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Paper 23
Date: January 6, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FRESENIUS KABI USA, LLC, and
FRESENIUS KABI SWISSBIOSIM GMBH
Petitioners,

v.

CHUGAI SEIYAKU KABUSHIKI KAISHA,
Patent Owner.

IPR2021-01024
Patent 7,521,052 B2

Before ERICA A. FRANKLIN, JOHN G. NEW, and ZHENYU YANG, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Fresenius Kabi USA, LLC, Fresenius Kabi SwissBioSim GmbH. ("Petitioners") filed a Petition requesting an *inter partes* review of claim 1 of U.S. Patent No. 7,521,052 B2 (Ex. 1001, "the '052 patent"). Paper 3 ("Petition" or "Pet."). Chugai Seiyaku Kabushiki Kaisha, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). With our authorization, Ex. 3001, Petitioners filed a Reply to the Preliminary Response to address further issues raised by Patent Owner involving the Board's discretion to deny institution under 35 U.S.C. § 314(a). Paper 13. Patent Owner filed a Sur-reply in response. Paper 14.

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314 (2018). Upon considering the parties' arguments and evidence, we determine that Petitioners have demonstrated a reasonable likelihood that it would prevail in showing the unpatentability of the one claim challenged in the Petition. Accordingly, we institute an *inter partes* review.

A. Real Parties-in-Interest

Petitioners identify the real parties-in-interest as Fresenius Kabi USA, LLC, Fresenius Kabi SwissBioSim GmbH, Fresenius Kabi AG, Fresenius Kabi Pharmaceuticals Holding, Inc., Fresenius Kabi Deutschland GmbH and Fresenius SE & Co. KGaA. Pet. 6. Patent Owner identifies itself as the real party-in-interest, noting that it is also called Chugai Pharmaceutical Co., Ltd. Paper 5, 1. Patent Owner further identifies Genentech, Inc., as a real party-in-interest. *Id.*

B. Related Matters

Petitioners assert that the '052 patent is not currently the subject of any litigation or post-grant proceedings. Pet. 6. Petitioners note that they

are seeking *inter partes* review of US Patent No. 10,744,201 ("the '201 patent") which claims priority to the '052 patent. *Id.*, *see* IPR2021-01025, Paper 3 (petition seeking *inter partes review* of the '201 patent). Patent Owner identifies a number of patent applications and issued patents that relate to US Patent Application No. 10/554,407, which issued as the '052 patent. Paper 5, 1–3. Patent Owner also notes that the '201 patent is the subject of IPR2021-01025. *Id.* at 2–3.

C. The '052 Patent

The '052 patent relates to methods for treating interleukin-6 (IL-6) related diseases with a combination of an IL-6 antagonist and immunosuppressants. Ex. 1001, 1:7–11. IL-6 is a multifunctional cytokine which affects functions of various cells, including inducing maturation of T lymphocyte lineage cells. *Id.* at 1:18–22. The IL-6 receptor, a ligand binding protein, is one manner by which IL-6 transmits its biological activity. *Id.* at 1:23–25. The use of anti-IL-6 receptor antibodies, such as humanized anti-IL-6R antibodies and chimeric anti-IL-6R antibodies, to prevent or treat rheumatoid arthritis and other diseases attributed to IL-6 production has been known in the art. *Id.* at 1:32–63. The Specification describes the specific preferable anti-IL-6R antibody for the present invention is, for example, humanized PM-1 antibody. *Id.* at 2:36–37.

According to the Specification, it was not previously known that: (a) synergistic effects can be obtained when treating IL-6 related diseases by using a combination of an anti-IL-6R antibody with immunosuppressants, such as methotrexate (MTX); (b) an immunosuppressant, such as MTX, can reduce or prevent allergic reactions when treating rheumatoid arthritis with an anti-IL-6R antibody; and (c) high dose anti-IL-6R antibody treatment of rheumatoid arthritis can reduce or prevent allergic reactions associated with

the use of an IL-6 antagonist for the treatment of IL-6 related diseases, including rheumatoid arthritis. *Id.* at 1:63–2:5, 2:14–20.

D. Challenged Claim

Petitioners challenge claim 1, the only claim recited in the '052 patent. Claim 1 is set forth below.

> 1. A method for treating rheumatoid arthritis, comprising administering an effective amount of an anti-IL-6 receptor antibody (anti-IL-6R antibody) and an effective amount of methotrexate (MTX) to a patient in need thereof, wherein the anti-IL-6R antibody is a humanized PM-1 antibody.

Ex. 1001, 22:31–35.

E. Asserted Grounds of Unpatentability

Petitioners assert that claim 1 is unpatentable on the following three grounds:

Claim Challenged	32 U.S.C. §[1]	Reference(s)
1	102(b)	Yoshizaki[2]
1	102(b)	Nishimoto[3]
1	103	Nishimoto and Weinblatt[4]

[1] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '052 patent issued has an effective filing date prior to that date, the pre-AIA version of §§ 102 and 103 applies.

[2] Kazuyuki Yoshizaki et al., *Therapy of Rheumatoid Arthritis by Blocking IL-6 Signal Transduction with a Humanized Anti-IL-6 Receptor Antibody*, SPRINGER SEMINARS IN IMMUNOPATHOLOGY 20:247–259 (1998) (Ex. 1005, "Yoshizaki").

[3] Norihiro Nishimoto, *Anti-IL-6 Receptor Antibodies, Usefulness and Issues in Rheumatoid Arthritis*, THERAPEUTICS 36(12):1264-1267 (2002) (certified English Translation) (Ex. 1006, "Nishimoto").

[4] Michael E. Weinblatt et al., *Adalimumab, a Fully Human Anti-Tumor Necrosis Factor α Monoclonal Antibody, for the Treatment of Rheumatoid*

Claim Challenged	32 U.S.C. §[1]	Reference(s)

Petitioners also rely upon the Declaration of Thomas M. Zizic, M.D. (Ex. 1002).

II. ANALYSIS

A. Person of Ordinary Skill in the Art

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1323 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioners assert that a person of ordinary skill in the art (POSA) at the time of the invention "would have had been an individual with an M.D. specializing in the treatment of autoimmune disorders and having several years of experience treating patients with such disorders, including rheumatoid arthritis, or having several years of experience researching treatments for autoimmune disorders, including rheumatoid arthritis." Pet. 13 (citing Ex. 1002 ¶ 30). At this stage in the proceeding, Patent Owner does not dispute Petitioners' description of the level of ordinary skill in the art. Prelim. Resp. 16

Because Petitioners' uncontested definition of one of ordinary skill in the art is reasonable and consistent with the '052 patent and the prior art of record, we adopt Petitioners' definition for purposes of this Decision.

