

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HOPEWELL PHARMA VENTURES, INC.,
Petitioner,

v.

MERCK SERONO S.A.,
Patent Owner.

IPR2023-00480
Patent 7,713,947 B2

Before ZHENYU YANG, ROBERT A. POLLOCK, and TIMOTHY G.
MAJORS, *Administrative Patent Judges*.

MAJORS, *Administrative Patent Judge*.

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

I. INTRODUCTION

Hopewell Pharma Ventures, Inc. (“Petitioner” or “Hopewell”) filed a Petition (Paper 2, “Pet”) requesting *inter partes* review of claims 36, 38, 39, and 41–46 of U.S. Patent No. 7,713,947 B2 (Ex. 1001, “the ’947 patent”). Pet. 1, 33. Merck Serono S.A. (“Patent Owner” or “Merck”) filed a Preliminary Response (Paper 8, “Prelim. Resp.”).

Under 35 U.S.C. § 314(a), an *inter partes* review may not be instituted unless it is determined that there is a reasonable likelihood that the petitioner will prevail with respect to at least one of the claims challenged in the petition. Considering the parties’ arguments and evidence, for the reasons set forth below, we conclude that Petitioner demonstrates a reasonable likelihood of prevailing with respect to at least one of the ’947 patent’s challenged claims. We decline to deny the Petition on the basis of discretion under 35 U.S.C. § 325(d) as sought by Patent Owner. We therefore institute an *inter partes* review on all challenged claims. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1355 (2018).

Any findings and conclusions at this stage are preliminary and based on the current record. This is not a final decision on the patentability of the challenged claims. Any such final decision will be based on a complete record developed through trial.

II. BACKGROUND

A. *Real Parties-in-Interest*

Petitioner identifies itself and the following entities as real parties-in-interest: Hopewell Pharma Ventures LLC; Levy SPV, LLC; GLS Capital Partners Fund I, LP; GLS Capital Partners GP, LLC; and GLS Capital, LLC. Pet. 68–69. Merck identifies itself along with Merck KGaA and Ares Trading SA as the real parties-in-interest. Paper 3, 1.

B. Related Matters

The parties identify the following lawsuits involving assertions of the '947 patent: *Merck KGaA et al. v. Accord Healthcare, Inc. et al.*, 1-22-cv-00974 (D. Del.); *Merck KGaA et al. v. Hopewell Pharma Ventures, Inc.*, 1-22-cv-01365 (D. Del.); *Merck KGaA et al v. Aurobindo Pharma USA, Inc. et al.*, 1-23-cv-00039 (D. Del.). Pet. 69; Paper 3, 1.

The parties also identify other related matters before the Board. Pet. 69–70; Paper 3, 1–2. Those matters include IPR2023-00481, filed by Hopewell, challenging U.S. Patent No. 8,377,903 (“the ’903 patent”), in which we institute trial concurrent with this decision.¹ Paper 3, 1. Additionally, the parties identify IPR2023-00049 and IPR2023-00050, which were filed by a different petitioner (TWi Pharmaceuticals, Inc. (“TWi”)), challenging the ’947 and ’903 patents.² *Id.* at 1–2; Pet. 69.

C. The ’947 Patent & Technology Background

The ’947 patent, titled “Cladribine Regimen for Treating Multiple Sclerosis,” issued on May 11, 2010. Ex. 1001, codes (45), (54). The application that matured into the ’947 patent was filed December 20, 2005, and claims the priority benefit of a provisional patent application filed December 22, 2004. *Id.* at codes (22), (60).³

¹ IPR2023-00482 involved the same parties (or their RPIs) and a patent on related subject matter, but that case terminated on August 16, 2023, before institution due to settlement. IPR2023-00482, Paper 12.

² The Board denied institution on the TWi-filed petitions. *See* IPR2023-00049, Paper 10; IPR2023-00050, Paper 8.

³ Although not conceding that the ’947 patent is entitled to claim priority to the date this provisional application was filed (Pet. 7–8 n.3), Petitioner applies that date (December 22, 2004) in explaining the state of the art at that time and for its obviousness analysis. *Id.* at 2–4, 13–28. In determining

According to the '947 patent, the “invention relates to the use of multiple doses of Cladribine for the treatment of multiple sclerosis, especially relapsing-remitting multiple sclerosis or early secondary progressive multiple sclerosis.” Ex. 1001, 1:17–20.

Cladribine is a chlorinated purine analogue, 2-chloro-2'-deoxyadenosine (also known as 2-CdA). *Id.* at 2:24–27. Cladribine was known in the prior art, as were oral, i.v., and subcutaneous formulations including it. *See, e.g., id.* at 6:20–25 (noting oral formulations described in, for example, WO 2004/087101, which is the Bodor reference asserted in this proceeding). As background, the '947 patent also notes that cladribine has been suggested previously as useful for treating multiple sclerosis. *Id.* at 2:24–3:21 (discussing prior studies on cladribine's use, in various forms including delivery via oral and subcutaneous routes, in patients with multiple sclerosis); *see also* Pet. 19–21; Ex. 1002 ¶¶ 33–52 (testimony of Dr. Aaron Miller on studies by Beutler, Stelmasiak, Rice, and others).

As described in the '947 patent, “[m]ultiple sclerosis (MS) is the most known chronic inflammatory demyelinating disease of the central nervous system in humans.” Ex. 1001, 1:25–27. “Over time, MS may result in the accumulation of various neurological disabilities” and “[c]linical disability in MS is presumed to be a result of repeated inflammatory injury with subsequent loss of myelin and axons, leading to tissue atrophy.” *Id.* at 1:30–34. The patent states that “MS is manifested in physical symptoms (relapses and disability progression), Central Nervous System (CNS) inflammation, brain atrophy and cognitive impairment.” *Id.* at 1:35–37.

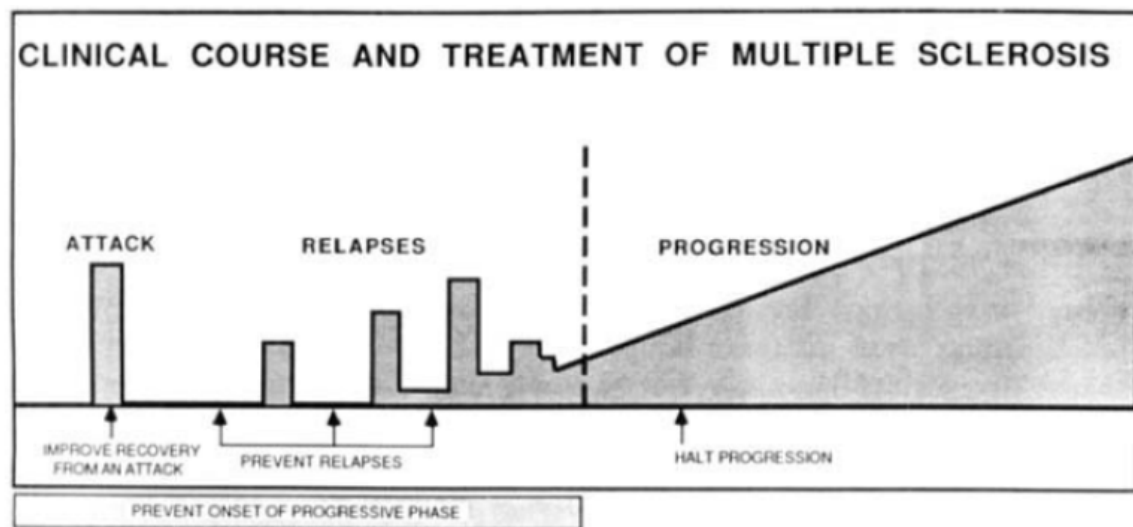
whether Petitioner has shown a reasonable likelihood that it would prevail herein, we will likewise apply that date.

Before December 2004, it was known that lymphocytes (or T cells), which cells are part of the body's acquired immune system, play a role in the pathophysiology of MS. Ex. 1002 ¶¶ 28–29. According to Dr. Miller, “[p]atients with MS ‘harbor T cells that react with CNS autoantigens’” and, “[a]lthough these T cells (a type of lymphocyte) may ‘remain dormant for decades, at some point they are activated in the periphery,’” allowing the cells to “‘migrate through the blood-brain barrier to the brain and spinal cord.’” *Id.* (citing Ex. 1044, 1–3; Ex. 1007, 131). “Once these T cells are reactivated in the CNS . . . they ‘release pro-inflammatory Th1 cytokines and orchestrate the destruction of the myelin sheath by various types of immune cells.’” *Id.* (citing Ex. 1007, 131). As Dr. Miller further explains, inflammation and resulting demyelination creates “lesions” in the affected tissues that can be detected and monitored. Ex. 1002 ¶¶ 15, 24, 27 (discussing detection of active/enhancing lesions using MRI).

According to the '947 patent, MS is “considered to be a multi-phasic disease and periods of clinical quiescence (remissions) occur between exacerbations. Remissions vary in length and may last several years but are infrequently permanent.” Ex. 1001, 1:43–46. Moreover, the patent states, “[f]our courses of the disease are individualized: relapsing-remitting (RR), secondary progressive (SP), primary progressive (PP) and progressive relapsing (PR) multiple sclerosis.” *Id.* at 1:47–50. “More than 80% of patients with MS will initially display a RR course with clinical exacerbation of neurological symptoms, followed by recovery that may or may not be complete.” *Id.* at 1:51–56 (noting that disability arises from incomplete recovery from relapses). “Approximately, half of the patients with RRMS switch to a progressive course, called SPMS, 10 years after the disease[] onset.” *Id.* at 1:57–62 (noting that worsening of disability in the progressive

phase results from “accumulation of residual symptoms after exacerbation but also from insidious progression between exacerbations”).

There is no known cure for MS. Ex. 1002 ¶ 22 (citing Ex. 1024, 35). Because MS is a chronic autoimmune disease, Dr. Miller explains, patients ordinarily require ongoing care and repeated treatments designed to alter or suppress the immune system. Ex. 1002 ¶ 53 (citing Ex. 1008, 211–213). Dr. Miller identifies Figure 1 of Weiner (Ex. 1008), which is reproduced below.



Ex. 1008, 212, Fig. 1. Figure 1, above, is titled a “clinical course and treatment of multiple sclerosis” and shows a common MS disease course, with the horizontal axis representing time and the vertical axis the level of disability. *Id.* (capitalization omitted). The figure includes an early “attack” followed by multiple “relapses,” shown by vertical bars of different heights on the left half of the figure; then, at the time represented by a vertical dashed line near the middle of the figure, the onset of a progressive phase of the disease with persistent disability steadily increasing as shown by the upwardly sloping line as one moves to the figure’s right. *Id.* (including, below the horizontal axis, a treatment strategy (e.g., improve recovery from

attack, etc.) for the disease stage). According to Dr. Miller, as reflected in the figure above, “different therapies are designed to treat acute attacks, prevent or decrease the number of relapses, and prevent onset of or halt the progressive phase.” Ex. 1002 ¶ 53 (citing Ex. 1008, 212–213).

As Dr. Miller further explains, “[b]ecause of the role the immune system plays in the underlying pathophysiology of MS, [administering] immunosuppressive drugs was ‘[t]he most common therapeutic approach’ for treating MS before December 2004.” *Id.* ¶ 16 (citing Ex. 1013, 4; Ex. 1007, 131); *see also id.* ¶ 30 (“Because of the role autoantigen-specific T lymphocytes were known to play in MS, suppressing these lymphocytes was a target of [prior] MS therapies”). According to Dr. Miller, “[b]ecause cladribine caused ‘prolonged, profound suppression of lymphocyte counts,’ researchers began studying it in MS.” *Id.* ¶ 16 (citing Ex. 1016, 420). Indeed, Dr. Miller testifies that “[i]n early studies, cladribine was shown to ‘modulat[e] autoimmune processes involving lymphocyte abnormalities such as MS’ and ‘impressively decrease[]’ relapse rates” in MS patients. *Id.* (citing Ex. 1018, 1146; Ex. 1013, 5, 7). Dr. Miller testifies that, “[d]uring treatment, neurologists commonly assessed the therapeutic effect of cladribine by monitoring a patient’s lymphocyte count, with a sustained reduction of lymphocytes, e.g., below 1000 [cells]/μL, being characteristic of a treatment response.” *Id.* (citing Ex. 1018, 1146; Ex. 1013, 5; Ex. 1014, 1717).

