficient to show that the information contained therein was publicly available before the July 19, 2002 priority date Petitioner asserts for its ground, albeit in German language instead of English language. For example, each page of the article indicates that it was published in the peer-reviewed scientific journal "Akt

Rheumatol" in 2000. *See, e.g.*, Ex. 1021, 83 ("Akt Rheumatol [Rheumatology Today] *2000*; 25: 83-88"). At this stage of the proceeding, such information is sufficient on its own to establish that the reference is a prior art printed publication.

Third, assuming that Petitioner intended to rely on the 2000 date included in the original German version of Rau, which it did not provide as an exhibit when it filed the Petition, such an omission is not fatal to Petitioner's asserted ground. *See Lumentum Holdings, Inc. v. Capella Photonics, Inc.*, Case IPR2016-00739, Paper 38, 4 (PTAB Mar. 4, 2016) (precedential) (explaining that a lapse in compliance with the requirements set forth in 35 U.S.C. § 312(a) does not "preclude the Board from permitting such lapse to be rectified"). Accordingly, to the extent that Petitioner intends to rely on the 2000 date in the original German version of Rau to establish that Exhibit 1021 is prior art to the '992 patent, Petitioner is authorized to file a copy of that version as an exhibit in this proceeding within five days of this decision.

We now turn to the asserted references.

2. Mease 2004 (Ex. 1056)

Mease 2004 describes a study to evaluate the "efficacy and safety over 24 weeks of 40 mg adalimumab administered subcutaneously every other week . . . compared with placebo in patients with active PsA." Ex. 1056, 4097. The study was a Phase III, placebo-controlled double-blind study in which adult patients were eligible to enroll if they had active PsA, i.e., ≥ 3 swollen and ≥ 3 tender joints, and had failed NSAID therapy. *Id.* Patients were assessed for efficacy and safety outcomes using the ACR response criteria and other assessment scales. *Id.*

Mease 2004 provides data showing that: (1) 57% of patients receiving adalimumab achieved an ACR20 response at week 24, compared to 15% of patients receiving placebo; and (2) 23% of patients receiving adalimumab achieved an ACR70 response at week 24, compared to 1% of patients receiving placebo. *Id.* Mease 2004 concludes that "[a]dalimumab treatment was effective in treating the signs and symptoms of PsA. Overall, treatment was well-tolerated, with a similar safety profile as that observed in patients with [RA]." *Id.*

3. 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.*

4. 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 inhibitors, including for patients with PsA and psoriasis. *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 four 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 received 5 mg/kg of infliximab at weeks 0, 2, and 6. *Id.* at S18. Baseline Psoriasis Area and Severity Index 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 PsA, eight patients achieved ACR70 after ten weeks of treatment, and six patients maintained that improvement to week 54. *Id.* Further, "magnetic resonance imaging showed an 82% reduction in perfusion of inflamed joints." *Id.*

In a first study evaluating etanercept, eight out of ten PsA patients experienced improvement in Physician's Global Assessment scores after

twelve months of treatment with 25 mg etanercept administered twice weekly. *Id.* at S18.

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. Further, 73% of etanercept-treated patients achieved ACR20 compared with 13% of patients in the placebo group. *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.*

5. Mease 2000 (Ex. 1017)[10]

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 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

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

25 mg administered twice weekly via subcutaneous injection for twelve weeks. *Id.* at 385–386. The median duration of PsA was 10 years. *Id.* at 387. The primary endpoint with respect to efficacy in PsA was the proportion of patients who met the Psoriatic Arthritis Response Criteria ("PsARC") at 12 weeks. *Id.* at 386. A secondary endpoint was the proportion of patients meeting the ACR20, ACR50, and ACR70 criteria (designed for the assessment of RA) at 12 weeks. *Id.* The study also assessed individual measures of arthritis disease activity. *Id.*

The trial determined that etanercept-treated patients "had statistically better outcomes for all clinical endpoints," including ACR response rates. *Id.* at 387; *see id.* at Fig. 2 (depicting the percentage of patients with ACR20, ACR50, and ACR70 responses at 12 weeks). Mease 2000 concludes 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.