Arthritis in Patients Taking Concomitant Methotrexate, ARTHRITIS & RHEUMATISM 48(1):35–45 (2003) (Ex. 1008, "Weinblatt").

B. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 100(b) (2019). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17).

Petitioners propose constructions for several claim terms. *See* Pet. 14–21. In the following discussion, we address those proposed constructions and Patent Owner's preliminary responses to them.

1. "A method for treating rheumatoid arthritis . . . in a patient"

Petitioners assert that "[t]he plain and ordinary meaning of the phrase '[a] method for treating rheumatoid arthritis . . . in a patient' is 'a method attempting to cause a therapeutic improvement in rheumatoid arthritis in a patient,'" as it "does not require actually causing a therapeutic benefit in that particular patient." Pet. 14 (citing Ex. 1002 ¶ 120). Patent Owner does not contest Petitioners' proposed construction for this phrase. *See* Prelim. Resp. 17 n.3.

Based on the current record, we agree with Petitioners and find that the plain and ordinary meaning of the phrase reciting "[a] method for treating rheumatoid arthritis . . . in a patient" does not require achieving a

recognizable therapeutic benefit in the patient, but instead only requires attempting to cause such a therapeutic improvement in the patient's disease.

2. "administering an . . . anti-IL-6 receptor antibody . . . and methotrexate (MTX)"

Petitioners assert the phrase "administering an . . . anti-IL-6 receptor antibody . . . and methotrexate (MTX)" "should be construed to include administration of two drugs either simultaneously or sequentially (i.e., in which one drug is administered first, followed by administration of the second drug)." Pet. 16. In support of that proposed construction, Petitioners refer to the Specification disclosure that "[t]he anti-IL-6R antibody and the immunosuppressant are administered simultaneously or with a time interval," without placing any restriction on such time interval within which the two drugs are administered. *Id.* (citing Ex. 1001, 3:63–64; Ex. 1002 ¶¶ 123–126).

Additionally, Petitioners assert that its proposed construction is supported by the file history for the '052 patent. *Id.* at 16. In particular, Petitioners note that "[d]uring prosecution, applicant pursued a separate dependent claim to 'simultaneously administering' and administering 'with in a time interval' and anti-IL-6 receptor antibody and methotrexate," while the independent claim encompassed both the simultaneous and sequential administrations schedules. *Id.* at 16–17 (citing Ex. 1003, 326–328, 351, 359–363). Petitioners assert that the dependent claims were subsequently cancelled and the independent claim was amended, but continued to encompass administering the drugs either simultaneously or sequentially. *Id.* at 17–18 (citing Ex. 1003, 363, 381).

Patent Owner agrees that the claim phrase "does not literally require the patient to receive both drugs at once." Prelim. Resp. 19. However, Patent Owner contends that the claim phrase should be construed "to require that the anti-IL-6 receptor antibody and MTX be administered as part of the same treatment regimen." *Id.* at 17. In support of that contention, Patent Owner asserts that the Specification describes that only patients who continued to receive MTX during the course of the clinical trial, in the same treatment regimen as MRA, were categorized as being within the "MTX-combined groups." *Id.* at 18. According to Patent Owner, the Specification reference to administering the two drugs "with a time interval" "cannot possibly mean that *any* 'time interval' between the administration of the two drugs falls within the claim—otherwise the three cohorts of 'MRA only' patients could not have been formed from those enrolled in the trial." *Id.* at 18–19.

Based on our review of the Specification and consideration of the arguments and the evidence, we agree with Petitioners that phrase "administering an . . . anti-IL-6 receptor antibody . . . and methotrexate (MTX)" includes administering two drugs either simultaneously or sequentially, i.e., with an interval, to a patient. As recognized by the parties, the Specification discloses that "[t]he anti-IL-6R antibody and the immunosuppressant are administered simultaneously or with a time interval." Ex. 1001, 3:63–64; *see* Pet. 16; *see* Prelim. Resp. 19. Insofar as the parties dispute whether such sequential dosing includes "any" time interval, we find that Patent Owner has the better position. As Patent Owner asserts, the Specification exemplifies only patients who continued to receive MTX during the course of the clinical trial, in the same treatment regimen as MRA, as within the "MTX-combined groups." Prelim. Resp. 18; Ex. 1001,

16:25–42 (Example 1); 17:21–26. Similarly, when referring to the combination therapy elsewhere in the disclosure, the Specification describes patients receiving MTX and MRA during the same treatment regimen, rather than referring only to some historical or prior treatment with MTX along with a current use of MRA alone. *See, e.g.*, Ex. 1001, 3:55–64.

Accordingly, at this stage in the proceeding, we preliminarily construe the claim phrase "administering an . . . anti-IL-6 receptor antibody . . . and methotrexate (MTX)" as meaning "administering the anti-IL-6 receptor antibody and methotrexate to a patient either simultaneously or sequentially, i.e., with an interval, wherein such interval occurs within a treatment regimen comprising the two drugs."

3. "an effective amount of an anti-IL-6 receptor antibody"/ "an effective amount of methotrexate (MTX)"

Petitioners contend that a POSA would have understood, in the context of the Specification, the plain meaning of the term "effective amount" to include amounts known to be effective in treating RA, regardless of whether it has such an effect on the particular patient to whom the drug is administered." Pet. 18–19 (citing Ex. 1002 ¶¶ 128, 131). For the anti-IL-6R antibody, Petitioners assert that such effective amounts for treating RA were known in the art and should be construed to include at least the amounts reported as effective for treating RA, and the range of dosages identified by the '052 patent: e.g., 0.02 to 150 mg/kg administered intravenously every four weeks. *Id.* at 19 (citing Ex. 1001, 3:55–62; Ex. 1002 ¶¶ 128–130).

Similarly, Petitioners assert that such effective amounts of methotrexate for treating RA were known in the art and should be construed "to include at least the amounts known to be effective for treating RA, and the range of dosages identified by the '052 patent: *e.g.*, 1 to 100 mg/body

per week when administered orally." *Id.* at 20–21 (citing Ex. 1001, 4:43–47; Ex. 1002 ¶¶ 131–133).

Patent Owner contends that "[b]ecause the claim requires administering MTX and an anti-IL-6R antibody together [to treat RA], the 'effective amount' of each drug must be effective to achieve that purpose when the drugs are administered together." Prelim. Resp. 20. Patent Owner asserts that the clinical trial designed by the inventors and discussed in the Specification was "*to determine the optimum dose* of MRA given alone *and* in combination with methotrexate for the treatment of rheumatoid arthritis." *Id.* at 20–21 (quoting Ex. 1001, 16:15–24) (emphasis added by Patent Owner). According to Patent Owner, "there is no suggestion that those two amounts are or would be the same—the optimal dosage of the drugs given in monotherapy would not necessarily match the optimal dosage when administered 'in combination.'" *Id.* at 21.