The ’947 patent describes, in an example, a treatment regimen for patients with MS. Ex. 1001, 14:19–16:23 (Example 1). In a study on sixty patients with relapsing forms of MS, the patients were sorted into three groups: for the first year, Group 1 patients received placebo for 4 months followed by 8 months of no treatment; Group 2 patients received daily oral

administration of cladribine (10 mg tablets) for about 5 days a month for 2 months, followed by placebo for 2 months, and 8 months of no treatment (“total dose of about 1.75 mg/kg”); and Group 3 patients received daily oral administration of cladribine (10 mg tablets, as above) for about 5 days a month for 4 months followed by 8 months of no treatment (“total dose of about 3.5 mg/kg”). *Id.* In the second year (starting month 13), the patent discloses that all three groups received oral cladribine for about 5 days a month for 2 months at the lower dose (i.e., total of “about 1.75 mg/kg” over the 2 months) followed by 10 months of no treatment.⁴ *Id.* (disclosing, *inter alia*, that lymphocyte markers are monitored and that “[p]atients in Groups 2 and 3 have a decrease in brain lesions”); *see also* Ex. 1001, 5:52–6:12 (disclosing that “[e]fficacy” of cladribine for MS treatment can be measured by, for example, frequency of relapses, reduction of MRI-detectable lesions, or improvements in clinical assessments, like the “Expanded Disability Status Scale (EDSS)”).

D. Illustrative Claims

Claim 36, reproduced below, is the only independent claim challenged in this proceeding. It reads:

36. A method of treating multiple sclerosis comprising the oral administration of a formulation comprising cladribine following the sequential steps below:

- (i) an induction period lasting from about 2 months to about 4 months wherein said formulation is orally administered and wherein the total dose of cladribine reached at the end of the induction period is from about 1.7 mg/kg to about 3.5 mg/kg;
- (ii) a cladribine-free period lasting from about 8 months to about 10 months, wherein no cladribine is administered;

⁴ The ’947 patent indicates that the course of treatment continues into a third year (starting at month 25) that essentially repeats the regimen given during the second year. Ex. 1001, 16:4–9.

(iii) a maintenance period lasting from about 2 months to about 4 months, wherein said formulation is orally administered and wherein the total dose of cladribine reached at the end of the maintenance period is about 1.7 mg/kg; [and]

(iv) a cladribine-free period wherein no cladribine is administered.

Ex. 1001, 19:14–30. Illustrating some of the challenged dependent claims, claim 39 depends from claim 36 and adds “wherein the total dose of cladribine reached at the end of the induction period is about 1.7 mg/kg,” claim 41 depends from claim 36 and adds “wherein the cladribine-free period (ii) lasts about 10 months,” and claim 45 depends from claim 36 and adds “wherein the formulation is orally administered at a daily dose of 10 mg cladribine.” *Id.* at 20:5–7, 20:11–12, 20:20–22.

E. Prior Art and Asserted Ground

Petitioner asserts that claims 36, 38, 39, and 41–46 are unpatentable based on the following ground:

Claims Challenged	35 U.S.C. § ⁵	References/Basis
36, 38, 39, 41–46	103	Bodor, ⁶ Stelmasiak ⁷

Petitioner also submits testimony from Aaron E. Miller, M.D., in support of its challenge. Ex. 1002 (Miller Decl.).

⁵ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 285–88 (2011), revised 35 U.S.C. §§ 102, 103 effective March 16, 2013. The ’947 patent issued from an application filed before March 16, 2013, so pre-AIA §§ 102 and 103 apply. Ex. 1001, code (22).

⁶ Bodor et al., WO 2004/087101 A2, published Oct. 14, 2004 (“Bodor” (Ex. 1022)).

⁷ Zbigniew Stelmasiak, *A pilot trial of cladribine (2-chlorodeoxyadenosine) in remitting-relapsing multiple sclerosis*, 41:1 Med. Sci. Monit. (March 1, 1998) (“Stelmasiak” (Ex. 1013)).

III. ANALYSIS

A. *Legal Standards*

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3)).

A claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the relevant art. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations of nonobviousness when presented. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

Moreover, “[a]n 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) (internal quotation marks and citation omitted).

B. *Level of Ordinary Skill in the Art*

In determining the level of skill in the art, we consider the problems encountered in the art, the art’s solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the

educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986).

Petitioner proposes that the person of ordinary skill in the art (“POSA”) would have a “high” level of skill. Pet. 28. In more detail, Petitioner contends:

A POSA here would have drawn upon the knowledge and experience of related disciplines of a multi-disciplinary team that might lie outside the POSA’s primary training. . . . A POSA for the ’947 patent would have the knowledge of multiple disciplines, such as immunology, biochemistry, and human physiology and anatomy, and also typically [would] be a clinician with experience and/or training in neurology. . . . The POSA typically would be a medical doctor with a specialty in neurology, specifically in treating autoimmune disorders of the nervous system, such as multiple sclerosis, and typically at least 2 years of experience with administering treatments to patients and evaluating results of such treatments, as well as experience or knowledge in related research and development.

Id. at 28–29 (citing Ex. 1002 ¶¶ 20–21).

Patent Owner does not contest Petitioner’s definition for the POSA. Prelim. Resp. 5. For purposes of this decision, we apply Petitioner’s proposed POSA level, which appears consistent with the skill level reflected in the prior art.

C. *Claim Construction*

In *inter partes* review, we construe claims using the same claim construction standard used to construe claims in a civil action before the courts under 35 U.S.C. § 282(b), including construing claims in accordance with the ordinary and customary meaning as understood by the POSA and the patent’s prosecution history. 37 C.F.R. § 42.100(b). We need only construe terms that are in controversy and only as needed to resolve the

matters in dispute. *Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019).

Petitioner proposes constructions for the following terms: (a) “total dose of cladribine”; (b) “an induction period”; and (c) “maintenance period.” Pet. 29–33. There is no dispute at this stage that turns on interpretation of a “total dose of cladribine,” and we see, as pointed out by Petitioner, that “total dose” is defined in the ’947 patent. Ex. 1001, 4:19–26 (defining “total dose” as the “cumulative dose,” i.e., “the total dose of Cladribine administered during the treatment, i.e. the dose reached at the end of the treatment that is calculated by adding the daily doses”). We need not further address the interpretation of this term at this time.

We discuss the terms “induction period” and “maintenance period” in greater detail below, starting with the “maintenance period,” which is the focus of the parties’ claim construction arguments.

1. maintenance period

The parties’ argument on the term “maintenance period” concerns a comparison between the total amount of cladribine reached at the end of the induction and maintenance periods. More specifically, whether “maintenance period” should be construed as a retreatment period “during which the total dose of cladribine is **lower** than the total dose in the induction period”—Petitioner’s position. Pet. 30–33 (emphasis added). Or, whether the “total cladribine dosing during a maintenance period can be either the **same as or lower than** the total dose of cladribine administered during the induction period”—Patent Owner’s argument. Prelim. Resp. 10. The parties cite intrinsic evidence that allegedly supports their respective interpretations. Pet. 30–33; Prelim. Resp. 6–15.

It is not wholly clear that “maintenance period” must be further interpreted to resolve Petitioner’s challenge. Patent Owner’s interpretation is broader and encompasses Petitioner’s interpretation. Nevertheless, to address the arguments made and give guidance for trial, we determine that the weight of the evidence on this preliminary record supports Patent Owner’s interpretation, and we conclude that the dosing of cladribine given during the “maintenance period” can be same as or lower than the total dose given during the induction period. We explain below.

First, the language of the claims supports Patent Owner’s interpretation. Claim 36 expressly recites that the total dose reached at the end of the induction period (step (i)) “is from about 1.7 mg/kg to about 3.5 mg/kg.” *See supra* Section II(D). Claim 36, step (iii), recites that the total dose of cladribine reached at the end of the maintenance period “is about 1.7 mg/kg.” The plain language of claim 36, thus, indicates that the cladribine dosing given during the induction period and the maintenance period can be the same—each “about 1.7 mg/kg.” Claim 36 also encompasses regimens where the maintenance period dosing (e.g., 1.7 mg/kg) is lower compared to the induction period dosing (e.g., 3.5 mg/kg). But the plain language of the claims does not *require* a lower total dose in the maintenance period. Petitioner’s construction narrows the claims and, in effect, asks us to rewrite the lower bound of the range recited in claim 36’s induction period step to be some value higher than “about 1.7 mg/kg.” We decline to do so.

Petitioner’s interpretation is also at odds with dependent claim 39, which specifies that the total dose of cladribine reached at the end of the induction period “is about 1.7 mg/kg.” Thus, in claim 39, the same dosing amount is recited for the induction and maintenance periods (“about

1.7 mg/kg,” given the dependency from claim 36). Petitioner does not explain how its proposed “lower than” construction can be reconciled with the express language of claim 39.

In addition, other claims (not challenged in this proceeding) expressly require that the “total dose of cladribine is *lower than* the total dose of cladribine reached at the end of the induction period.” *See, e.g.*, Ex. 1001, 18:7–24 (claim 20, which is otherwise substantially identical to claim 36, apart from using the “lower than” language not the language “about 1.7 mg/kg” for the maintenance period) (emphasis added). The patent applicant, thus, knew how to draft independent claims *requiring* the maintenance period dosing be lower. But that language was not used in independent claim 36, which instead sets forth the amount of cladribine reached at the end of the maintenance period using different, numerical terms. Under such circumstances, Petitioner does not persuade us that we should construe claim 36 to insert a “lower than” requirement.

Second, the Specification of the ’947 patent supports Patent Owner’s interpretation. Petitioner cites a definition of “Maintenance Treatment” that describes a maintenance period in which the total cladribine dosage is “orally administered at a lower dose than the Cladribine dose orally administered during the induction treatment.” Ex. 1001, 5:6–11.⁸ That the maintenance period dosing *may be* lower than the induction period dosing is uncontroversial. The question is whether it must always be so. And the Specification answers this question: “no.” Indeed, the ’947 patent includes an example where the cladribine dose reached at the end of the induction

⁸ Petitioner’s declarant, Dr. Miller, testifies that “[t]he ’947 patent does not explicitly define ‘maintenance period.’” Ex. 1002 ¶ 70.

period and the maintenance period is the same (1.75 mg/kg in both periods) or it may alternatively be lower (1.75 mg/kg in the maintenance period and 3.5 mg/kg in induction). Ex. 1001, 15:50–16:3 (describing the dosing regimen for Group 2 and Group 3 patients versus a placebo group). Petitioner’s claim construction argument never addresses this disclosure in the ’947 patent. There is no adequate basis on this record to construe “maintenance period” in claim 36 such that it would exclude the broader maintenance period dosing in the patent’s example.

Lastly, the prosecution history does not, on balance, justify interpreting “maintenance period” in the manner urged by Petitioner. Petitioner argues that, during prosecution of the ’947 patent, Patent Owner accepted the Examiner’s finding that the applied prior art did not “teach that the total dose of cladribine reached at the end of the maintenance phase is *lower* than the total dose reached at the end of the induction phase.” Pet. 31–32 (citing Ex. 1004, 248⁹). According to Petitioner, the Examiner’s finding and Patent Owner’s alleged acceptance of it reflect Patent Owner’s own understanding of the claimed invention. *Id.* The flaw with Petitioner’s argument is that “the Examiner’s characterization [of the art and claims] aligned with the scope of the then-pending claims” that were subject to the Examiner’s rejection. Prelim. Resp. 11 (citing Ex. 1004, 3–6 (pending claim 18, for example, expressly included the “lower than” language)). Claim 36 was added via a proposed amendment (as application claim 54) and was not, at any time during the ’947 patent’s prosecution, rejected by the Examiner. Ex. 1004, 243 (proposed amendment adding new claim 54, dated

⁹ Citations to the prosecution histories of the ’947 and ’903 patents use the page numbering added to the exhibit copy, not the native pagination.

Dec. 18, 2009); *see also id.* at 298 (Notice of Allowance dated Mar. 22, 2010, following applicant’s Dec. 18, 2009, proposed amendment and remarks). The Examiner, thus, never characterized claim 36 as requiring a “lower” maintenance period dose compared to the induction period dose.

Petitioner also cites statements made during prosecution of the child application that matured into the related ’903 patent. Pet. 31–32. According to Petitioner, Patent Owner “argued that the maintenance period is characterized by administration of a lower total dose of cladribine compared to the induction period (even for the pending claims that did not expressly require a *lower* dose, e.g., claim 17 and 20).” *Id.* at 32. Petitioner highlights argument raised during prosecution that “one skilled in the art **would not have had any reason to reduce the dosage of cladribine administered during the ‘maintenance period’ as recited in the claims,**” and that Patent Owner made this argument for the group of “claims 1, 4, 5, 9, 10, 17, 20 or 21.” *Id.* (quoting Ex. 1025, 151) (emphasis added by Petitioner). Here, the prosecution colloquy cited by Petitioner comes closer to supporting Petitioner’s claim construction position. Immediately before applicant made the argument cited above, however, it argued “that nowhere in the teachings of the reference is there any discussion about repeating a treatment course at any point in time *at either the original dosage or at a lower dosage in a manner that could be construed as a ‘maintenance period’* as defined by the subject application.” Ex. 1025, 151 (emphasis added); Prelim. Resp. 12–13 (citing same and contending “PO never argued the maintenance period must always use a total dose lower than the induction period dose”). The prosecution history of the related ’903 patent is, at best for Petitioner, ambiguous on revealing any narrowed meaning of the “maintenance period.” This record does not, overall, support Petitioner’s interpretation on the basis

of any alleged disclaimer, disavowal, or estoppel. *Continental Circuits LLC v. Intel Corp.*, 915 F.3d 788, 798 (Fed. Cir 2019) (“[T]o operate as a disclaimer, the statement in the prosecution history must be clear and unambiguous, and constitute a clear disavowal of scope.”).