6. Dechant 2000 (Ex. 1029)

Dechant 2000 explains that infliximab "proved to be highly effective" in treating RA. Ex. 1029, S102. Because it was known that TNFα is elevated in the synovial fluid and skin lesions of PsA patients, Dechant 2000 describes a study designed to determine whether infliximab could also be successful in treating PsA. *Id.* Dechant 2000 describes a study in which 10 patients with severe PsA received 5 mg/kg of infliximab at weeks 0, 2, and 6. *Id.* "At week 10 all patients showed a dramatic[] response to infliximab treatment with reduction of signs and symptoms and serological activity." *Id.* After week 10, infliximab treatment was adapted to the individual needs of the patients, who were followed for up to one year by evaluating ACR

responses. *Id.* Dechant 2000 concludes that the results show "infliximab was effective over one year. Therefore infliximab seems to be effective in the treatment of severe [PsA] as well." *Id.*

7. Rau (Ex. 1021)

Rau discloses several clinical studies in which patients were administered adalimumab (D2E7). *See generally* Ex. 1021. Patients were assessed for progression of structural damage using an X-ray, both prior to and during treatment. *Id.* at 85–86. X-ray images were evaluated to quantify the degree of joint surface destruction using the Ratingen Score, the Sharp Erosion Score, and the Sharp Joint Space Narrowing Score. *Id.* at 85. Rau describes each of those scores and how the evaluation is graded according to each score. *Id.* at 85–86.

Rau discloses that, prior to treatment with adalimumab, "an increase in [Ratingen] scores could be seen in nearly all patients, but in almost none of the patients during the treatment." *Id.* at 86. "In the Sharp Erosion Score, one sees in the pre-treatment phase a strongly significant increase," but there was "almost no change during the treatment with [adalimumab]." *Id.* Rau explains that "the same is true for the Joint Space Narrowing Score." *Id.* In summarizing the X-ray results, Rau states "before the start of treatment there is a progression in the Ratingen Score of 4.5% of the maximum possible score per year," which fell to "-0.75% per year" during treatment with adalimumab. *Id.* "In the Sharp Erosion Score the increase shrank from 6.5% of the maximum possible score per year, to 0.9%." *Id.*

E. Asserted Anticipation of Claims 1, 5, and 6 by Mease 2004

Petitioner asserts that claims 1, 5, and 6 of the '992 are unpatentable under 35 U.S.C. § 102 because Mease 2004 anticipates those claims. Pet.

40–41. Petitioner's arguments are based on its proffered May 16, 2006 priority date—an alternative priority date that assumes the clinical outcomes recited in those claims are limitations entitled to patentable weight. *See id.* at 6, 12–13, 40. Patent Owner opposes. Prelim. Resp. 47–50. 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 ground.

1. Analysis of Petitioner's Anticipation Ground

Petitioner asserts that Mease 2004 describes the same clinical study that was added as an example to the '992 patent in a continuation-in-part application filed May 16, 2006. Pet. 40. In particular, Petitioner points to: (1) the patient eligibility criteria, i.e., patients who suffered from moderate to severe active PsA (as indicated by ≥ 3 swollen and ≥ 3 tender joints) and had failed NSAID therapy; (2) the treatment protocol, i.e., patients were treated with 40 mg of adalimumab administered subcutaneously every other week; and (3) the clinical outcomes, i.e., 23% of patients treated with adalimumab achieved a 70% reduction in ACR score and 39% of patients treated with adalimumab achieved a 50% reduction in ACR score after 24 weeks of treatment. *Id.* at 40–41 (citing Ex. 1056, 4097).

At this stage of the proceeding, Patent Owner does not contest Petitioner's showing regarding Mease 2004's disclosure. Having considered Petitioner's arguments, and based on our review of Mease 2004, we are persuaded that Petitioner shows sufficiently how Mease discloses each limitation of claims 1, 5, and 6. That does not end our inquiry with respect to Petitioner's asserted ground, however, as Patent Owner raises a procedural issue, which we address below.