Additionally, Patent Owner asserts that construction of an "effective amount" of each drug means that "the combined doses of the two drugs actually impart a therapeutic effect on the patient." *Id.* at 22. Patent Owner contends that the Specification's disclosure of exemplary dosage ranges for MTX and an anti-IL-6R antibody "provide only guidance to the POSA in selecting an 'effective amount' for a patient." *Id.* To support that contention, Patent Owner notes that the Specification "never says that every dose within those exemplary ranges is an 'effective amount' for any given patient and indeed the reported clinical trial data confirms that some were not." *Id.*

Patent Owner also refers to the prosecution history of the '052 patent, noting that it argued that a cited reference did "not suggest the combined use of an anti-IL-6 receptor antibody [with MTX] provides *a better therapeutic*

effect in comparison with the use of an anti-IL-6 receptor antibody alone." *Id.* at 23 (citing Ex. 1003, 351). Patent Owner contends "[t]hat distinction would have been meaningless if . . . the claimed combination need not be effective and could even be unsafe." *Id.*

Based on our review of the Specification and consideration of the arguments and the evidence, we do not find adequate support for Patent Owner's contentions that the claim phrases "an effective amount of an anti-IL-6 receptor antibody" and "an effective amount of methotrexate (MTX)" requires that each drug must be an amount that is effective, based on their administration together, and that such amounts must actually impart a therapeutic effect on a patient.

To begin, the claim does not recite or refer to any required *combined effectiveness amount*. Nor does the claim refer to any "optimum" or "optimal" dosages, a feature that Patent Owner appears to improperly import from Example 1 in the Specification. *See CollegeNet, Inc. v. ApplyYourself, Inc.*, 418 F.3d 1225, 1231 (Fed. Cir. 2005) (holding that it is improper to "import limitations from the specification into the claims"). Rather, the claim distinctly and separately recites administering "an effective amount" of each drug. We find no description in the Specification that the effective amounts of those drugs are co-dependent on each other. Instead, when describing the typical dosage of the antibody when administered in combination with MTX, there is no discussion of adjusting the dose of the antibody to account for the MTX therapy. *See, e.g.*, Ex. 1001, 2:38–48. Similarly, when discussing the dose of MTX, there is no discussion of adjusting that dose to account for the amount of the antibody therapy. *See id.* at 2:60–67.

Further, in the Phase II trial of MRA described in Example 1 of the Specification, for those patient groups receiving a combination of MRA and MTX, only the amounts of the MRA are varied, i.e., either 2 mg/kg, 4 mg/kg, or 8 mg/kg, while the amount of MTX combined remains in the same dosage range for each group, i.e., 10-25 mg/week. The Specification does not describe adjusting that dosage in that constant dosing range for MTX based on the amount or effectiveness of the MRA. Indeed, the results of the trial are relayed as demonstrating "[a] clear dose-response" for MRA monotherapy and for MRA combined with methotrexate, and that "[t]he effectiveness of MRA to treat patients with rheumatoid arthritis was confirmed for both MRA monotherapy and for MRA combined with methotrexate," without any discussion of the actual dosage of MTX administered or any indication that such dosage impacted the results. Thus, we do not see from the Phase II trial disclosed in the Specification any suggestion that an effective amount of the two drugs are co-dependent.

Regarding the parties' dispute whether "an effective amount" of each drug includes amounts of each drug known to be effective in treating RA, as Petitioners assert, or requires that such amounts must actually impart a therapeutic effect on a patient, as Patent Owner asserts, we find that Petitioners have the better position. Petitioners provide expert testimony that a POSA would have understood the plain meaning of the term to include amounts known to be effective in treating RA, regardless of whether it has such an effect any one particular patient to whom the therapy is administered. Pet. 18–20 (citing Ex. 1003 ¶¶ 128, 131). Based on the current record, we find that unrebutted testimony persuasive. Moreover, the Specification discloses specific dosage ranges for each drug recited in the challenged claim. For the antibody, the Specification states,

> When administered in combination with MTX, the dosage of the anti-IL-6R antibody is typically, for example, in the case of the rheumatoid arthritis treatment, the dosage more than 0.5 mg/kg per week or the dosage showing an equivalent or more anti-rheumatic effect. For instance, when the intravenous administration is carried out once four weeks, the dosage is from 0.02 to 150 mg/kg, preferably from 0.5 to 30 mg/kg, and more preferably from 2 to 8 mg/kg.

Ex. 1001, 3:55–62; *see also id.* at 2:38–48 (referring also to "the dosage showing the anti-IL-6R antibody concentration in blood equivalent thereto").

For the immunosuppressant, i.e., MTX, the Specification states,

> When MTX is used as the immunosuppressant, the dosage of MTX is, for example, from 1 to 100 mg/body/weeks or the dosage showing the MTX concentration in blood equivalent thereto, preferably from 4 to 50 mg/body/week or the dosage showing the MTX concentration in blood equivalent thereto, and particularly preferably from 10 to 25 mg/body/weeks or the dosage showing the MTX concentration in blood equivalent thereto.

Id. at 2:60–67; *see also id.* at 4:43–47. Based on those disclosures, we agree with Petitioners that "an effective amount" for each drug encompasses at least the dosage range amounts set forth in the Specification. Based on our reading of the Specification, those dosage ranges are expected to provide a therapeutic effect in patients. We gain that understanding from the Specification description that, even beyond the dosage ranges disclosed, "the dosage showing [the drug] concentration in blood equivalent thereto" would be suitable. Notably, the Specification explains that "[t]he dosage showing the drug" means "a dosage giving an *equivalent therapeutic effect*," which we interpret to mean a therapeutic effect equivalent to what the specifically disclosed dosage ranges are expected to provide. *Id.* at 3:1–8 (emphasis added).

Accordingly, at this stage in the proceeding, we preliminarily construe "an effective amount" recited in the claim phrases "an effective amount of an anti-IL-6 receptor antibody," and "an effective amount of methotrexate (MTX)" as "an amount of the recited drug known in the art to be typically effective in achieving a therapeutic effect in RA, including the dosage range amounts identified by the '052 patent, regardless of whether such dosage amount is shown to provide a therapeutic effect in a particular patient to whom the drug is administered."