Considering the totality of the intrinsic evidence and argument of record, we conclude that, as recited in claim 36, the total dose of cladribine reached at the end of the “maintenance period” *need not be lower* than the total dose reached at the end of the induction period. It may be the same (i.e., about 1.7 mg/kg) for both periods as discussed above.

2. *induction period*

The parties’ dispute about the meaning of “induction period” flows inescapably from their arguments about the maintenance period. That is, if the maintenance period dose must be *lower*, the induction period dose is “higher,” according to Petitioner. Pet. 29–30. Patent Owner, conversely, contends that the induction period’s total cladribine dose may be higher, but it may also be the same as the maintenance period dose. Prelim. Resp. 15. On this record, we agree with Patent Owner for the same reasons discussed above concerning the maintenance period.

D. *Obviousness over Bodor and Stelmasiak*

Petitioner contends that claims 36, 38, 39, and 41–46 would have been obvious over the combined teachings of Bodor and Stelmasiak. Pet. 33–61.

Petitioner contends that Bodor and Stelmasiak are prior art to the ’947 patent and Patent Owner provides no argument otherwise. *Id.* at 22, 24. On this record, we agree that Bodor and Stelmasiak qualify as prior art.

We summarize the asserted prior art below before turning to the parties’ further arguments and our analysis.

1. Bodor (Ex. 1022)

Bodor is an international patent application that was filed March 26, 2004, and published October 14, 2004. Ex. 1022, codes (22), (43). Bodor relates to “compositions of cladribine and cyclodextrin which are especially suited for the oral administration of cladribine.” *Id.* at Abstr.

Bodor teaches that “[o]ral delivery of drugs is often preferred to parenteral delivery for a variety of reasons.” *Id.* at 2:9–10. “[F]oremost,” among the reasons given by Bodor, is “patient compliance.” *Id.* “Patient compliance is enhanced insofar as oral dosage forms alleviate repeated health care provider visits, or the discomfort of injections or prolonged infusion times associated with some active drugs.” *Id.* at 2:11–13.

“However,” Bodor teaches, “to date the oral delivery of cladribine has been plagued by low bioavailability . . . and suboptimal interpatient variation.” *Id.* at 2:22–25. Bodor teaches that “[i]t has now been found that amorphous cyclodextrins can be combined to form a particularly advantageous product which can be incorporated into a solid oral dosage form.” *Id.* at 5:2–4. “This product is a [] cladribine-cyclodextrin complex, and solid oral dosage form containing it improves oral bioavailability and/or achieves lower interpatient and/or inpatient variation of the drug.” *Id.* at 5:4–7; *see also id.* at 11:27–12:3 (describing a cladribine and cyclodextrin complex “associated with improved cladribine absorption, as reflected by higher bioavailability and/or lower interpatient variation”).

Bodor teaches that cladribine has “been used as an immunosuppressive agent and as a modality for the treatment of a variety of autoimmune conditions including . . . multiple sclerosis.” *Id.* at 2:1–5. Bodor discloses that “an effective amount of the complex cladribine-cyclodextrin . . . is used (e.g., an amount effective for the treatment of

multiple sclerosis[)].” *Id.* at 22:11–15. Bodor further teaches that “[t]herapeutically effective dosages described in the literature include those for . . . multiple sclerosis (from about 0.04 to about 1.0 mg/kg/day (see U.S. Patent No. 5,506,214)).” *Id.* at 22:17–22 (defining “therapeutically effective amount”); *see also id.* at 22:27–23:6 (noting “various dosage amounts and dosing regimens have been reported in the literature for use in the treatment of multiple sclerosis,” and listing references).¹⁰

Bodor discloses that, “[a]t the present time, it is envisioned that, for the treatment of multiple sclerosis, 10 mg of cladribine in the instant [] cladribine-cyclodextrin complex in the instant solid dosage form” would be given. *Id.* at 23:15–17. Further, Bodor teaches, this dosage form “would be administered once per day for a period of five to seven days in the first month, repeated for another period of five to seven days in the second month, followed by ten months of no treatment.” *Id.* at 23:17–20; *see also id.* at 23:20–24 (disclosing an alternative regimen where 10 mg of cladribine is given once per day for five to seven days per month over six months, followed by eighteen months of no treatment).

Bodor teaches that the dosing regimen can be tailored to suit the needs of the patient. Specifically, Bodor teaches that “one of skill will appreciate that the therapeutically effective amount of cladribine . . . may be lowered or increased by fine tuning and/or by administering cladribine . . . with another active ingredient.” *Id.* at 24:1–6 (“The invention . . . provides a method to tailor the administration/treatment to the particular exigencies specific to a

¹⁰ U.S. Patent No. 5,506,214 issued April 9, 1996, and names Ernest Beutler as the inventor. Ex. 1026, codes (45), (75). Several other references identified in Bodor are also of record, including Rice (Ex. 1018), Romine (Ex. 1031), Selby (Ex. 1047), and Tortorella (Ex. 1015).

given mammal.”). Furthermore, Bodor teaches that “[t]herapeutically effective amounts may be easily determined for example, empirically by starting at relatively low amounts and by step-wise increments with concurrent evaluation of beneficial effect.” *Id.* at 24:6–9.

2. *Stelmasiak (Ex. 1013)*

Stelmasiak is a paper about a pilot trial describing cladribine’s use in patients with remitting-relapsing multiple sclerosis (RRMS), which paper published in 1998. Ex. 1013, 4–5 (“In the present study we tested clinical efficacy of cladribine in remitting-relapsing form of MS in a two-year open-label pilot clinical trial.”).

In its Introduction, Stelmasiak teaches that “multiple sclerosis (MS) is an autoimmune disease in which abnormalities in immune regulation lead to the lymphocyte-dependent demyelination process in the central nervous system.” *Id.* at 4. As further background, Stelmasiak teaches that “[c]ladribine . . . is a purine analog with a potent and clinically useful activity against some indolent leukemias and lymphomas” and “[t]he drug displays a highly selective toxicity toward malignant lymphocytes, and normal lymphocytes are also subject to the cytotoxic effect of the drug.” *Id.*

Stelmasiak teaches that, in its study, cladribine was used in a solution form for both oral and subcutaneous administrations. *Id.* at 5. “The drug was prepared as a sterile solution in isotonic saline, 1 mg/ml for oral use and 2.5 mg/ml . . . for subcutaneous injections.” *Id.* Stelmasiak discloses that its study group comprised “10 patients (eight females and two males)” with “body weight 52-75 kg (median: 66 [kg]).” *Id.*

According to Stelmasiak, “[s]ix cladribine courses were given at monthly intervals, and two additional courses were given at 9 and 12 or 15 months,” where “[e]ach course consisted of five doses of the drug taken

once daily on consecutive days.” *Id.* Six of the patients received the subcutaneous dosing (5 mg per day), and four patients received oral dosing (10 mg per day). *Id.* The patients were monitored for 24 months from the start of treatment. *Id.* at Abstr., 5–7.

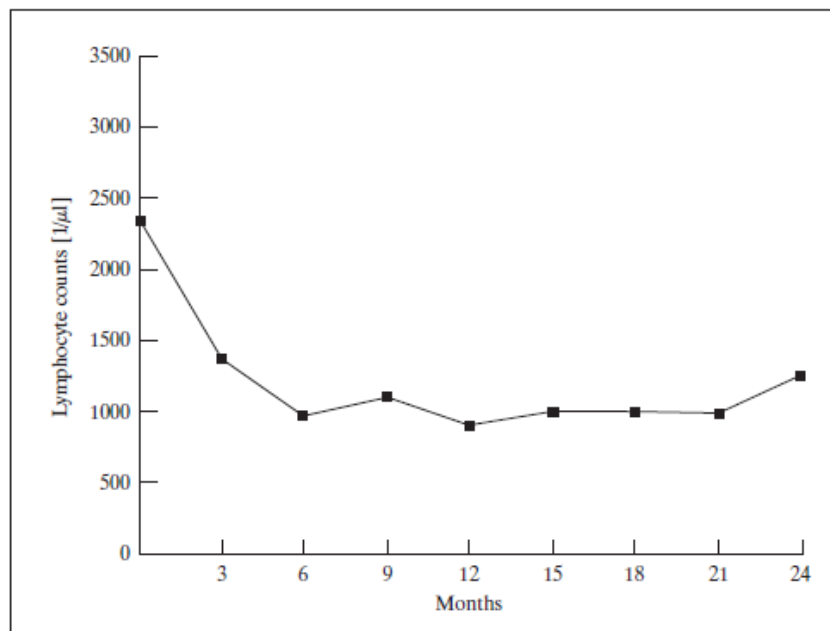
Stelmasiak reports that compliance and tolerance to the therapy were “good” and “side effects were mild.” *Id.* Stelmasiak teaches that, in patients with RRMS, “treatment with cladribine decreases lymphocyte counts in peripheral blood, to 1/3 of the initial values on average.” *Id.* Stelmasiak teaches that the “therapy appeared to be effective in seven patients who reported a very marked (almost five-fold on average) reduction in the relapse rate during the 2 years.” *Id.* at 7; *see also id.* (“The relapse rate in some (but not all) patients is impressively decreased.”). Stelmasiak discloses that, among a “responders” sub-group, the seven patients had “reported a total of 29 relapses during the two preceeding [sic] years . . . and a total of 6 relapses during the two-year study period.” *Id.* at 6. Stelmasiak further discloses that responding patients “showed also a somewhat more pronounced improvement in their neurological status as measured by EDSS scores.” *Id.* at 7; *see also id.* at 6 (“Analysis of the data for the whole group revealed that EDSS scores were significantly reduced during the treatment compared to the initial values . . . and that the decreases observed at the third to fifteenth month were significant.”). Stelmasiak teaches that “[a]long with clinical evaluation in MS, the detailed pattern of cladribine-induced immunosuppression in clinical conditions deserves further study.” *Id.* at 7.

The therapy given in Stelmasiak’s study appeared effective in seven of the patients, but Stelmasiak reports that it “seemed ineffective in the remaining three” patients. *Id.* at 7. The Stelmasiak authors report that they “were unable to identify any factor which would differentiate between the

‘responders’ and the ‘non-responders.’” *Id.* (reporting, for example, that “[t]here was no indication that a ‘good response’ is related to the actual cladribine dose per body weight”).

Further, with respect to lymphocyte counts, Stelmasiak includes Figure 1, reproduced below.

Figure 1. Average lymphocyte counts during and after treatment with cladribine.



Id. at 5. Figure 1, above, is a graph of average lymphocyte counts during the 2-year treatment course, with the number of lymphocytes (1/μl) plotted on the vertical axis versus time (months) on the horizontal axis. *Id.* Stelmasiak teaches that “[l]ymphocyte counts dropped from the initial count of 2336 ± 595 per μl (mean $\pm$ S.D.) to 968 ± 229 per μl at 6 months, and remained at approximately 1000 per μl for the next 15 months.” *Id.* at 5–6 (“A tendency toward normalization of lymphocyte counts became evident only at the end of the 2-year observation period.”).

3. *Petitioner's Argument: Claim 36*

Petitioner contends that claim 36 would have been obvious over Bodor and Stelmasiak. Pet. 33–54; Ex. 1002 ¶¶ 77–119. Patent Owner's counterargument at this stage (discussed below in Sections III(D)(4)-(5)) addresses the challenged claims as a group, with no distinct argument for any dependent claims. *See generally*, Prelim. Resp. The discussion and analysis below focuses on independent claim 36 as illustrative.

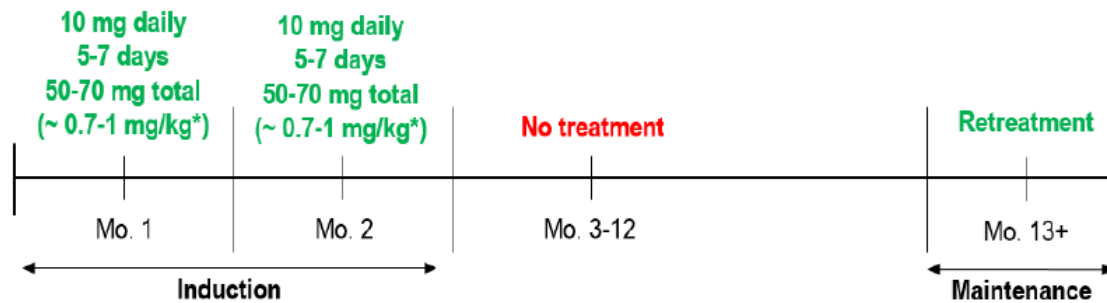
According to Petitioner, Bodor teaches treating MS by orally administering cladribine as recited in claim 36's preamble. Pet. 45, 47 (citing, e.g., Ex. 1022, 23:15–20). Petitioner contends that Stelmasiak similarly teaches treating MS, specifically patients with RRMS, using an oral formulation of cladribine. *Id.* at 47–48 (citing Ex. 1013, Abstr.).