2. Whether Petitioner's Anticipation Challenge is Inconsistent with Petitioner's Obviousness Challenges

Patent Owner argues that we should deny institution of the asserted ground because Petitioner's anticipation challenge is "irreconcilable with Petitioner's position [in its obviousness challenges] regarding the effect of the ACR outcome language in the claims." Prelim. Resp. 47. More specifically, Patent Owner argues "Petitioner seeks to have it both ways" in its asserted grounds because Petitioner first argues that the earliest effective filing date of claims 1, 5, and 6 is the date the applicant allegedly added the ACR outcomes to the specification, but then separately argues that the ACR outcomes are statements of intended result that cannot impart patentability to the claims. *Id.* at 47–48. In other words, Patent Owner contends that Petitioner argues inconsistently that "the ACR outcomes are limiting where they help the petition (establishing a later priority date) but that they are not limiting where they hurt the petition (reading prior art onto the claims)." *Id.* at 48.

We are not persuaded that Petitioner's arguments regarding the ACR outcomes recited in claims 1, 5, and 6 are "irreconcilable" or "inconsistent" as Patent Owner argues. We find, instead, that Petitioner's arguments regarding the ACR limitations are permissible alternative arguments at this stage of the proceeding because they are based on different asserted priority dates. For this asserted ground, Petitioner assumes that the ACR outcomes are entitled to patentable weight and argues that they lacked support in the written description of the '992 patent until May 16, 2006, when the applicant added them to the disclosure and claims in a continuation-in-part application. Pet. 6, 12–13. Alternatively, Petitioner's two asserted obviousness grounds assume that the ACR outcomes are not entitled to

patentable weight and, therefore, do not require written-description support. Consequently, Petitioner asserts earlier effective filing dates for those grounds. *See id.* at 9 (asserting July 18, 2003 and July 19, 2002 as the assumed priority date for the asserted obviousness grounds). As explained above, however, we construe the ACR outcomes to be substantive limitations of claims 1, 5, and 6. Accordingly, we do not find Petitioner's alternative arguments insufficient to support its anticipation challenge. As such, we are persuaded that Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that Mease 2004 anticipates claims 1, 5, and 6.

F. Asserted Obviousness of Claims 1, 2, and 5–7

Petitioner asserts that claims 1, 2, and 5–7 of the '992 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 Mease 2000; or (2) Keystone, Mease 2000, and Dechant 2000 and, for claim 7, Rau. Pet. 41–57, 62–66 (claim charts). Petitioner's arguments for both grounds are substantively similar, except that Petitioner replaces the teachings of Lorenz with the teachings of Dechant 2000 and adds Rau for claim 7. *See Id.* at 50. Patent Owner opposes, addressing both asserted grounds together. Prelim. Resp. 21–46. 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. 25–27 (referring to Ex. 1034; Ex. 1049). Patent

Owner contends that "[e]ven for [] alleged 'background' references, Petitioner must meet its burden of making a threshold showing that alleged prior art was available as a printed publication." *Id.* at 25 (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,[11] 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 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

[11] Notably, Patent Owner relies on one of those background references—the Humira Press Release (Ex. 1049)—to support its argument that the prior art articulated the differences between RA and PsA. Prelim. Resp. 31–32.

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, 2, 5, and 6

For both asserted grounds, Petitioner argues that the "only difference" between Keystone and the dosing regimen recited in independent claims 1 and 2 is that the claimed dosing regimen recites treating PsA instead of treating RA. Pet. 43; *see id.* at 54 (citing Ex. 1003, A481). Petitioner further contends that Mease 2000 teaches the patient enrollment criteria and "moderate to severe active [PsA]" limitations of claim 1. *Id.* at 46–47 (citing Ex. 1001, 37:31–33; Ex. 1017, 385). And Petitioner argues that the combined teachings of the asserted references disclose or suggest the ACR outcomes recited in claims 1, 5, and 6 because those outcomes are the inherent results of practicing the claimed method, i.e., administering 40 mg adalimumab every other week. *Id.* at 48, 56. Alternatively, Petitioner contends that the prior art "makes clear" that the recited ACR outcome is the "obvious result of TNF-α inhibition in PsA patients." *Id.* at 49, 56. To support its alternative argument, Petitioner points to the ACR outcomes reported in Keystone (for treating RA with adalimumab), as well as the ACR outcomes reported in Mease 2000 and Lorenz or Dechant 2000 (for treating PsA with TNFα inhibitors infliximab and etanercept). *Id.* at 49–50, 56 (citing Ex. 1002 ¶¶ 34, 128–130, 147; Ex. 1017, Table 2; Ex. 1028, S18); *see* Ex. 1003, A481 (Table 1).