C. Anticipation by Yoshizaki

Petitioners assert that claim 1 is anticipated by Yoshizaki. Pet. 22–29. Patent Owner disagrees. Prelim. Resp. 24–28.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Schering Corp. v. Geneva Pharms*, 339 F.3d 1373, 1379 (Fed. Cir. 2003) (quoting *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

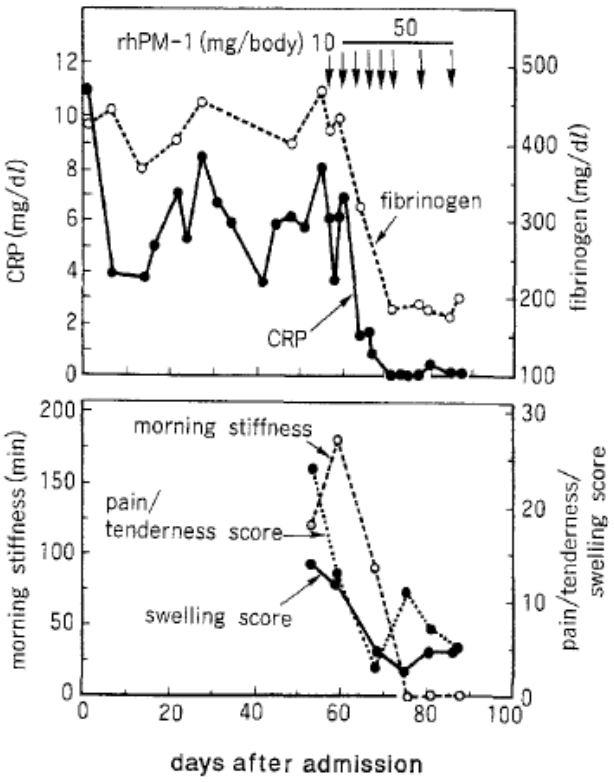
1. Yoshizaki

Yoshizaki is a review article that discusses the role of IL-6 in the pathogenesis of RA and a new approach for treating the disease based on blocking IL-6 signal transduction with a humanized anti-IL-6 receptor antibody because it is "now known that de-regulated cytokine production plays a major role in the pathogenesis of chronic inflammatory autoimmune diseases." Ex. 1005, 3.[5] Yoshizaki explains that such new therapeutic strategies are needed because "conventional therapy with non-steroid anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs

[5] We refer to page numbers assigned to Exhibit 1005 by Petitioners.

DMARDs combined with methotrexate (MTX) and/or steroids in RA is still unsatisfactory." *Id.* at 6.

Yoshizaki describes evaluating the therapeutic effects of humanized anti-IL-6R antibody, i.e., remodeled human anti-IL-6R antibody (rhPM-1), by administering rhPM-1 to patients with severe RA who were resistant to any conventional therapy. *Id.* at 10. Yoshizaki explains that those patients suffered from continuous arthralgia and symptoms of general fatigue, low appetite, loss of weight and subfever, "despite treatment with NSAIDs, DMARDs, MTX and maintenance doses of steroids." *Id.* Yoshizaki states that "rhPM-1, 1-50 mg in 50 ml of saline was intravenously injected once or twice a week. The results were positive in all of the patients." *Id.* at 11. Yoshizaki explains that "[t]he representative clinical course of a rhPM-1 treated patient is shown in Figure 8." *Id.* Yoshizaki's Figure 8 is set forth below.



Ex. 1005, Fig. 8. Yoshizaki Figure 8 depicts the "clinical course of laboratory and symptomatic findings in a patient with severe RA treated with rhPM-1." *Id.* Yoshizaki describes that patient as "[a] 67 year-old woman with severe RA given NSAIDs, DMARDs, MTX and 15 mg predomizolone[6] received 50 mg rhPM-1 twice a week or once a week combined with the conventional treatment. The clinical and laboratory abnormalities improved after the rhPM-1 therapy." *Id.* Yoshizaki explains that the therapeutic effects depicted in Figure 8 "did not decrease even after continuous 6-month treatment, in which the maintenance dose was 50 mg of rhPM-1 and the total amount was almost 1.2–2.4 g." *Id.* at 11. Additionally, Yoshizaki explains that "[n]o major side effects were observed except for the appearance of anti-idiotypic antibody in one case." *Id.* According to Yoshizaki, "[t]he results of this open study suggest that rhPM-1 is effective, safe and useful for the treatment of RA, and that IL-6 is a pathogenic key cytokine as an effector in RA." *Id.*

2. Discussion

Petitioners identify the disclosures in Yoshizaki that Petitioners assert disclose each limitation of claim 1. Pet. 23–29. Specifically, Petitioners assert that Yoshizaki's disclosure of treating an RA patient with a combination of rhPM-1 and methotrexate anticipates challenged claim 1. *Id.* at 23. In particular, Petitioners assert that Yoshizaki discloses administering an effective amount of each drug by disclosing that the patient had previously been treated with a number of RA drugs, including methotrexate,

[6] It is unclear from the reference whether the term "predomizolone" is a typographical error of the term "prednisolone," a well-known glucocorticoid commonly used in the treatment of RA. That issue, however, does not impact our analysis of Yoshizaki or the parties' arguments.

and that treatment with 50 mg of rhPM-1 was combined with the "conventional treatment" to treat her RA. *Id.* at 24–25. Petitioners assert that the 50 mg of the anti-IL-6R antibody, rhPM-1, administered once or twice a week was an effective amount, as Yoshizaki disclosed that such dose was "effective, safe and useful for the treatment of RA." *Id.* at 25 (citing Ex. 1005, 11. Further, Petitioners assert that the dosage of 50 mg once a week corresponds to a dosage within the range disclosed in the '052 patent. *Id.* (citing Ex. 1002 ¶ 138).

As for methotrexate, Petitioners assert that Yoshizaki administered methotrexate in accordance with "conventional treatment," and that a POSA would have understood that such conventional treatment with methotrexate means an amount of methotrexate known to be effective for treating RA. *Id.* at 27. Further, Petitioners assert that at the time of Yoshizaki's publication, the conventional methotrexate treatment for RA was between 7.5 and 20 mg per week, which is within the dosage range for methotrexate disclosed in the '052 patent. *Id.* (citing Ex. 1002 ¶¶ 136–141).