Petitioner argues that Bodor and Stelmasiak teach an induction period, and that Bodor teaches an induction period dosage that overlaps with claim 36's recitation in step (i) that the total cladribine dose reached at the end of the induction period is about 1.7 mg/kg to about 3.5 mg/kg. *Id.* at 48–49 (citing Ex. 1022, 23; Ex. 1013, Abstr., 5). Specifically, Petitioner contends, Bodor teaches an induction period spanning two months wherein 10 mg of cladribine is administered once daily for five to seven days in the first month and repeated for five to seven days in the second month. Ex. 1022, 23. As Dr. Miller explains, that Bodor regimen provides a total cladribine dose of 100–140 mg (e.g., 7 days x 10 mg x 2 months = 140 mg) at the end of the induction period and, for a patient of average weight, mathematically corresponds to a range of about 1.4 mg/kg to 2 mg/kg (e.g., $140 \text{ mg} \div 70 \text{ kg} = 2 \text{ mg/kg}$). Pet. 49; Ex. 1002 ¶ 83 (citing Exhibit 1050 for an average adult weight and showing the respective calculations).

Petitioner contends that Bodor further teaches a cladribine-free period after the induction period that satisfies claim 36's step (ii). Pet. 49–50. Petitioner cites Bodor's teaching that the two-month induction period discussed above is "followed by ten months of no treatment." *Id.* (citing Ex. 1022, 23:15–20). According to Petitioner, Bodor's cladribine-free period is within the scope of the claimed "cladribine-free period lasting from about 8 months to about 10 months." *Id.*; Ex. 1002 ¶ 85.

Furthermore, Dr. Miller opines that a POSA would have understood that Bodor teaches or suggests a retreatment period after the cladribine-free period. Ex. 1002 ¶ 86 (discussing an alternative regimen in Bodor with an eighteen-month cladribine-free period (Ex. 1022, 23:15–24) and testifying that a POSA would understand Bodor to teach a cyclical cladribine regimen, with a subsequent retreatment phase "otherwise, the specified length of time of the cladribine-free period is meaningless"). Moreover, Dr. Miller explains, a POSA would have known that MS is a disease without a cure that needs ongoing treatment and, reading Bodor in that context, would have "thought to re-administer cladribine again after the specified cladribine-free period." *Id.* ¶ 87 (testifying that "MS patients typically receive more than one course of drug therapy to treat active relapses, prevent relapses, and/or prevent or slow further progression of the disease"); *see also id.* ¶¶ 53–59.

Accordingly, Petitioner contends, the skilled artisan would have understood Bodor as teaching a cladribine dosing regimen for the treatment of MS as shown below.

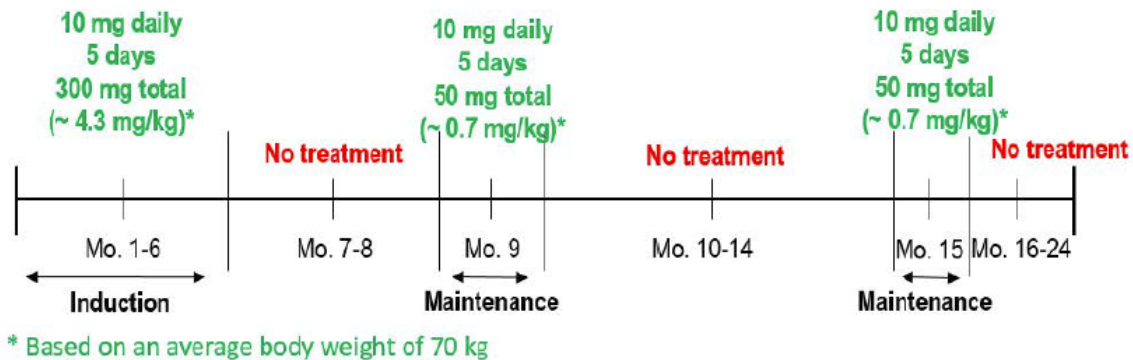


* Based on an average body weight of 70 kg

Pet. 49–51 (citing Ex. 1002 ¶ 84). The image above is a schematic/timeline prepared by Dr. Miller that shows an induction period (months one and two), a subsequent “No treatment” period of ten months, and then a “Retreatment” or “Maintenance” phase starting in the thirteenth month. Ex. 1002 ¶ 84 (testifying this “schematic . . . illustrate[s] how a POSA would have understood Bodor’s dosing regimen”). The schematic further shows daily and monthly cladribine doses in each of the first two months (~ 0.7–1 mg/kg for each month based on the average-weight patient). *Id.*; *see also id.* ¶¶ 86–87 (testifying that the POSA would have understood Bodor to suggest re-administering cladribine after the specified cladribine-free period).

Petitioner argues that Stelmasiak also teaches a cyclical cladribine regimen with retreatment or “maintenance” periods. Pet. 52–53. Petitioner contends that Stelmasiak teaches, for instance, a regimen (“Regimen 2”) involving administration of cladribine for the first six months, a no-treatment period in months seven and eight, a retreatment at month nine, followed by another no-treatment period between months ten to fourteen, then another cladribine retreatment at month fifteen, which is again followed by a no-treatment period that spans months sixteen to twenty-four. *Id.*; Ex. 1013, Abstr., 5. Dr. Miller’s schematic illustrating this dosing regimen from Stelmasiak is reproduced below.

Regimen 2



Ex. 1002 ¶ 89. The schematic above shows the periods in which cladribine is administered (with specific dosing amounts in green font) occurring in months one through six, and at months nine and fifteen; following each of the periods in which cladribine is administered are “No treatment” periods (red font) lasting a certain number of months. Dr. Miller opines that a POSA would have understood the first six months as being an induction period and that the retreatments at month nine and fifteen would be understood as “Maintenance” treatments. Ex. 1002 ¶¶ 88–89. Further, Petitioner argues, Stelmasiak discloses a “maintenance period” where a lower dosage is given because Stelmasiak “teaches administering a lower total dose of cladribine (50 mg) after the initial induction dose (300 mg).” Pet. 53. Although the duration and total dosing of Stelmasiak’s alleged “maintenance period” does not correspond to claim 36’s step (iii), Petitioner argues that a POSA would have found it routine to tailor and optimize the length of administration and cladribine dose during a maintenance period and arrive at the claimed duration and dosing. *Id.* (citing Ex. 1002 ¶¶ 91–93); *see also id.* at 40–43 (providing argument on routine optimization).

Petitioner contends that Stelmasiak also teaches a cladribine-free period after a maintenance period as recited in claim 36’s step (iv). Pet. 54. Petitioner argues that a POSA would have understood the observation

periods in Stelmasiak, such as the months-long interval following the cladribine administration at month nine to be a cladribine-free period that follows a maintenance period. *Id.* (citing Ex. 1013, 5; Ex. 1002 ¶¶ 94–95).

Petitioner further contends that a POSA would have had reasons for combining the teachings of Bodor and Stelmasiak to arrive at the method of claim 36. Pet. 33–43.

According to Petitioner, a POSA would have been motivated to use Bodor’s oral cladribine solid dosage form, citing its “improved cladribine absorption,” and would have administered that dosage form for two months followed by ten months of no treatment, as recommended by Bodor. Pet. 33–34 (citing, e.g., Ex. 1022, 12, 23; Ex. 1002 ¶¶ 79, 97, 99; Ex. 1048, 122¹¹). Further, Petitioner contends, a POSA would have expected some or all patients treated with the Bodor “two months on/ten months off” cycle to experience breakthrough disease or relapse that would require an ongoing treatment. *Id.* at 35 (citing Ex. 1002 ¶ 100 (testifying, with citation to supporting literature, that cladribine treatment is disease modifying but not permanent and that it was recognized that retreatment would be important)). As explained by Petitioner with Dr. Miller’s supporting testimony, signs or symptoms of relapse may include, e.g., worsening neurologic function on physical examination or inflammatory demyelination (i.e., new lesion formation) on MRI scan. *Id.* (citing Ex. 1002 ¶ 100; Ex. 1016, 420; Ex. 1013, 6–7).

¹¹ Jan Liliemark, *The Clinical Pharmacokinetics of Cladribine*, 32(2) *Clinical Pharmacokinetics*, 120–131 (1997) (Ex. 1048, “Liliemark 1997”). Liliemark 1997 discloses that “[t]he oral bioavailability [of cladribine] . . . varies from 37% to 51% when the saline solution for intravenous administration is given to patients to drink.” Ex. 1048, 122.

Because a POSA would have expected relapse, to improve patient status and decrease the incidence of relapse, Petitioner contends a POSA would have retreated with cladribine, such as taught in Stelmasiak. *Id.* at 35–36 (citing Stelmasiak’s reporting of a five-fold reduction in relapse rate, and improvements in patient EDSS scores). Petitioner contends a POSA, thus, would have had reasons to continue treating patients with cladribine after the induction/cladribine-free periods of Bodor. *Id.* at 36; Ex. 1002 ¶ 101. Indeed, Petitioner contends, retreatment, including with cladribine, was evidenced in various MS therapies described in the art. Pet. 36 (citing Ex. 1026, 11:5–7; Ex. 1022, 23; Ex. 1013, Abstr.; Ex. 1018, Abstr.; Ex. 1002 ¶¶ 101–102).

Petitioner further contends a POSA would have followed a retreatment or maintenance period with another cladribine-free period. *Id.* at 36. According to Petitioner, a POSA would have been motivated to do so to better manage side effects (e.g., hematological toxicity/bone marrow suppression). *Id.*; Ex. 1013, 5; Ex. 1002 ¶¶ 103–105 (testifying that drug-free periods would have been seen as a desirable aspect of the regimen to mitigate toxicity and infections arising from immunosuppressive effects of cladribine).

Continuing, Petitioner contends a POSA would have had reasons for lowering the total dose of cladribine in the maintenance period compared to the induction period. Pet. 37–39.¹² Citing Stelmasiak’s data, specifically the reported drop in lymphocyte count during a higher-dose induction phase and stabilization of the lowered count over time with “lower” maintenance

¹² Petitioner, in a footnote, contends that “POSAs may have also considered administering cladribine in the maintenance period at the same dose as in the induction period.” Pet. 37 n. 10 (citing Ex. 1002 ¶ 89).

doses of cladribine, Petitioner contends a POSA would have expected that a “lower dose . . . would suffice” and “be enough for maintaining the lowered count.” *Id.* at 38 (citing Ex. 1002 ¶ 108; Ex. 1013, Fig. 1, 7). Lowering the dose would also have been considered, argues Petitioner, to keep toxicity effects from cladribine low. *Id.*; Ex. 1002 ¶ 118.

Petitioner also contends that the claimed dose of cladribine reached at the end of the induction and maintenance periods would have been prima facie obvious over the prior art’s teachings. Pet. 39–43. Petitioner cites an overlapping range with Bodor’s 1.4 mg/kg to 2.0 mg/kg induction dosing compared to the range of “about 1.7 mg/kg to about 3.5 mg/kg” as claimed. *Id.* at 39 (citing Ex. 1002 ¶ 107). Moreover, Petitioner contends, Bodor “suggests a retreatment” and evidences that the duration of treatment and dosage amount were known variables subject to tailoring and routine optimization. *Id.* at 40–41 (citing Ex. ¶¶ 91–92, 99, 109–110; Ex. 1022, 2, 11–12, 23); *see also id.* (citing Bodor’s definition (Ex. 1022, 22) for “therapeutically effective amount”). Indeed, Petitioner argues, Bodor expressly teaches that “one of skill will appreciate that the therapeutically effective amount of cladribine administered . . . may be *lowered or increased* by fine tuning” and it was similarly known that “one can *tailor the dosage and duration* for which [cladribine] is administered to the stage of the disease and the condition of the patient being treated.” *Id.* (quoting Ex. 1022, 24:1–3; Ex. 1026, 5:22–25) (emphasis added by Petitioner). Thus, Petitioner argues, it was known that cladribine’s dose and length of administration are result-effective variables that could be modified to achieve immunosuppression and therapeutic efficacy, which can be measured, for example, by changes in a patient’s lymphocyte counts. *Id.* at 41 (“And Rice uses two different cladribine doses, 0.7 mg/kg and 2.1 mg/kg,

with the higher dose having a higher suppression of lymphocyte counts”) (citing Ex. 1018, Fig. 4).