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, 2, 5, and 6. We find, on the current record, that Petitioner shows sufficiently that Keystone, Lorenz, and Mease 2000, or Keystone, Mease 2000, and Dechant 2000, 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 PsA; and (b) a reason to use, or a reasonable expectation of success in using, 40 mg adalimumab administered every other week to treat PsA. We address both of those issues below.

a. Reasonable expectation of success in using adalimumab to treat PsA

With respect to a reasonable expectation of success in using adalimumab to treat PsA, Petitioner asserts that the prior art taught that adalimumab was a prime candidate to treat PsA. Pet. 32, 43–44. 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 32 (citing Ex. 1028, S17–18). Petitioner also argues that Lorenz "restated the known relationship between TNF-α 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.* (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." *Id.* at 44 (citing Ex. 1002 ¶ 90).

For its asserted ground relying on Dechant 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 PsA" based on "(1) Keystone's description of adalimumab's success in treating RA"; and "(2) the teachings of Mease 2000 and Dechant 2000 that the TNF-α inhibitors etanercept and infliximab were successful in treating RA and PsA." *Id.* at 55 (citing Ex. 1002 ¶ 146); *see also id.* at 54 (describing the disclosures of Mease 2000 and Dechant 2000).

Patent Owner responds that the asserted art fails to disclose that adalimumab would treat PsA. *Id.* at 21–24. Patent Owner notes that Keystone—the only asserted reference disclosing an adalimumab dosing regimen—is not directed to treating PsA, but rather, to treating RA. *Id.* at 21. Patent Owner further asserts that none of Petitioner's references discusses any connection between adalimumab and PsA, "adalimumab's effect on or distribution to all of the tissues affected by PsA, or whether adalimumab could inhibit the progression of structural damage in PsA patients." *Id.* at 22–23. Patent Owner also argues that the general disclosures in Lorenz, Dechant 2000, and Mease 2000 regarding the use of other TNFα inhibitors (infliximab and etanercept) "are insufficient to bridge this gap" because they do not compare adalimumab to infliximab or etanercept. *Id.* at 22–24.

Similarly, Patent Owner argues that Petitioner's reliance on references disclosing that infliximab and etanercept were effective in treating PsA, "ignores the substantial complexity of PsA and differences between adalimumab and other anti-TNFα agents." *Id.* at 29–30. In that regard, Patent Owner contends that Petitioner fails to address any differences between the structures, administration, tissue distribution, or pharmacokinetic properties of the different drugs, which is insufficient to establish a reasonable expectation of success in using adalimumab to treat PsA. *Id.* Patent Owner also argues that Petitioner does not show a reasonable expectation of success because it omits from the analysis a discussion of the differences between RA and PsA, and their respective treatments. Prelim. Resp. 30–34.

We are not persuaded, on the current record, that Petitioner's failure to address the structures, distribution, or pharmacokinetic parameters, or compare the effect of the different TNFα inhibitors negates a showing of reasonable expectation of success in using adalimumab to treat PsA. Nor are we persuaded that the differences between RA and PsA dictate a finding that Petitioner fails to show a reasonable expectation of success. 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 PsA, Patent Owner does not direct us to evidence in the current record to support sufficiently its argument.

Rather, as Petitioner argues and Dr. Helfgott testifies, 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 PsA (Pet. 30–31; Ex. 1002 ¶¶ 74–81); (2) were using

TNFα inhibitors, such as infliximab and etanercept, to treat RA and to treat PsA based on the known role of TNFα in those conditions (Pet. 33–34; Ex. 1002 ¶¶ 82–89); and (3) would have predicted success in using adalimumab—one of the handful of TNFα inhibitors already known to treat RA—in treating PsA based on the successes of infliximab and etanercept in treating both RA and PsA (Pet. 32; Ex. 1002 ¶¶ 90, 92). For example, 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 PsA received the same dose of etanercept. Ex. 1017, 385, 389. Dechant 2000 explains that infliximab "proved to be highly effective" in treating RA. Ex. 1029, S102. Because it was known that TNFα is elevated in the synovial fluid and skin lesions of PsA patients, Dechant 2000 designed a study to determine whether infliximab could also be successful in treating PsA. *Id.* Based on ACR50 and ACR70 responses the patients in the study achieved and maintained, Dechant 2000 concluded that "infliximab seems to be effective in the treatment of severe [PsA] as well [as RA]." *Id.* Similarly, Lorenz provides a review of clinical studies in which infliximab and etanercept—already known to be effective in treating RA—were shown to be effective in treating PsA and suggests that other known TNFα inhibitors, such as adalimumab, would provide encouraging results in similar studies. Ex. 1028, S17–19.