Based upon our review and consideration of the current record, we determine that Petitioners have demonstrated a reasonable likelihood of prevailing in showing that claim 1 is anticipated by Yoshizaki. In particular, as Petitioners assert, Yoshizaki discloses, as the representative clinical course of the patient treatment in the Osaka University rhPM-1 study, that "[a] 67 year-old woman with severe RA given NSAIDs, DMARDs, MTX and 15 mg predomizolone received 50 mg rhPM-1 twice a week or once a week combined with the conventional treatment." Ex. 1005, 11. Based on the current record, we credit Dr. Zizic's currently unrebutted testimony that a person having ordinary skill in the art at the time of the invention would have understood Yoshizaki's reference to "conventional treatment" of

methotrexate to mean the amount of methotrexate known to be effective in treating RA at that time. *See* Ex. 1002 ¶ 137. Additionally, we credit Dr. Zizic's currently unrebutted testimony that the dosage of rhPM-1 administered to the patient in Yoshizaki falls within the dosage range disclosed in the '052 patent for the anti-IL-6R antibody. *Id.* ¶¶ 138–139. Yoshizaki reports that "[t]he clinical and laboratory abnormalities improved after the rhPM-1 therapy." Ex. 1005, 11. Further, as correctly noted by Petitioners and Dr. Zizic, Yoshizaki concludes that "[t]he results of this open study suggest that rhPM-1 is effective, safe and useful for the treatment of RA." *Id.*; Pet. 25; Ex. 1002 ¶140.

In reaching our determination that Petitioners have demonstrated a reasonable likelihood of prevailing in it challenge of claim 1, we considered Patent Owner's arguments, which we address in the following discussion.

Patent Owner contends that Yoshizaki does not disclose administering MTX and an anti-IL-6R antibody in the same treatment regimen. Prelim. Resp. 26. In particular, Patent Owner asserts that Yoshizaki's disclosure that a patient's conventional treatment continued when she received the rhPM-1 antibody was not a disclosure of the claimed combination therapy. *Id.* Patent Owner characterizes Yoshizaki as merely describing "many different medicines that could form a part of the 'conventional' treatment this particular patient received, including, in addition to MTX, at least two NSAIDs, at least two DMARDs, and 'predomizolone.'" *Id.* at 26–27 (citing Ex. 1005, 10–11). According to Patent Owner, "[t]here is no statement or suggestion [in Yoshizaki] that the 'conventional treatment' this patient received included *all* of these drugs *at the same time*," and that "*Yoshizaki* is simply silent on whether this patient ever received the experimental antibody and MTX at the same time." Prelim. Resp. 27.

Insofar as Patent Owner asserts that Yoshizaki does not disclose whether the patient identified as representing the clinical course of a patient in the Osaka University study received the antibody and MTX "*at the same time*," we note that argument lacks merit as our preliminary construction regarding the administration of the two drugs to a patient either simultaneously or sequentially within a treatment regimen comprising both drugs. Thus, administration of the two drugs need not be "at the same time" to meet the administration step of the claim.

Additionally, based upon our reading of Yoshizaki, we do not see any ambiguity as to whether the patient described by Yoshizaki received MTX along with rhPM-1. Yoshizaki states, "A 67 year-old woman with severe RA given NSAIDs, DMARDs, MTX and 15 mg predomizolone received 50 mg rhPM-1 twice a week or once a week combined with the conventional treatment." Ex. 1005, 11. We understand the reference to "conventional treatment" refers back to the itemized treatments in the same sentence, i.e., NSAIDs, DMARDs, MTX and 15 mg predomizolone. Those treatments are linked or connected together with the usage of commas and the conjunction "and." *See id.* Moreover, Yoshizaki discusses conventional therapy, including NSAIDs, DMARDs, MTX, and/or steroids for treating RA. *Id.* at 6. Thus, based on the current record, we find Patent Owner's assertions that Yoshizaki does not disclose that the patient received NSAIDs, DMARDs, MTX and predomizolone along with rhPM-1, and that such therapy would be "shocking" and "not 'conventional,'" *see* Prelim. Resp. 27, is unsupported attorney argument.

Next, Patent Owner contends that Yoshizaki fails to disclose an "effective amount" of MTX because the reference does not disclose the dosage of MTX administered as part of the prior "conventional treatment"

that failed or in combination with the current antibody therapy, assuming that MTX was included such combination therapy. Prelim. Resp. 27–28. Although recognizing that Petitioners may use extrinsic evidence "to reveal what a § 102 reference would have meant to a POSA," Patent Owner asserts that Petitioners improperly seek to use such evidence to supply missing claim limitations. *Id.* at 28. Further, Patent Owner asserts that Petitioners have not identified "*any* reference disclosing the dosage of MTX that is 'effective' when *combined* with an anti-IL-6R antibody." *Id.*

At this stage in the proceeding, we find Patent Owner's arguments to be insufficient to outweigh the strength of Petitioners' arguments and evidence for institution. Insofar as Patent Owner argues that Petitioners have not shown that any reference discloses the dosage of MTX that is effective when combined with an anti-IL-6R antibody, we note that argument lacks merit as we have determined, at this stage of the proceeding, that claim 1 does not recite or refer to any required "combined" effectiveness amount, or that the recited "effective amount" of the two drugs are co-dependent.

Additionally, Patent Owner's argument that Yoshizaki does not disclose a dosage for MTX dismisses Petitioners' evidence to the contrary. Petitioners provide expert testimony that a POSA would have understood Yoshizaki's disclosure of administering "the conventional treatment" to include administering methotrexate in an amount known to be effective for treating RA at that time. *Id.* at 27 (citing Ex. 1002 ¶¶136–137). Further, Petitioners provide expert testimony that, at the time of Yoshizaki's publication, the conventional methotrexate treatment for RA was known to be between 7.5 and 20 mg per week, which is within the dosage range for methotrexate disclosed in the '052 patent. *Id.* (citing Ex. 1002 ¶¶ 136–141).

Thus, Petitioners appear to properly rely on currently unrebutted expert testimony, along with the additional cited references supporting that testimony, to demonstrate what a POSA would have understood from Yoshizaki's express disclosure of administering "the conventional treatment" for RA. In doing so, Petitioners have shown sufficiently for institution that Yoshizaki discloses each limitation of claim 1.

Accordingly, based on the information presented at this stage of the proceeding, we determine that Petitioners have demonstrated a reasonable likelihood that it would prevail in showing that independent claim 1 is anticipated by Yoshizaki.

D. Anticipation by Nishimoto

Petitioners assert that Nishimoto anticipates claim 1. Pet. 29–34. Patent Owner disagrees. Prelim. Resp. 28–32.

1. Nishimoto

Nishimoto is a journal article that discusses the role of IL-6 in the pathology of rheumatoid arthritis and the usefulness of anti-IL-6 receptor antibodies as a novel treatment for the disease. Ex. 1006, 3–4.[7] Nishimoto explains that, prior to clinical studies, MRA was used at Osaka University from 1995 to 1997 "to treat patients with intractable rheumatism who were resistant to anti-rheumatics including methotrexate." *Id.* at 4. That MRA treatment was administered by drip infusion of 50 mg twice a week or 100 mg once a week. *Id.* Nishimoto discloses that such MRA treatment "not only caused a dramatic normalization of inflammatory markers . . . but also rapidly improved joint symptoms and general symptoms." *Id.*

[7] We refer to page numbers assigned to Exhibit 1006 by Petitioners.