Accordingly, Petitioner argues, it would have been routine and well within the ordinary capabilities of the POSA to “fine tune” the total dose and length of cladribine administration, including during a maintenance period. *Id.* at 42; Ex. 1002 ¶ 93. Dr. Miller opines that “it would have been logical for a POSA to have used Bodor’s 2-month treatment period as a starting point, knowing that it could be optimized.” Ex. 1002 ¶ 102. And Petitioner cites Bodor’s teaching that “[t]herapeutically effective amounts may be easily determined, for example, empirically by starting at relatively low amounts and by step-wise increments with concurrent evaluation of beneficial effect.” Ex. 1022, 24:6–9; Pet. 42. Hence, Petitioner contends, a POSA would have arrived at suitable doses and durations of cladribine administration for MS treatment by, for example, regularly measuring the patient’s lymphocyte counts and evaluating the efficacy of a given dose based on changes in the count. Pet. 42 (citing Ex. 1002 ¶ 102); *see also id.* at 42–43 (arguing that there is no evidence of “criticality” to the duration and dosage for the maintenance period of claim 36, citing precedents).

Lastly, Petitioner contends a POSA would have had a reasonable expectation of success in arriving at the subject matter of claim 36. Pet. 43–45 (citing Ex. 1002 ¶¶ 111–119). Petitioner contends the POSA’s skill level is “high,” that the POSA would have “followed the instructions in Bodor to orally administer the dosage forms following the disclosed regimen” disclosed as suitable for treatment of MS. *Id.* at 44. Petitioner contends a POSA would have predictably included a maintenance and secondary cladribine-free period “because it was standard practice in the field to retreat MS patients over the course of the disease,” and optimized the duration and

dosing of such maintenance period as appropriate. *Id.* (citing Ex. 1013, Abstr.; Ex. 1002 ¶ 114). And, Petitioner contends, a POSA would have reasonably expected that the claimed cladribine regimen would be effective because it was known that cladribine can cause a “prolonged, profound suppression of lymphocyte counts,” and “researchers published several clinical studies reporting on the efficacy of cladribine in MS patients.” *Id.* at 44–45 (citing Ex. 1016, 420–421; Ex. 1013, 4, 7; Ex. 1022, 1–2, 23; Ex. 1014, 1719–20; Ex. 1023, Abstr.; Ex. 1002 ¶¶ 35–49, 115–116).

4. *Patent Owner’s Counterargument*

Patent Owner contends that Petitioner has not shown any reasonable likelihood that Petitioner would prevail on its challenge to claim 36. Prelim. Resp. 1–3, 16–51. Patent Owner contends that Bodor and Stelmasiak teach “flat” dosing not “weight-based” dosing of cladribine and that there is no sufficient reason to modify the regimen of Bodor or Stelmasiak to arrive at the method of claim 36. *Id.* at 16–39. Patent Owner argues that, even if the art was combined, a POSA would not have reasonably expected success in arriving at the induction period dosing, the duration of the cladribine-free period, or the maintenance period dosing as claimed. *Id.* at 44–51. And, Patent Owner argues, Petitioner’s arguments concerning routine optimization should fail given the “infinite number” of hypothetical dosage/duration regimens available. *Id.* at 39–44. Patent Owner also alludes to alleged objective indicia of nonobviousness, reserving its right to argue such indicia later if the Board institutes trial. *Id.* at 52. For reasons

discussed below, none of these reasons undermines Petitioner’s threshold showing at this stage.¹³

5. *Analysis: Claim 36*

Based on the present record, Petitioner persuades us that it is reasonably likely to prevail in establishing that claim 36 would have been obvious over Bodor and Stelmasiak. We agree with Petitioner’s showing that Bodor teaches a method for treating MS by orally administering cladribine tablets over a two-month induction period at a total dose of between 100 mg to 140 mg (equivalent to 1.4–2.0 mg/kg for the average patient) and, thus, satisfies claim 36’s preamble¹⁴ and step (i). *See, e.g.*, Pet. 45–49. Bodor also expressly teaches such an induction period is followed by a ten-month cladribine-free period—meeting claim 36’s step (ii) (reciting a cladribine-free period of between about 8–10 months), as argued by Petitioner. *Id.* at 49–50; Ex. 1022, 23:15–20.

Although Bodor does not explicitly describe a subsequent “maintenance period” or a secondary cladribine-free period, we find it logical, credible, and consistent with Dr. Miller’s testimony, that a POSA would have understood Bodor to suggest retreatment and that a POSA would know that retreatment is often needed given the chronic, incurable nature of MS. *See, e.g.*, Ex. 1002 ¶¶ 86–87, 100–102 (testifying that a POSA would have thought to readminister cladribine according to Bodor’s initial treatment regimen, disclosed as suitable for MS treatment, and optimize if

¹³ This paragraph is a high-level summary of Patent Owner’s argument (Prelim. Resp. 1–3, 51); we discuss Patent Owner’s argument in more detail in our analysis below but summarize here to reduce repetition.

¹⁴ We need not determine whether the preamble is limiting because, at this stage, there is no dispute that it is taught or suggested in the asserted art.

needed). Moreover, Petitioner provides evidence-backed reasoning supporting why it would have been routine and obvious to “tailor” the dosage, including by starting with a lower dose and “step-wise” increase it until a desired therapeutic effect is achieved. *See, e.g.*, Ex. 1022, 24:1–9;¹⁵ Ex. 1002 ¶ 93. The POSA would have also been aware, from at least Stelmasiak, that it’s possible to give lower amounts of cladribine in a maintenance phase versus an induction phase, keeping lymphocyte counts in a suppressed state, and providing therapeutic benefits even over extended periods where no cladribine is administered. Ex. 1013, 5–7 (describing a decrease in relapse rate and EDSS improvements over a twenty-four month study period). That, combined with Bodor’s teachings and an expectation that a lower dose and intermittent cladribine-free periods would help manage potential side effects, supports Petitioner’s challenge. *See, e.g.*, Ex. 1002 ¶¶ 50–52, 91, 95, 103. Based on Petitioner’s evidence and reasoning, we find it reasonably likely that a POSA would have found it obvious to modify Bodor’s method to arrive at steps (iii) and (iv) of claim 36.

We also find that the preliminary record, on balance, supports Petitioner’s contention that the POSA would have reasonably expected success in modifying the art to arrive at the subject matter of claim 36. Bodor discloses a method for treating MS with administration of oral cladribine and provides further guidance for adjusting the dosage or duration as needed to produce a desired therapeutic result. *See, e.g.*, Ex. 1022, 22:18–22, 23:15–20, 24:1–9. Stelmasiak further evidences efficacy in

¹⁵ *See also* Ex. 1022, 26:2–8 (teaching that dosages are given with concomitant, continuous clinical evaluations by a skilled practitioner to “determine subsequent therapy” and “evaluating whether to increase, reduce or continue a particular treatment dose”).

treating MS with cladribine administration, including in oral and parenteral forms. Ex. 1013, 7. And neither Bodor nor Stelmasiak stands alone; as pointed out by Petitioner and Dr. Miller, several studies predating the '947 patent describe the use of cladribine for treating MS, and such studies inform the POSA's background knowledge—a necessary consideration in any obviousness analysis. *See* Pet. 19–21, 44; Ex. 1002 ¶¶ 35–49, 115; *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) (“[T]he knowledge of such an artisan is part of the store of public knowledge that must be consulted when considering whether a claimed invention would have been obvious.”). Indeed, many of these studies are incorporated by reference into Bodor. Ex. 1022, 22:27–23:6 (incorporating, e.g., Romine (Ex. 1031) and Rice (Ex. 1018), after teaching that “various dosage amounts and dosing regimens have been reported in the literature for use in the treatment of multiple sclerosis”).

Patent Owner argues that Petitioner's challenge must fail because it is based solely on art teaching “*flat* dosing” and, therefore, does not establish a teaching or suggestion of “weight-based dosing” as allegedly required in claim 36's induction and maintenance period steps. Prelim. Resp. 16–20. We disagree. As explained above, Bodor discloses an illustrative regimen where 100–140 mg of cladribine is given over the course of two months. Ex. 1022, 23:15–20. And Dr. Miller testifies persuasively that a POSA would understand that this is readily convertible to a dose reported on a mg/kg basis simply by dividing milligrams of the drug given by a patient's weight. *See, e.g.*, Ex. 1002 ¶ 83. For an average weight patient, Bodor's dosage is equivalent to between 1.4–2.0 mg/kg—materially overlapping the “about 1.7 mg/kg to about 3.5 mg/kg” range recited in claim 36. *Id.* Patent Owner argues it is “hindsight” to “arbitrarily limit[]” Bodor's regimen to the

average-weight patient. Prelim. Resp. 19. But Patent Owner’s reading of Bodor would *exclude* the average-weight patient from Bodor’s disclosed method for treating MS.¹⁶ That makes no sense. There is no evidence to show that a POSA, who is one of “ordinary creativity, not an automaton,” would read Bodor that way. *KSR*, 550 U.S. at 421.

Patent Owner contends that Bodor only “mentions” weight-based cladribine dosages but never suggests dosing based on weight. Prelim. Resp. 18. This argument is weak. Bodor does not simply “mention” so-called weight-based dosing; it uses it in defining the terms “therapeutically effective amount” and “effective amount.” Ex. 1022, 22:17–22 (citing the mg/kg/day dosing recited in Beutler (Ex. 1026), which Bodor incorporates by reference); *see also id.* at 22:27–23:6 (incorporating-by-reference other references that report “dosage amounts and dosing regimens . . . for use in the treatment of multiple sclerosis” including, e.g., Rice (Ex. 1018, Abstr. (teaching dosing (s.c.) of 0.7 mg/kg and 2.1 mg/kg)). This preliminary record, thus, reinforces that skilled artisans used so-called “flat” and “by-weight” expressions of total cladribine dosages interchangeably when describing dosages suitable for treating MS.¹⁷

¹⁶ Insofar as Patent Owner is suggesting that the dosing overlap only arises in narrow circumstances (e.g., administration to a patient weighing 70 kg), such a suggestion fails. Indeed, by way of example, giving 140 mg to any patient weighing between 50–80 kg (about 110 to 176 pounds) would result in an induction dosage within the expressly recited bounds of claim 36. Notably, the ’947 patent also appears to treat such bounds rather loosely. *See, e.g.*, Ex. 1001, 15 (Table 3 (target dose of “1.75 mg/kg”): suggesting, e.g., a patient receiving 14 tablets (each with 10 mg cladribine) and weighing between 85–89.9 kg would fit the criteria, which conversion produces a total dose range of about 1.56–1.65 mg/kg).

¹⁷ It is also not evident the claims require any active, *a priori*, steps of determining an individual patient’s weight and performing calculations to

Patent Owner argues that Stelmasiak is deficient too because, “like Bodor, it teaches flat cladribine dosing.” Prelim. Resp. 20 (“Stelmasiak does not teach or suggest weight-based dosing at all.”). The ’947 patent reveals the flaws with this argument. As “Background,” the ’947 patent describes “Grieb,” which Patent Owner asserts “has substantially the same disclosure” as Stelmasiak” (*id.* at 31), and the ’947 patent states “Grieb . . . reported a small trial . . . wherein Cladribine has been orally administered during 6 monthly courses of 5 days at a total dose of about 4–5.7 mg/kg (patients of about 52 and about 75 kilos, respectively).” Ex. 1001, 3:3–21 (describing Grieb and citing Stelmasiak). Nowhere, however, does Grieb expressly report a total dosage in the range of 4–5.7 mg/kg. *See generally* Ex. 1023. The ’947 patent simply makes the basic mathematical conversion from Grieb’s express disclosure (much like Bodor’s cited regimen) of giving a certain cladribine dosing (e.g., 10 mg/day) over a specified timeframe. Ex. 1023, 324. And the patent’s discussion of Grieb’s mg/kg range as part of the background prior art is tantamount to an admission that a POSA would recognize that mg/kg dosing *is taught* in Grieb and equally Stelmasiak, which describes the *same* regimen of 10 mg oral cladribine for five days per month for six months given to patients weighing between 52–75 kg. *Compare* Ex. 1023, 324, *with* Ex. 1013, 5. We are unpersuaded on this record that, if there is a distinction between “flat” and “by-weight” dosing, that the skilled artisan would consider it anything more than residing

arrive at a mg/kg dosing before any drug is administered (claim 36, for example, passively recites that the “total dose of cladribine *reached* at the end of the induction period is from about 1.7 mg/kg to about 3.5 mg/kg”). Ex. 1001, 19:17–21. Even if that were a requirement in the claims, the evidence points to the simplicity and obviousness of such determination.

in a simple, straightforward conversion; the '947 patent itself supports this conclusion.

Patent Owner argues that, even considering body weight, Stelmasiak's total dose would correspond to an induction-period dose outside the claimed range. Prelim. Resp. 20 (4.0–5.8 mg/kg versus about 1.7–3.5 mg/kg). This argument does not undermine Petitioner's showing because Petitioner relies on the lower dosing amounts in Bodor's disclosed induction period.