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 PsA.

b. Reason to treat PsA 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 PsA given: (1) TNFα's role in the pathogenesis of both RA and PsA; (2) the use of TNFα inhibitors infliximab and etanercept to treat both RA and PsA with the same doses and dosing regimens; and (3) adalimumab's known potential for treating PsA. Pet. 46, 51–53 (referring to Petition §§ VI.C.2–VI.C.3, VI.C.5–VI.C6, and evidence cited therein, and citing Ex. 1002 ¶¶ 130, 134–135, 151). Petitioner further contends that the numerous prior art references demonstrating the successful treatment of PsA with the same infliximab and etanercept doses and dosing regimens that had been used to treat RA would have provided the ordinarily skilled artisan with a reasonable expectation of success in treating PsA with the claimed dosing regimen. *Id.* at 52–53; *see id.* at 33–39.[12]

Patent Owner responds that Petitioner fails to support its rationale for reasonable expectation of success in using the same dose of 40 mg adalimumab every other week that had been used to treat RA to treat PsA because Petitioner's references describing infliximab and etanercept dosing confirm the uncertainty of dosing that existed in the art. Prelim. Resp. 34. In that regard, Patent Owner contends that Lorenz, Dechant 2000, and Petitioner's background references disclose treating PsA with 5 mg/kg of

[12] Petitioner also points to small molecule drugs that Petitioner contends were used to treat both RA and PsA at the same or similar doses and dosing regimens to support a reasonable expectation of success. Pet. 39–40. 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. 37.

infliximab, which is "not the same as the 3 mg/kg infliximab dose approved by the FDA for the treatment of RA." *Id.* at 35 (citing Ex. 1027, 1085, 1087). Patent Owner further argues that Petitioner's citation to multiple references with different infliximab dosing regimens "confirms the uncertainty regarding dosing for PsA in the art." *Id.* Patent Owner makes similar arguments with respect to Mease 2000's etanercept study. *Id.* at 36.[13]

Patent Owner's arguments appear to assume that the Food and Drug Administration ("FDA") approved dose is the 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 PsA based on the prior art's disclosure of using the same or similar doses and dosing regimens to effectively treat both

[13] Additionally, Patent Owner argues, again, that Petitioner fails to point to anything in its asserted references that compares infliximab's or etanercept's effect on or distribution to the tissues that PsA affects with that in the tissues that RA affects. Prelim. Resp. 36. Although a fruitful issue to explore during trial, we find this argument unpersuasive on this record for the reasons set forth *supra* in § III.E.2.a.

disorders. *See* Pet. 33–39, 45–46. For example, Petitioner directs us to the 2001 Remicade Package Insert,[14] 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 combination with methotrexate to treat RA. Pet. 35, 37–38 (both citing Ex. 1027, 1087). Petitioner and Dr. Helfgott also point to a 2002 study by Marzo-Ortega,[15] which was designed to assess whether infliximab was effective in treating PsA using the same dosing regimen that that the Remicade Package Insert discloses, i.e., 3 mg/kg administered at weeks 0, 2, 4, 6, and 14. Pet. 35, 37–38 (citing Ex. 1004, 6[16]); *see also* Ex. 1002 ¶¶ 95–99 (Dr. Helfgott's testimony regarding the prior art use of 3 mg/kg infliximab to treat RA and PsA). Marzo-Ortega determined that 3 mg/kg infliximab was effective at treating PsA—results showed "a dramatic beneficial effect on skin and joint disease in patients with PsA and skin psoriasis"—and explained that the reduced infliximab dose "also has considerable cost-saving implications." Ex. 1004, 6.