According to Nishimoto, based on the effectiveness of MRA treatment observed in those patients as Osaka University, phase I clinical studies were initiated in 1997 in healthy individuals in Japan and in rheumatism patients in the United Kingdom. *Id.* Nishimoto describes the phase I study in the United Kingdom as "a double-blind study by single administration of 0.1, 1.5 or 10 mg/kg of body weight of MRA or a placebo." *Id.* Nishimoto states that "[o]n day 2 after MRA administration in the 5 mg/kg dose group, efficacy was observed with about 56% of patients satisfying the American College of Rheumatology Criteria ACR 20." *Id.*

Nishimoto also describes a phase I/II study of MRA in rheumatoid arthritis patients in Japan that began in 1999. *Id.* In that open-label study, patients were administered 2, 4, or 8 mg/kg body weight of MRA every two weeks by intravenous drip infusion. *Id.* at 54. Nishimoto reports that "[t]he percentage achieving ACR 20 was 60% in week 6 and 80% in month 6, and the percentage achieving ACR 50 was 6.7% in week 6 and 40% in month 6, confirming excellent treatment efficacy." *Id.* at 4. Nishimoto explains that, based on these study results, "a placebo-controlled late phase II study was performed in Japan and on the basis of its results, treatment with 8 mg/kg of body weight of MRA every 4 weeks was recommended." *Id.*

Additionally, Nishimoto mentions that "a phase II study of coadministration with methotrexate is currently underway in several European countries." *Id.*

2. Discussion

Petitioners identify the disclosures in Nishimoto that Petitioners assert disclose each limitation of claim 1. Pet. 30–34. Specifically, Petitioners assert that Nishimoto's disclosure that "a phase II study of the coadministration [of MRA] with methotrexate is currently underway in

several European countries" anticipates challenged claim 1. *Id.* at 30–31 (citing Ex. 1006, 5). Petitioners also rely on Nishimoto as disclosing, based on results of another series of clinical studies, a recommended dosage regimen of treating RA with 8mg/kg of body weight of MRA every four weeks. *Id.* at 31–32 (citing Ex. 1006, 5). Based on those disclosures, Petitioners assert that "Nishimoto discloses administering MRA in combination with methotrexate, according to the recommended dosage regimen, *i.e.*, 8 mg/kg administered intravenously every four weeks, which is an 'effective amount' of MRA within the meaning of claim 1." *Id.*

As for methotrexate, Petitioners assert that "a POSA would have known that methotrexate was administered at a dose of between 7.5 mg and 25 mg once weekly to treat RA, whether as monotherapy or in combination with other drugs." *Id.* (citing Ex. 1002 ¶ 147). Petitioners assert also that a POSA would have known that same dosage range was used for clinical trials involving methotrexate in combination with other RA drugs. *Id.* at 33 (citing Ex. 1002 ¶ 147). Based on those assertions, Petitioners contend that "a POSA would have reasonably inferred that the phase II study disclosed by Nishimoto involved administering methotrexate orally at a dose between 7.5 mg and 25 mg, which is an 'effective amount' within the meaning of claim 1." *Id.* (citing Ex. 1002 ¶ 147).

Patent Owner argues that Petitioners have not shown that Nishimoto anticipates claim 1 because Nishimoto does not disclose the MRA or MTX dosing used in the relied upon phase II study of the coadministration of those two drugs that was currently underway in several European countries. Prelim. Resp. 29. We agree. Nishimoto provides no details about the clinical course of the combination therapy in the European phase II study beyond the fact that it involved coadministration of MRA and MTX. *See*

Ex. 1006, 5. As Patent Owner asserts, it is unclear whether the MRA dosage amount disclosed by Nishimoto was known, much less employed, by those conducting the phase II study in Europe. Additionally, there is no indication in Nishimoto that the phase II study employed a MTX dosage amount used in conventional treatment. As Patent Owner asserts, Petitioners' argument that claim 1 is anticipated by Nishimoto is improperly based largely on supposition and speculation, rather than on disclosures by Nishimoto. *See* Prelim. Resp. 29–30. For that reason, we determine that Petitioners have not shown sufficiently for institution that Nishimoto discloses each limitation of claim 1.

Accordingly, based on the information presented at this stage of the proceeding, we determine that Petitioners have not demonstrated a reasonable likelihood that it would prevail in showing that independent claim 1 is anticipated by Nishimoto.

E. Obviousness over Nishimoto and Weinblatt

Petitioners assert that claim 1 would have been obvious over the combined teachings of Nishimoto and Weinblatt. Pet. 34–45. Patent Owner disagrees. Prelim. Resp. 32–39. We incorporate our description of Nishimoto in Section II.D.1. here.

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007).

"An obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art

references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *CRFD Research, Inc. v. Matal*, 876 F.3d 1330, 1340 (Fed. Cir. 2017) (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–1368 (Fed. Cir. 2016)).

Notwithstanding what the teachings of the prior art would have suggested to one with ordinary skill in the art at the time of the patent's invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the challenged claims would not have been obvious to one with ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984). Objective evidence of nonobviousness, so called "secondary considerations," may include long-felt but unsolved need, failure of others, unexpected results, commercial success, copying, licensing, and praise. *See Graham*, 383 U.S. at 17–18; *Leapfrog Enters., Inc. v. Fisher–Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).[8]

1. Weinblatt

Weinblatt is a journal article describing a 24-week, randomized double-blind, placebo-controlled trial of adalimumab with concomitant MTX therapy performed in the United States and Canada, i.e., the "ARMADA" trial. Ex. 1008, 1–2.[9]

[8] At this stage of the proceeding, Patent Owner does not assert or present evidence of objective indicia supporting nonobviousness of the challenged claim. *See* Prelim. Resp. 32–39.
[9] We refer to page numbers assigned to Exhibit 1008 by Petitioners.