Bradium Techs. LLC v. Iancu, 923 F.3d 1032, 1050 (Fed. Cir. 2019) (“A finding of obviousness . . . cannot be overcome by attacking references individually where the rejection is based upon the teachings of a combination of references.”) (internal quotation marks omitted). There is no reasonable dispute that, for at least patients of average weight, administering Bodor's two-month oral tablet regimen would involve a total induction period cladribine dosage that overlaps with the claimed range. *Hewlett-Packard Co. v. Mustek Sys.*, 340 F.3d 1314, 1326 (Fed. Cir. 2003) (explaining that prior art that “sometimes, but not always, embodies a claimed method nonetheless teaches that aspect of the invention.”). And, consistent with Dr. Miller's unrebutted testimony, the skilled artisan would have recognized this in Bodor's teachings. Ex. 1002 ¶ 83. As Bodor also post-dates Stelmasiak by years and incorporates cladribine/MS studies conducted between 1999 through 2002—after Stelmasiak's publication in 1998—Bodor may be more probative on the full range of dosages that would have been thought suitable by December 2004. Ex. 1022, 22:27–23:6.

Patent Owner, further to its argument that Bodor teaches only “flat” dosing, cites the denial of institution in IPR2023-00049. *See, e.g.*, Prelim. Resp. 17–19 (“As the TWI Board explained, ‘Bodor's disclosure regarding a treatment dose does not include any consideration of a patient's weight’ and

‘Bodor . . . does not teach or suggest switching to a weight-based dosage.’”) (quoting, in part, IPR2023-00049, Paper 10 at 13, 19). The case before us is, however, a different proceeding with a different petitioner and a different record overall compared to IPR2023-00049. The Board’s panel here is also different, and we are not bound by the denial decision or subsidiary findings of the panel in the TWi matter (which decision is subject to a pending rehearing request). IPR2023-00049, Papers 11 and 13.

Patent Owner also argues that neither Bodor nor Stelmasiak teaches a “maintenance period” as claimed. Prelim. Resp. 21–28. Patent Owner contends Bodor is silent about any cladribine retreatment period, much less one with the claimed duration of two to four months and total dosage reached in such period of about 1.7 mg/kg. *Id.* at 21–22. This argument is unavailing on this record. As discussed above, Dr. Miller testifies that a POSA would have understood Bodor as suggesting a cyclical regimen where cladribine is readministered after the cladribine-free period (*see, e.g.*, Ex. 1002 ¶¶ 84–86 (“otherwise, the specified length of time of the cladribine-free period is meaningless”)), and Dr. Miller opines that a POSA would have thought to readminister cladribine in a maintenance period to help reduce relapse (*id.* ¶¶ 100–102 (testifying, *e.g.*, that it would have been logical to have used Bodor’s two-month treatment regimen as a starting point for optimization of known result-effective variables—duration and dosage)). Patent Owner’s attorney argument, urging that a POSA would interpret Bodor differently, is unpersuasive. *Gemtron Corp. v. Saint-Gobain Corp.*, 572 F.3d 1371, 1380 (Fed. Cir. 2009) (“[U]nsworn attorney argument . . . is not evidence and cannot rebut . . . other admitted evidence.”).

Patent Owner also cites disclosure in Bodor about administration of other active agents to suggest that “there is nothing in Bodor to suggest that

cladribine—and not one of the other active ingredients disclosed therein, if anything—is re-administered at the end of the cladribine-free period.”

Prelim. Resp. 21–22 (“[T]here is nothing in Bodor to suggest that the *same* cladribine dosing regimen would be used again.”). Not only is this argument unpersuasive at this time given Dr. Miller’s testimony to the contrary, it is also at odds with argument made by the patentee during prosecution of the related ’903 patent. There, it was argued that, if Bodor were understood to “imply” a retreatment (as the Examiner had indicated), “the teachings of the reference would suggest that the *same dosing regimen* be applied to the patient (10 mg of cladribine administered for 5-7 days each month for two consecutive months followed by another 10 month period of time in which the patient receives no treatment).” Ex. 1025, 100, 151 (arguing “[t]his would have resulted in the same total dose of cladribine being administered to the patient in both the induction phase and the maintenance phase”) (emphasis added). This concession aligns more closely with Dr. Miller’s testimony that Bodor’s initial cladribine regimen provides a logical starting point that a POSA would have considered for a retreatment phase.

Patent Owner argues that, contrary to Petitioner’s assertions, most MS treatments were not cyclical before the ’947 patent. Prelim. Resp. 22–23 (asserting, for example, “most FDA-approved MS drugs were not dosed cyclically”). Regardless of what “most” MS treatments allegedly may have involved, the evidence of record demonstrates that retreatments—and in particular retreatments with cladribine—were known in the art. *See, e.g.*, Ex. 1013, 5 (describing cladribine re-administration at months 9 and 12 or 15 after a six-month induction period); Ex. 1018, 1146 (describing a long-term extension phase with additional cladribine administration “provided at least 12 months had elapsed since the last dose of cladribine”). Moreover,

when obviousness is the issue, the teachings of the prior art are not limited to the “most” common approach—even assuming, for argument’s sake, that Patent Owner’s characterization of prior treatments was accurate. In any case, Patent Owner has no persuasive rebuttal at this stage to Dr. Miller’s testimony that a POSA would have known that MS is chronic and without a known cure and, relatedly, would have known that future treatment would likely be needed. Ex. 1002 ¶¶ 17, 53–59, 100–106.

Patent Owner argues that Stelmasiak does not “remedy the deficiencies of Bodor” because Stelmasiak’s cladribine retreatment or “maintenance” period starts sooner and at a lower dosage than required by claim 36. Prelim. Resp. 25–28. According to Patent Owner, Stelmasiak discloses retreatment starting two months (not 8–10 months) after the induction period, and this retreatment is a single 50 mg oral cladribine course over a single month (not 1.7 mg/kg over 2–4 months). *Id.* at 26–27. This argument, however, misconstrues Petitioner’s challenge. Petitioner is not urging a modification of Bodor’s method to incorporate Stelmasiak’s comparatively shorter cladribine-free period or the specific dosage given to patients in Stelmasiak’s one-month retreatment window. Instead, Petitioner cites Stelmasiak as evidence of a cyclical treatment regimen with “maintenance” periods and that “lower” dosages of cladribine may be given in maintenance periods. Pet. 35–39. As discussed above, Bodor teaches a MS treatment regimen involving a two-month induction period and longer (i.e., ten-month) cladribine-free period within claim 36’s scope. We see no deficiency at this stage in Bodor’s teachings. As for the maintenance period, including its length and dosing, as discussed above, the preliminary record supports Petitioner’s contention that Bodor suggests a retreatment or maintenance phase after the cladribine-free period, that a POSA would have

considered Bodor's initial regimen as a starting point for the retreatment and, as needed "fine tuning," and that a POSA would have had reasons to use lower doses and step-wise increase them while monitoring for efficacy and potential side effects.¹⁸

According to Patent Owner, Petitioner is picking from the art's teachings in "hindsight." Prelim. Resp. 25–26. We do not, at this stage, agree that Petitioner's challenge is infected with hindsight bias. As explained above, Petitioner's challenge relies on, *inter alia*, the MS treatment method taught in Bodor, modified to include a retreatment or "maintenance" phase, which the preliminary record evidences is at least suggested in Bodor. A need for retreatment and subsequent cladribine-free periods also finds support in Stelmasiak and the POSA's background knowledge as already discussed. Evidence also supports Petitioner's optimization rationale; Bodor instructs, for example, that therapeutically effective amounts are "easily determined" according to empirical methods known to the POSA. Ex. 1022, 24:1–9. Petitioner's reconstruction of the claimed subject matter, thus, takes into account knowledge that would have been within the level of ordinary skill, which knowledge is rooted in a sufficient evidentiary basis on this preliminary record. And Patent Owner

¹⁸ Patent Owner contends that Petitioner advances an "individualized retreatment theory" that is inconsistent with patients resuming cladribine therapy after a no-cladribine period. Prelim. Resp. 26. Again, this appears to misinterpret Petitioner's challenge, which is not based on the ad hoc administration of cladribine whenever a particular patient experiences a relapse within an otherwise designated cladribine-free window. *See, e.g.*, Pet. 36 ("Thus, a POSA would have had a reason to continue treating the patients with cladribine after the induction/cladribine-free cycle of Bodor.").

does not identify Petitioner’s reliance on knowledge that is gleaned only from the ’947 patent’s disclosure.

Patent Owner argues that Petitioner has not established a motivation to combine Bodor and Stelmasiak with a reasonable expectation of success in arriving at the subject matter of claim 36. Prelim. Resp. 29–51.¹⁹ We address Patent Owner’s arguments in turn below.

Patent Owner contends there is no reason for the POSA to have “shifted” to weight-based dosing, or reasonable expectation of success in doing so. *Id.* at 29–30, 45. On the record at this stage, we do not agree. As discussed above, a POSA would have understood that expressing a dosage in mg/kg involves only a simple mathematical conversion from the specific dosing described in both Bodor and Stelmasiak. *See, e.g.*, Ex. 1002 ¶ 83. Moreover, Patent Owner overstates the supposed need to “shift” to such dosing from what is already disclosed and would be understood in the art. As already explained, following the cited Bodor regimen, an average-weight patient receiving Bodor’s 140 mg of cladribine in the first two months would already fulfill the requirement that the total dosage reached at the end of the induction period be between about 1.7–3.5 mg/kg as claimed—in that case, Bodor’s patient would receive a 2.0 mg/kg induction dose. Dr. Miller testifies that this would be readily apparent to the skilled artisan. *Id.* Patent Owner submits no persuasive rebuttal evidence to the contrary.

¹⁹ Because there is significant overlap in Patent Owner’s arguments about the sufficiency of Petitioner’s showing of a “motivation” and “reasonable expectation of success,” we address that argument together. *See, e.g.*, Prelim. Resp. 29–30 (no motivation to adopt weight-based dosing), 45 (no reasonable expectation to arrive at weight-based dosing).

Patent Owner contends Stelmasiak “teaches away” from adopting weight-based dosing. Prelim. Resp. 29–30. According to Patent Owner, Stelmasiak remarks on there being “no correlation” between the magnitude of lymphocyte reduction and the drug dose expressed per kg of body weight; similarly, Patent Owner cites Stelmasiak’s disclosure that “there was no indication that a ‘good response’ is related to the actual cladribine dose per body weight.” *Id.* (citing Ex. 1013, 6–7) (emphasis omitted). We do not agree that this rises to a teaching away. These cited disclosures relate to Stelmasiak’s attempt to explain the observed variance in lymphocyte counts among its patients, and to identify “any factor” that might have differentiated between those patients that were responders versus the non-responders. Ex. 1013, 6–7. Stelmasiak was “unable” to identify such a factor. But Stelmasiak nowhere teaches that expressing dosages in mg/kg and administering those dosages would result in a less effective or ineffective MS treatment. To the contrary, at most, Stelmasiak suggests that doing so would not have changed the results for its study and patient group. We also note that other technical literature of record describes cladribine studies where dosages are expressed in mg/kg form and recognizes a dose-dependent effect, including on the level of lymphocyte reduction. *See, e.g.*, Ex. 1002 ¶¶ 91–92 (discussing Rice (Ex. 1018) (noting dose-dependent reduction in lymphocyte counts and lesion volume) and Selby (Ex. 1047)). Patent Owner’s “teaching away” argument is also weakened by Bodor, which, while teaching a regimen based on an alleged “flat” dosing (10 mg/day), defines “effective amount[s]” for MS treatment by referencing dosages expressed on a mg/kg basis—“from about 0.04 to about 1.0 mg/kg/day.” Ex. 1022, 22:17–22, 23:15–20. Whatever distinction Patent Owner seeks to erect between so-called “flat” and “weight-based” dosing is

not one that the art of record appears to recognize as a meaningful differentiator.

Patent Owner argues that a POSA would not have been motivated to combine the art to arrive at the induction dose, cladribine-free period of ten months, and maintenance dose as claimed. Prelim. Resp. 30–39. If anything, Patent Owner contends, had the POSA considered combining Bodor and Stelmasiak, the POSA would have started with Stelmasiak’s longer-duration initial 300 mg cladribine course, or would have increased the duration and dosage of Bodor’s regimen beyond the duration and dosage of the induction period claimed. *Id.* at 30–36. Continuing, Patent Owner argues, a POSA would not have been motivated to prolong Stelmasiak’s cladribine-free period to ten months like Bodor, but would have resumed treatment sooner—after two months, as in Stelmasiak. *Id.* at 36–38. And, Patent Owner argues, because a POSA would have believed that Bodor’s induction dosing (e.g., 100–140 mg over two months; about 1.4–2 mg/kg for a patient of average weight) would have been too low to induce adequate immunosuppression or therapeutic effect, the POSA would not have been motivated to reduce, or expected success in reducing, that dose even more in a retreatment phase to arrive at the claimed maintenance period dosage of “about 1.7 mg/kg.” *Id.* at 38–39.