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 PsA. Pet. 37. Mease 2000 determined that "etanercept resulted in significant clinical benefit in the composite measures (PsARC, ACR20, and ACR50) and in

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[14] PHYSICIANS' DESK REFERENCE, Remicade entry, 1085–1088 (55th ed. 2001) (Ex. 1027).
[15] 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).
[16] We refer to the page numbers that Petitioner added to the exhibit instead of the exhibit's original page numbers.

each individual factor of disease activity," with 73% of patients treated with etanercept achieving an ACR20 at 12 weeks, compared with 13% of patients in the placebo group. Ex. 1017, 388–389; *see* Ex. 1002 ¶ 109. 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 PsA with 40 mg adalimumab administered every other week with a reasonable expectation of success. Accordingly, Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the subject matter of claims 1, 2, 5, and 6 would have been obvious over the combination of Keystone, Lorenz, and Mease 2000 or Keystone, Mease 2000, and Dechant 2000.

3. Claim 7

Claim 7 depends from claim 2, which requires "reducing or inhibiting symptoms in a patient with [PsA]." Ex. 1001, 55:26–29. Claim 7 further recites that the "symptoms are progression of structural damage assessed by a radiograph." *Id.* at 56:25–26. Petitioner asserts that the subject matter of claim 7 would have been obvious over the combined teachings of Keystone, Lorenz, and Mease 2000, or Keystone, Mease 2000, Dechant 2000, and Rau. Pet. 50–51, 56–57, 65–66 (claim chart).

Petitioner argues that, like the ACR outcomes recited in claims 1, 5, and 6, reducing or inhibiting the progression of structural damage is the inherent result of practicing the claimed method. *Id.* at 50–51, 56. Alternatively, Petitioner asserts Lorenz (first asserted obviousness ground) and Rau (second asserted obviousness ground) taught that treating patients with TNFα inhibitors reduced the progression of structural damage in RA patients, as assessed by radiograph. *Id.* at 51 (citing Ex. 1028, S17), 56

(citing Ex. 1021, 86). Petitioner further relies on Dr. Helfgott's testimony that a person of ordinary skill in the art would have expected that treating PsA patients with TNFα inhibitors would similarly inhibit the progression of structural damage in view of the similarities between RA and PsA. *Id.* at 51, 57 (citing Ex. 1002 ¶¶ 140, 157).

Patent Owner responds that Petitioner fails to make a sufficient showing under either of its two theories. Prelim. Resp. 38–39. Regarding Petitioner's inherency theory, Patent Owner argues it is "entirely conclusory" because it does not cite data reflecting that any patient treated according to the claimed method would necessarily achieve the claimed structural damage outcome. *Id.* at 45–46.

Patent Owner's argument is unpersuasive at this stage of the proceeding. Rather, we agree with Petitioner on this record that reducing or inhibiting the structural damage merely recites the inherent result of practicing the claimed method. In other words, upon performing the method step of administering 40 mg adalimumab every other week to a patient with PsA, the record before us indicates that a patient will experience inhibition of structural damage. The claims do not recite any other step for this mechanism to occur. Because Petitioner makes a sufficient showing that the combined teachings of the prior art in both asserted grounds would have disclosed administering 40 mg adalimumab every other week to a patient with PsA, administering adalimumab in accordance with that disclosure necessarily would result in reducing or inhibiting the patient's structural damage.

Given the foregoing, we decline to address, at this stage of the proceeding, Petitioner's alternative theory that the subject matter of claim 7

would have been obvious based on the explicit teachings of the prior art. On the present record, Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the subject matter of claim 7 would have been obvious over the combination of Keystone, Lorenz, and Mease 2000, or Keystone, Mease 2000, Dechant 2000, and Rau.

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, 2, and 5–7 of the '992 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, 5, and 6 under 35 U.S.C. § 102 as anticipated by Mease 2004;

Claims 1, 2, and 5–7 under 35 U.S.C. § 103 as obvious over the combination of Keystone, Lorenz, and Mease 2000;

Claims 1, 2, 5, and 6 under 35 U.S.C. § 103 as obvious over the combination of Keystone, Mease 2000, and Dechant 2000; and

Claim 7 under 35 U.S.C. § 103 as obvious over the combination of Keystone, Mease 2000, Dechant 2000, and Rau;

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; and

FURTHER ORDERED that to the extent Petitioner intends to rely on the 2000 date in the original German version of Rau to establish that Exhibit 1021 is prior art to the ’992 patent, Petitioner is authorized to file a copy of that version as an exhibit in this proceeding within five days of this decision.

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