As background, Weinblatt explains that, although methotrexate had become the treatment of choice for RA, many patients continue to have some degree of disease activity despite receiving therapeutic doses of that drug. *Id.* at 2. "To enhance the clinical response, MTX is frequently combined with one or more other traditional disease-modifying antirheumatic drugs (DMARDs)." *Id.* Specifically, Weinblatt describes "the development of biologic DMARDs that bind to and inactivate the proinflammatory cytokine tumor necrosis factor α (TNFα)." *Id.* Weinblatt notes that there are two TNFα blockers that are commercially available, infliximab, a chimeric monoclonal antibody to TNFα, and etanercept, a recombinant human TNF receptor fusion protein. *Id.*

The focus of the current study discussed by Weinblatt was to evaluate the efficacy and safety of the first fully human monoclonal tumor necrosis factor α antibody, adalimumab. *Id.* at 1–2. In the study, patients with active rheumatoid arthritis, despite treatment with MTX, were randomly assigned to receive injections of 20 mg, 40 mg, or 80 mg of adalimumab subcutaneously, or placebo, every other week "while continuing to take their long-term stable dosage of MTX," i.e., 12.5–25 mg, or 10 mg if intolerant to higher doses). *Id.* at 1–2. Weinblatt reports that "the addition of adalimumab (subcutaneously every other week) to the MTX (orally or subcutaneously every week) therapy achieved significant, rapid, and sustained responses." *Id.* at 9. In particular, "[t]he 20-mg, 40-mg and 80-mg adalimumab dosage plus MTX groups achieved statistically superior ACR20 and ACR50 response rates compared with placebo plus MTX group." *Id.* According to Weinblatt, "[t]aken together, these findings indicate that addition of adalimumab to MTX therapy substantially and rapidly improves standard measures of disease activity, including signs and

symptoms, the acute-phase response, functional parameters fatigue scales, and quality of life scores in RA patients not adequately responding to therapy with MTX alone." *Id.*

2. Discussion

According to Petitioners, a POSA would have been motivated by the combined teachings of Nishimoto and Weinblatt "to administer an effective amount of an anti-IL-6R antibody with an effective amount of methotrexate, and would have had a reasonable expectation of success in so doing." Pet. 34 (citing Ex. 1002 ¶¶ 149–162). As in its anticipation challenge, Petitioners here again rely on Nishimoto's disclosure that "a phase II study of the coadministration [of MRA] with methotrexate is currently underway in several European countries" and Nishimoto's recommended treatment of RA with 8mg/kg of body weight of MRA every four weeks. *Id.* at 38 (citing Ex. 1006, 5). Petitioners assert that "[e]ven if Nishimoto did not expressly disclose the amounts or frequencies of administration of the combined regimen, selection of theses parameters [as claimed] would have been obvious." *Id.* at 40.

Specifically, regarding MRA, Petitioners assert that a POSA would have been motivated to use that recommended dosing that Nishimoto discloses for MRA, which is an "effective amount" within the meaning of claim 1, in a MRA-MTX combination therapy because it was known that "DMARDs are generally administered in the same dosage amount and frequency when given in combination with methotrexate as they are when given alone, and a POSA would have expected this to be the case for MRA." *Id.* at 40–41 (citing Ex. 1002 ¶159).

Regarding methotrexate, Petitioners assert that a POSA would have maintained the patient's existing methotrexate dosing regimen as disclosed

in Weinblatt, which was a common practice when supplementing methotrexate with a new drug. *Id.* at 41 (citing Ex. 1008, 2; Ex. 1002 ¶ 160). In particular, Petitioners point to Weinblatt's teaching that typical inadequate methotrexate responders receive oral doses between 10 and 25 mg once per week, which Petitioners assert encompasses the standard methotrexate dosing regimen for treating RA and is an "effective amount" within the meaning of claim 1. *Id.* (citing Ex. 1008, 2); Ex. 1002 ¶¶ 155–160.

Petitioners contend that a skilled artisan would have had a reasonable expectation that the combined regimen would successfully treat RA because both MRA and methotrexate were known to be individually effective for treating RA, and combining methotrexate with other RA drugs was known to 'improve disease control.'" *Id.* at 41 (citing Ex. 1002 ¶ 161). In other words, Petitioners assert that a POSA would have had a reasonable expectation that a combination of known efficacious regimens of MRA and methotrexate could be used to treat a patient with RA. *Id.* at 42–43 (citing *BTG Int'l Ltd. v. Amneal Pharm. LLC*, 923 F.3d 1063, 1074 (Fed. Cir. 2019) ("[T]he record shows that a PHOSITA would have a reasonable expectation of success in combining abiraterone and prednisone because they were both together and individually considered promising prostate cancer treatments at the time.").

Patent Owner responds that "Petitioners' references establish only that the POSA might be motivated to see whether there were 'effective amounts' of an anti-IL-6R antibody and MTX that could be administered in a combination therapy." Prelim. Resp. 38. However, Patent Owner asserts that, "[i]n light of the field's limited understanding of the pathology of RA, the mixed and unpredictable experience with prior MTX combination

treatments, and the novelty and complexity of anti-cytokine treatments for RA, Petitioners have not met their burden" of proving that a skilled artisan would have reasonably expected success in achieving that goal. *Id.* at 38–39, *see id.* at 33–38 (arguing that the track record of treating RA with MTX in combination with another compound was "replete with mixed and unpredictable results").

Having considered the parties' arguments and evidence, at this stage in the proceeding, we conclude that Petitioners have shown sufficiently for institution that, in view of Nishimoto and Weinblatt, a POSA would have had a reason to administer an effective amount of MRA and an effective amount of MTX as a combination therapy to treat RA in a patient in need thereof, with a reasonable expectation of success. To begin, Petitioners have provided ample support for its contention that Nishimoto alone, and in view of Weinblatt, would have provided sufficient motivation for a POSA to combine MRA and MTX to treat RA. *See* Pet. 34–41. Indeed, Patent Owner does not challenge Petitioners' contention in that regard, at this stage in the proceeding. *See* Prelim. Resp. 38 (acknowledging the motivation provided by Petitioners' cited references).

As for the dosage of MRA, Petitioners have shown that Nishimoto discloses a recommended dosage of MRA, i.e., 8mg/kg of body weight every 4 weeks, to treat RA. Pet. 38; Ex. 1006, 5. As Petitioners assert, Nishimoto explains that such dose was recommended based on study results that confirmed such treatment provided excellent efficacy. Pet. 38–41; Ex. 1006, 4–5. Based on those disclosures of Nishimoto, and our preliminary construction of the term "effective dose," discussed above in Section II.B.3., we find that Petitioners have shown sufficiently, based on the current record, that Nishimoto teaches or suggests an effective amount of MRA to treat RA,

as required by claim 1. Moreover, we credit Dr. Zizic's currently unrebutted testimony that "DMARDs are generally administered in the same dosage amount and frequency when given in combination with methotrexate as they are when given alone, and a POSA would have expected this to be the case for MRA." Ex. 1002 ¶ 159.