Those arguments from Patent Owner are based on two premises, neither of which we accept as established adequately at this stage. First, that the POSA would have understood that Stelmasiak’s orally-administered cladribine solution is superior to Bodor’s oral cladribine-cyclodextrin complex tablets—at least as to which formulation yields a higher bioavailability of cladribine. *Id.* at 30–33 (arguing that the bioavailability of cladribine in Stelmasiak’s saline solution when drank is 50% versus about

39–43% with Bodor’s tablets). Second, that the POSA would have believed that therapeutic efficacy requires a reduction of a patient’s lymphocyte counts to a level below 1000/ μ L. *Id.* at 33–36 (citing, e.g., Stelmasiak’s Fig. 1 (graphing average lymphocyte counts over time) and some of Dr. Miller’s testimony (Ex. 1002 ¶¶ 32, 91)).

With regard to bioavailability, Patent Owner contends that Stelmasiak’s formulation provides higher cladribine bioavailability (50%) compared to Bodor’s tablets (about 39.1–43.1%). *Id.* at 31–32. According to Patent Owner, if the POSA’s preference would have been for an increased bioavailability oral dosage form, as Petitioner asserts, the clear choice would have been Stelmasiak’s regimen, not Bodor. *Id.* at 32–33 (arguing, however, that Stelmasiak’s dosing regimen includes an induction duration and dosage that is longer and higher than recited in claim 36). It is, however, not evident that Stelmasiak tested its formulation for bioavailability or just assumed that it was 50%. Stelmasiak discloses that “[t]hese dosing regimens [(i.e., 5 mg per day subcutaneously, or 10 mg per day orally)] produce equivalent area under the concentration-time curve of the drug,” and cites a paper authored by Liliemark in support. Ex. 1013, 5, 8; *see also* Ex. 1023 (Grieb), 325, 327 (stating “oral bioavailability is approximately 50%,” citing Liliemark papers).

Bodor, on the other hand, studied the bioavailability of its formulations, which provide “improved cladribine absorption,” “higher bioavailability,” and “lower interpatient variation.” Ex. 1022, 11:25–12:3, 33–36 (Example 4). This would purport to be improvements versus what was otherwise known at the time, which was that “oral delivery of cladribine has been plagued by low bioavailability.” Ex. 1022, 2:22–25; Ex. 1002 ¶ 110. And Bodor cites some of the same Liliemark papers—the same as

relied on by Stelmasiak and Grieb concerning bioavailability—as indicative of prior oral formulations that had been “plagued” by low cladribine bioavailability. Ex. 1022, 2:22–25.

As Dr. Miller explains, citing the only Liliemark paper of record, the general knowledge at the time was that bioavailability of oral cladribine when given in a solution for the patient to drink (as in Stelmasiak) varied from 37–51%. Ex. 1002 ¶ 110 (citing, e.g., Ex. 1048 (Liliemark 1997), 122). Dr. Miller testifies that a POSA would have understood Bodor’s oral cladribine tablet to be advantageous, with “increased or enhanced bioavailability compared to earlier oral solutions known in the art,” thus suggesting its use over Stelmasiak’s oral solution, even at lower doses. *Id.* The only testimony of record at this time probative of the skilled artisan’s perspective on this question comes from Dr. Miller. The extent to which the bioavailability of Bodor’s tablets adds to or detracts from Petitioner’s motivation and reasonable expectation of success contentions are questions best resolved on a full record. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1327 (Fed. Cir. 2016) (“Whether an ordinarily skilled artisan would have been motivated to modify the teachings of a reference is a question of fact.”) (citations omitted); *Teva Pharm. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1380–1381 (Fed. Cir. 2021) (explaining that the presence or absence of a reasonable expectation of success is a question of fact).

From Patent Owner’s position that Bodor is giving a comparatively weaker dosage form (with less bioavailability) comes Patent Owner’s argument that the POSA would not believe that Bodor’s regimen could reduce lymphocytes to a level below 1000 cells/ μ L or produce therapeutic efficacy. Prelim. Resp. 33–36 (arguing it took six months at higher total dose (300 mg compared to 140 mg of Bodor) for Stelmasiak to reduce the

average lymphocyte count of its patient group below 1000 cells/ μ L). Resolution of this issue is premature at this stage for at least the reasons noted above about the comparison between Bodor's and Stelmasiak's formulations and their bioavailabilities. In addition, we question whether Patent Owner is overstating the supposed need to reduce lymphocytes to below 1000 cells/ μ L before a therapeutic response would be expected. We recognize how some language in the Petition and in Dr. Miller's testimony may be read as indicating that reduction below 1000 cells/ μ L is significant. *See, e.g.*, Pet. 16 n. 6. But it's not clear at this time that Petitioner is, in fact, proposing 1000 cells/ μ L as a bright-line threshold—below which efficacy would be expected and above which it would not. *See, e.g.*, Ex. 1002 ¶ 16 (testifying that “a sustained reduction of lymphocytes, *e.g.*, below 1000/ μ L” being characteristic of a therapeutic response) (emphasis added).

Moreover, based on the preliminary record, it is not evident that a sustained reduction to below 1000 cells/ μ L would be necessary before a therapeutic effect is observed. Stelmasiak, for example, discloses that a “significant” improvement (i.e., reduction) in EDSS scores was seen within three months of the start of treatment. Ex. 1013, 6. Yet looking at Patent Owner's annotated version of Stelmasiak's Figure 1, at three months the average lymphocyte count was still well above 1000/ μ L “(~ 1350 cells/ μ L),” and only about “150 mg” of cladribine would have been given via Stelmasiak's oral formulation.²⁰ Prelim. Resp. 35; *see also* Ex. 1002 ¶ 91

²⁰ Stelmasiak's graph also reflects “average” lymphocyte counts across a group of patients, and Stelmasiak reports a mean reduction with a standard deviation that would suggest some patients were above 1000/ μ L and some below. Ex. 1013, 5 (“968 $\pm$ 229”). We do not see that Stelmasiak teaches or suggests that patients could be sorted into responders and non-responders based on whether they were above or below 1000/ μ L. *Id.* at 7 (“We were

(reproducing a graph from Rice (Ex. 1018, Fig. 4), which appears to show a more rapid decrease in average lymphocyte counts (to at or below about 1000/ μ L) within two months with both the higher (2.1 mg/kg) and lower (0.7 mg/kg) doses), with the latter increasing above 1000/ μ L over time); *see* Ex. 1018, 1145, 1151 (noting that, while no significant treatment effects in terms of changes in EDSS or SNRS scores were seen, both doses produced and sustained significant reductions in the presence, number, and volume of brain lesions on MRI). As with the bioavailability issue, we will consider this question further, as appropriate, on a full evidentiary record.

Patent Owner argues that Petitioner's assertions of routine optimization should fail. Prelim. Resp. 39–44. Patent Owner argues that, if optimization were sought, a POSA would have used Stelmasiak's dosing regimen not Bodor's (citing the allegedly superior bioavailability of Stelmasiak's formulation). That argument is unavailing at this stage as discussed above.²¹ Patent Owner argues that “there is *no overlap* between Bodor's doses and the claimed doses.” Prelim. Resp. 39–40. We disagree. Bodor discloses a therapeutically effective range for treatment of MS (from about 0.04 to about 1.0 mg/kg/day) that broadly encompasses the claimed doses and, as explained above, more narrowly describes a preferred dosing regimen for treatment of MS where 100–140 mg of cladribine is given, which converts to 1.4–2.0 mg/kg for an average patient—overlapping with the doses recited in claim 36. Patent Owner argues that Petitioner “ignores

unable to identify any factor that would differentiate between the ‘responders’ and the ‘non-responders.’”).

²¹ The notion that only a “best” solution may be obvious is also legally untenable. *Intel Corp. v. Qualcomm Inc.*, 21 F.4th 784, 800 (Fed. Cir. 2021) (“[It is] not necessary to show that a combination is the best option, only that it be a suitable option.”) (internal quotation marks and citation omitted).

the infinite number of combinations” of dosing amounts and dosing durations available. *Id.* at 42. On the record at present, this argument exaggerates the options known in the art that a POSA would have readily considered. Petitioner provides, as discussed above, a reasoned and evidence-backed basis for why the POSA would have administered Bodor’s initial regimen (with an induction and cladribine-free period) and considered doing the same in the next year with “fine-tuning” of the dosage or duration if necessary while monitoring for efficacy.

Patent Owner argues that a POSA would not have expected a safe and effective method of treating MS in view of the prior art. Prelim. Resp. 49–51. According to Patent Owner, some earlier MS studies had remarked that cladribine was not found to be effective against clinical deterioration. *Id.* (citing, e.g., Ex. 1015, 1754; Ex. 1016, 425 (Table III)). Moreover, Patent Owner argues, a POSA would have been concerned with “cancer risks” with cladribine’s use. *Id.* (citing Ex. 1031, 43–44).

Patent Owner’s argument does not undermine Petitioner’s showing at this stage. Prior studies may not have universally pointed to cladribine’s promise or efficacy but much of the reporting in the literature did.²² *See, e.g.*, Ex. 1013, 7 (remarking that the relapse rate “impressively decreased” in some (but not all) patients); Ex. 1022, 22:8–23:6 (describing MS as a “cladribine-responsive disease” as “well-documented in the literature,” and citing work by Beutler, Romine, Rice, and Selby, among others); Ex. 1016, 420 (citing studies and noting that, although confirmation across a wider number of patients is needed, “cladribine therapy appears to have the

²² Notably, claim 36, although it recites a “method of treating” MS, does not recite any specific treatment or efficacy endpoint. And the patent defines efficacy broadly. *See, e.g.*, Ex. 1001, 5:52–6:15.

potential to slow the progression of MS, reduce CNS lesions in patients with either the chronic progressive or relapsing-remitting forms of the disease and improve neurological functioning in some of these patients”); Ex. 1031, Abstr. (“We conclude that cladribine shows promise as a treatment for relapsing-remitting multiple sclerosis.”). As for cladribine’s safety, Stelmasiak noted only “mild” side effects over its two-year study. Ex. 1013, 7; *see also* Ex. 1018, 1153 (reporting “no serious adverse events could be attributed to cladribine in this study”). Even if there were some risks, of cancer for example, it is telling that numerous studies on cladribine’s use for treating MS, nevertheless, continued apace before the ’947 patent. *See, e.g.*, Pet. 19–21 (listing prior studies). There is no persuasive evidence of record that such risks were thought to be so high as to discourage cladribine’s use or rendered it, on the whole, unsafe.

Lastly, Patent Owner’s argument about alleged objective indicia amounts to only a single sentence at this point. According to Patent Owner, the “FDA-approved method of using [Patent Owner’s] successful MAVENCLAD® product practices the method recited in the challenged claims, and has been shown to surprisingly ‘significantly lower[] the annualized relapse rate’ for treated patients and was approved by the FDA for treating MS patients.” Prelim. Resp. 52 (citing Ex. 2001, 5–6, 24–25).

Patent Owner has not established a sufficient nexus at this time between Mavenclad and the invention claimed. A patentee may, for example, be entitled to a rebuttable presumption of nexus “if the patentee shows that the asserted evidence is tied to a specific product and that the product ‘is the invention disclosed and claimed.’” *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019) (quoting *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988)).

But Patent Owner has not made such a showing on this record. *See Volvo Penta of the Americas, LLC, v. Brunswick Corp.*, No. 2022-1765 (Fed. Cir. Aug. 24, 2023) (“The Board correctly found the single, conclusory sentence and one-paragraph citation [to PO’s expert’s report] to be insufficient to show a presumption of nexus.”). The cited prescribing information about Mavenclad appears, for example, to be narrower than and not reasonably commensurate with the scope of claim 36. *See, e.g.*, Ex. 2001, 24 (describing a total, two-year, cumulative cladribine dose of 3.5 mg/kg). Moreover, counsel’s characterization of a lower relapse rate as “surprising” is not *evidence* of the POSA’s perspective on the issue. It is also contrary to Dr. Miller’s present opinion noting the absence of any unexpected results. Ex. 1002 ¶¶ 83, 138, 140.

We also agree with Petitioner here that it should be afforded an opportunity to test Patent Owner’s argument about any alleged objective indicia and develop rebuttal evidence through trial. Pet. 60–61 (citing *Amneal Pharms., LLC v. Supernus Pharms., Inc.*, IPR2013-00368, Paper 8 at 12–13 (PTAB Dec. 17, 2013)). We will reevaluate argument about objective indicia of nonobviousness on a fully-developed record.

For the reasons above, based on the record at this stage, we determine that Petitioner has met its threshold showing and established a reasonable likelihood that it will prevail on its challenge to claim 36.