As for the dosage of MTX, Petitioners have demonstrated persuasively, at this stage in the proceeding, that a POSA would have maintained a patient's existing methotrexate dosing regimen when supplementing that medication with an additional drug, including MRA. *See* Pet. 41 (citing Ex. 1008, 2; Ex. 1002 ¶¶ 155–160). Additionally, Petitioners have shown sufficiently at this stage that the typical dosage of methotrexate used to treat RA was between 10 and 25 mg once per week, as disclosed, for example, in Weinblatt. *Id.* Based on that showing, including the testimony of Dr. Zizic regarding the same, and our preliminary construction of the term "effective dose," discussed above in Section II.B.3., we find that Petitioners have shown persuasively, based on the current record, that Weinblatt and the knowledge in the art teaches or suggests an effective amount of MTX to treat RA, as required by claim 1.

The parties' dispute in this ground centers upon whether a POSA would have had a reasonable expectation of success in treating RA by administering effective amounts of MRA and MTX. We have considered each of Patent Owner's arguments, *see* Prelim. Resp. 33–39, but do not find them sufficient at this stage of the proceeding to deny the Petition.[10] As discussed in our claim construction analysis, we have made a preliminary

[10] As noted above, Patent Owner does not assert or present evidence of objective indicia supporting nonobviousness of the challenged claim in its Preliminary Response. *See* Prelim. Resp. 32–39.

determination that the recited method for treating RA only requires attempting to cause a therapeutic improvement in the patient's disease and that the effective amounts of each drug administered are amounts known in the art to be typically effective in achieving a therapeutic effect in RA. Based on those preliminary claim constructions, we find that Petitioners have shown adequately for institution that a POSA would have had a reasonable expectation of successfully treating RA by administering the known effective amounts of MRA and MTX, for the reasons discussed by Petitioners, i.e., because both drugs "were known to be individually effective for treating RA, and combining methotrexate with other RA drugs was known to 'improve disease control.'" *See* Pet. 42 (citing Ex. 1002 ¶ 161).

Based on the current record, Patent Owner's arguments to the contrary establish at most that a POSA would have "know[n] to proceed with caution" in combining the drugs based on the alleged safety concerns associated with each drug. However, Patent Owner has not identified evidence sufficient to establish that such concerns or unpredictability involved in the combined therapy would have caused a POSA to not have even a reasonable expectation of success with such therapy. In any event, Patent Owner may develop those arguments at trial.

Accordingly, based on the information presented at this stage of the proceeding, we determine that Petitioners have shown sufficiently that there is a reasonable likelihood that it would prevail in showing that claim 1 is rendered obvious by the combination of Nishimoto and Weinblatt.

F. Discretion to Institute under 35 U.S.C. § 314(a)

Institution of *inter partes* review is discretionary:

> The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that 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). This language provides the Director with discretion to deny institution of a petition. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) ("[T]he agency's decision to deny a petition is a matter committed to the Patent Office's discretion."); Patent Trial and Appeal Board Consolidated Trial Practice Guide ("CTPG") at 55 (November 2019), *available at* https://www.uspto.gov/TrialPracticeGuideConsolidated. The Director has delegated his authority under § 324(a) to the Board. 37 C.F.R. § 42.4(a) ("The Board institutes the trial on behalf of the Director.").

The Leahy-Smith America Invents Act was "designed to establish a more efficient and streamlined patent system that will improve patent quality and limit unnecessary and counterproductive litigation costs." H.R. Rep. No. 112−98, pt. 1, at 40 (2011), 2011 U.S.C.C.A.N. 67, 69 (reviews were meant to be "quick and cost effective alternatives to litigation"); *see also* S. Rep. No. 110−259, at 20 (2008); CTPG 56. The Board recognized these goals, but also "recognize[d] the potential for abuse of the review process by repeated attacks on patents." *General Plastic Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19, 16−17 (PTAB Sept. 6, 2017) (precedential).

In *NHK Spring Co. v. Intri-Plex Technologies, Inc.*, IPR2018-00752, Paper 8 (PTAB Sept. 12, 2018) (precedential), the Board determined that the advanced state of a parallel proceeding is an additional factor weighing in favor of denying institution under 35 U.S.C. § 314(a). *Id.* at 19–20. In *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019 ("*Fintiv*"), Paper 11 (PTAB Mar. 20, 2020) (precedential), the Board articulated a list of factors that we consider in determining whether to exercise discretion to deny institution based on an advanced stage of a parallel proceeding:

> 1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
>
> 2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
>
> 3. investment in the parallel proceeding by the court and the parties;
>
> 4. overlap between issues raised in the petition and in the parallel proceeding;
>
> 5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
>
> 6. other circumstances that impact the Board's exercise of discretion, including the merits.

Fintiv, Paper 11, 5–6. "These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding." *Id.* In evaluating these factors, we take "a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review." *Id.* (citing CTPG 58).

Patent Owner asserts that we should decline to institute under *NHK Spring/Fintiv*. Prelim. Resp. 39–41. However, as Patent Owner admits, there is no pending litigation between the parties. *Id.* at 39. Nevertheless, Patent Owner urges that we could deny institution under *Fintiv* "because of the near-certainty of parallel, duplicative proceedings." *Id.* In particular, Patent Owner asserts that "[t]he absence of any pending litigation between the parties does not mean they do not have a dispute." *Id.* According to Patent Owner, "[t]he statutory scheme governing biosimilars like Petitioners' copy of Actemra® [Patent Owner's product comprising tocilizumab, i.e., MRA] all but guarantees patent litigation between Petitioners and Patent Owner." *Id.* Specifically, Patent Owner contends,

> Once Petitioners seek approval from FDA for their copy of Actemra®, the parties' patent disputes are likely to explode into full-blown district court litigation, including, potentially, preliminary injunction proceedings on patents like the '052 patent. By refusing to hold off serving its notice of intent to market until this proceeding concludes, Petitioners virtually guarantee that the trial court and the Board will be addressing the '052 patent in parallel.

Id. at 40.

As noted above, the Board's discretionary denial analysis, set forth in *NHK Spring/Fintiv* pertains to matters before us that involve a parallel proceeding—typically an ongoing lawsuit in court. Here, Patent Owner has identified, at best, a hypothetical future district court litigation. Because Patent Owner has not identified an existing parallel proceeding to consider, we decline Patent Owner's invitation for us to consider discretionary denial of the institution under *Fintiv*.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioners have established a reasonable likelihood of prevailing in its assertion that claim 1 of the '052 patent is unpatentable. Accordingly, in light of *SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348, 1354 (2018), and the Patent Trial and Appeal Board Consolidated Trial Practice Guide 64 (Nov. 2019), *available at* https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf, we institute an *inter partes* review of the challenged claim on all asserted grounds.

Our determination in this Decision is not a final determination on either the patentability of any challenged claims or the construction of any claim.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claim 1 of the '052 patent on all grounds set forth in the Petition is instituted, commencing on the entry date of this decision; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of review.

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