6. *Other claims*

Petitioner contends that claims 38, 39, and 41–46 would also have been obvious over Bodor and Stelmasiak. Pet. 55–60; Ex. 1002 ¶¶ 120–139. We have considered Petitioner’s argument and evidence, which is presently un rebutted except for the argument of Patent Owner addressed above. We

determine that Petitioner has shown that it is reasonably likely to prevail in showing the unpatentability of one or more of these additional claims.

7. *Conclusion*

For the reasons above, we determine that Petitioner is reasonably likely to prevail in establishing the unpatentability of at least one of claims 36, 38, 39, and 41–46 for obviousness over Bodor and Stelmasiak.

IV. DISCRETION ISSUES

The Board has discretion under 35 U.S.C. § 325(d) to reject a petition when the same or substantially the same prior art or arguments were presented previously in another proceeding before the Office.²³ The relevant portion of that statute reads:

In determining whether to institute or order a proceeding . . . , the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

35 U.S.C. § 325(d). In evaluating whether to deny institution under 325(d), the Board has considered several non-exclusive factors: (a) the similarities and material differences between the asserted art and the prior art involved during examination; (b) the cumulative nature of the asserted art and the prior art evaluated during examination; (c) the extent to which the asserted art was evaluated during examination; (d) the extent of the overlap between the arguments made during examination and the manner in which a petitioner relies on the prior art or a patent owner distinguishes the prior art; (e) whether a petitioner has pointed out sufficiently how the Office erred in

²³ Patent Owner urges discretionary denial on the basis of § 325(d) alone. Prelim. Resp. 52–64. On this record, we do not further address Petitioner’s arguments about other bases for discretionary denial. Pet. 65–68 (arguing against discretionary denial due to parallel litigation or serial petitions).

evaluating the asserted prior art; and (f) the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments. *See Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first para.).

Factors (a), (b), and (d) relate to whether the art or arguments in the Petition are the same or substantially the same as those previously presented to the Office. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 10 (PTAB Feb. 13, 2020) (precedential) (“*Advanced Bionics*”). Factors (c), (e), and (f) “relate to whether the petitioner has demonstrated a material error by the Office” in the Office’s prior consideration of that art or arguments. *Id.*

Under *Advanced Bionics*’s two-part framework, we first determine whether the same or substantially the same art or arguments previously were presented to the Office. *Id.* at 8, 10. If “either condition of [the] first part of the framework is satisfied,” we then determine whether material error by the Office has been shown. *Id.* at 8, 10.

Patent Owner argues that the Petition should be discretionarily denied under § 325(d). Prelim. Resp. 52–63; Pet. 61–65 (opposition to § 325(d) denial). Patent Owner argues that substantially the same prior art or arguments were raised during prosecution. Prelim. Resp. 52–57. We agree with Patent Owner that the same art and at least some of the same arguments were presented previously to the Office during prosecution. Indeed, the Examiner cited Bodor against the pending claims in the prosecution of both the ’947 and ’903 patents. *See, e.g.*, Ex. 1004, 220 (Office Action rejecting

claims as obvious over Bodor, Beutler, and Bloom)²⁴; Ex. 1025, 103 (Office Action rejecting claims as obvious over Bodor, Grieb, and Bloom).

Stelmasiak is also listed in an Information Disclosure Statement (Ex. 1004, 17) and in the “References Cited” section of the ’947 patent (Ex. 1001, code (56) (second page)). *Advanced Bionics* at 7–8 (stating “previously presented art” includes art provided to the Office by an applicant in an IDS). Although Stelmasiak was not cited by the Examiner against the claims at any point, Patent Owner contends that Grieb’s and Stelmasiak’s disclosures are not materially different, and that Grieb was cited in a rejection during the related ’903 patent’s prosecution. Prelim. Resp. 53–54.

Because we agree that Bodor and Stelmasiak were presented previously to the Office, we turn to part two of the *Advanced Bionics* framework—whether there was a material error by the Office.

Patent Owner addresses three areas of potential error raised by Petitioner. Prelim. Resp. 57–63. The first concerns whether the Examiner erred in confusing monocytes and lymphocytes when addressing a rejection over Bodor, Beutler, and Bloom. *Id.* at 60–61; Pet. 62–64 (arguing the Examiner and Patent Owner repeatedly conflated monocytes and lymphocytes in their analysis of whether POSAs would have a reasonable expectation of success relative to keeping cell numbers down with cladribine therapy); Ex. 1002 ¶¶ 28, 38 (testimony of Dr. Miller, with citation to literature, explaining the differences in these immune cell types); Ex. 1004, 225 (Examiner discussing monocytes and lymphocytes).

According to Petitioner, this confusion is material because, had the Examiner recognized the differences between monocytes and lymphocytes

²⁴ Beutler and Bloom are, respectively, Exhibits 1026 and 1033 here.

(and had the confusion not been compounded by Patent Owner’s repetition of the error), it would have refuted the applicant’s argument raised prior to allowance of the claims. Pet. 63. In particular, applicant argued that a POSA “would not have had a reasonable expectation of success in maintaining lower *lymphocyte* numbers” because Beutler taught that “monocyte numbers rebound to pretreatment levels about two weeks after cladribine administration is stopped.” Ex. 1004, 251–252. Petitioner points out that, irrespective of what Beutler says about monocytes, Beutler teaches that “absolute *lymphocyte* counts [were] suppressed 0.5 to about 10 percent *for more than one year.*” Pet. 63 (quoting Ex. 1026, 13:34–36 (Petitioner’s emphasis)).

We agree with Petitioner that the Examiner erred in conflating monocytes and lymphocytes. Patent Owner does not argue otherwise. We also agree with Petitioner that, absent this error, the applicant could not have maintained some of the arguments raised in response to the Examiner’s rejection—including the argument noted above.

Patent Owner, however, argues that any such error is “immaterial.” Prelim. Resp. 60–61. The crux of Patent Owner’s position is that Beutler’s teaching of a sustained suppression of lymphocytes (e.g., about 10%) is too low to have given a POSA a reasonable expectation of success in providing an effective MS treatment. *Id.* (citing Stelmasiak’s average baseline lymphocyte level of 2336 cells/ μ L, which would only decrease to about 2100 cells/ μ L at a 10% reduction; citing Bloom’s disclosure about reduction to 500 cells/ μ L). Patent Owner’s arguments might have had merit and perhaps could have convinced the Examiner to allow the claims. The problem, however, is that such arguments were never raised with the Examiner in the ’903 patent’s prosecution. So, we can only speculate about

how the Examiner might have responded. It is clear on this record that the Examiner erred in confusing monocytes and lymphocytes, which error was compounded by the applicant's embrace of it. It is also clear that some of the applicant's arguments were incorrect in view of the error. What is less clear is the materiality of this error and the extent to which it would have impacted patentability of the claims. In any case, the error weighs somewhat against denying the Petition under § 325(d).

Patent Owner next turns to Petitioner's argument that the Examiner erred by not applying Stelmasiak in a rejection, especially as to Stelmasiak's teachings about administering a lower cladribine maintenance dose. Prelim. Resp. 62; Pet. 61. According to Patent Owner, the Examiner already relied on Bloom for the point about administering a lower dose in a retreatment phase, rendering Stelmasiak "cumulative" and, further, during prosecution of the related '903 patent, the Examiner applied Grieb (alleged to have a substantially similar disclosure to Stelmasiak) in a rejection but the applicant overcame it. Prelim. Resp. 59, 62. Patent Owner is correct that the Examiner cited Bloom for the proposition that it would have been obvious to administer a "lower intensity treatment" in a maintenance phase. Ex. 1004, 224. We do not necessarily agree, however, that Stelmasiak and Bloom (or the argument about Bloom) are cumulative. To the contrary, in response to the rejection over Bodor, Beutler, and Bloom, the applicant argued Bloom fails to disclose any sequential high-dose, no-dose, low-dose regimen; applicant argued that, if anything, Bloom suggested a "higher intensity" treatment in a maintenance phase that used combinations of other active agents (i.e., AZA (azathioprine) and prednisone); and applicant argued that Bloom was non-analogous art. *Id.* at 253–254. Because the Examiner did not enter any reasons for allowance, we cannot know whether any of those

arguments were found persuasive. But none of those arguments about Bloom have relevance to Stelmasiak, which plainly teaches administering a high initial dose of cladribine (300 mg) followed by a no-cladribine period, then a maintenance period at a lower cladribine dose (50 mg). *See supra* Section III(D)(3). The Examiner appears to have overlooked Stelmasiak and the relevant teachings noted above in the prosecution of the '947 patent.

In any case, Patent Owner contends, Grieb (and effectively Stelmasiak given its similar disclosure) were thoroughly considered during the related '903 patent's prosecution. The record suggests otherwise. It is true that the Examiner rejected pending claims over Bodor, Grieb, and Bloom. *See, e.g.*, Ex. 1025, 100. In doing so, however, the Examiner discussed Bodor and Grieb and then remarked "neither of the above references teach that the total dose of cladribine reached at the end of the maintenance phase is lower than the total dose reached at the end of the induction phase." *Id.* at 103. That is wrong. Grieb (like Stelmasiak) teaches a lower total dose in a maintenance period, as already explained. Ex. 1023, 324. Had the Examiner appreciated such teachings in Grieb, Bloom would have been unnecessary. And we do not see this oversight on the Examiner's part as being immaterial, especially with the applicant arguing, for example, that modifying Bodor or Grieb such that either regimen would have a higher initial loading dose followed by lower maintenance doses (as evidenced by Bloom, according to the Examiner) would have been inconsistent with Bodor and Grieb. Ex. 1025, 151–152 ("[S]uch a modification of the teachings of Bodor . . . or Grieb . . . is not supported by the teachings of the individual references and one skilled in the art, in view of Bodor . . . and/or Grieb . . . would not have been motivated to reduce the dosage of cladribine administered to a patient.").

Lastly, Patent Owner challenges Petitioner’s assertion that, during prosecution, “Merck did not, and could not, dispute that Bodor taught cyclical treatment of MS using cladribine.” Prelim. Resp. 63 (quoting Pet. 10). Instead, Patent Owner contends, during prosecution the applicant argued that “there is no teaching in Bodor . . . regarding ***repeated treatment cycles*** comprising the administration of cladribine after the 10-month cladribine free period.” *Id.* (citing Ex. 1004, 247–249). This raises another aspect of Examiner error. The Examiner could have and should have recognized that Bodor at least suggested a subsequent retreatment phase after the 10-month cladribine-free period, but the Examiner made no such finding in the ’947 patent’s prosecution. We know the Examiner could have made such a finding because, in fact, the Examiner did so during prosecution of the ’903 patent. *See, e.g.*, Ex. 1025, 100 (“Here, because Bodor states ‘10 months of no treatment’, it is implied that following these 10 months, treatment with cladribine is resumed.”), 137 (“Bodor does implicitly teach that cladribine administration may be repeated following the ‘ten months of no treatment.’”). There is also new evidence of record in this proceeding—expert testimony from Dr. Miller—on precisely this point, which merits considering the issue further through trial. *See, e.g.*, Ex. 1002 ¶¶ 86, 102.

That the applicant may have overcome the rejections made during the ’903 patent’s prosecution does not persuade us of the absence of material error on this point. The Examiner focused on whether the art disclosed *lowering* the maintenance period dosage. *See, e.g.*, Ex. 1025, 103. But that was not required of all the claims presented for examination and, as Patent Owner has argued persuasively here, is not required in challenged claim 36. *See supra* Section III(C)(1). In short, the Examiner should have appreciated that Bodor “implied” a retreatment with cladribine and raised the issue

during the '947 patent's prosecution. And, as to applicant's response on that point (such as made during the '903 patent prosecution) that, if this implied teaching is accepted, it would only suggest that Bodor's "same dosing regimen" be applied in the induction and maintenance phases (Ex. 1025, 151), the Examiner should have recognized how that response impacted the patentability of those claims that encompass a method where the dose and duration of the induction period is repeated in the maintenance period.

Altogether, we find that there is a sufficient showing of material error in the Office's previous consideration of the prior art that we decline to deny the Petition on a discretionary basis under § 325(d).

V. CONCLUSION

We determine that there is a reasonable likelihood that Petitioner would prevail with respect to at least one of the claims challenged in the Petition. We further decline to deny the Petition on a discretionary basis. We, thus, institute *inter partes* review.

Any argument not raised in a Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived even if asserted in the Preliminary Response. In addition, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board's Rules.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review of all challenged claims of the '947 patent is instituted on all grounds of unpatentability set forth in the Petition.

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

IPR2023-00480
Patent 7,713,947 B2

FOR PETITIONER:

Eldora L. Ellison
Olga A. Partington
Chandrika Vira
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
eellison-ptab@sternekessler.com
opartington-ptab@sternekessler.com
cvira-ptab@sternekessler.com

FOR PATENT OWNER:

Emily R. Whelan
Deric Geng
Cindy Kan
WILMER CUTLER PICKERING HALE AND DORR LLP
emily.whelan@wilmerhale.com
deric.geng@wilmerhale.com
cindy.kan@wilmerhale.com