Trials@uspto.gov
571-272-7822

Paper 11
Date: September 23, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,
Petitioner,

v.

THE JOHNS HOPKINS UNIVERSITY,
Patent Owner.

IPR2024-00625
Patent 11,339,219 B2

Before DEBORAH KATZ, SUSAN L.C. MITCHELL, and DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

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

I. INTRODUCTION

Merck Sharp & Dohme LLC ("Petitioner") filed a Petition requesting *inter partes* review of claims 1–8 of U.S. Patent No. 11,339,219 B2 (Ex. 1001, "the '219 patent"). (Petition ("Pet."), Paper 1.) The Johns Hopkins University ("Patent Owner") filed a Preliminary Response identifying itself as the owner of the '219 patent. (Preliminary Response ("Prelim. Resp."), Paper 5.) In addition, as authorized (*see* Order, Paper 7), Petitioner filed Petitioner's Reply to Patent Owner's Preliminary Response regarding discretionary denial under 35 U.S.C. § 314(a) ("Pet. Reply," Paper 8), and Patent Owner filed Patent Owner's Sur-Reply ("PO Sur-Reply," Paper 10).

The Director may not authorize an *inter partes* review "unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). We determine whether to institute a post grant review on behalf of the Director. *See* 37 C.F.R. § 42.4(a).

The following findings of fact and conclusions of law are not final, but are made for the sole purpose of determining whether Petitioner meets the threshold for initiating review. Any final decision shall be based on the full trial record, including any response timely filed by Patent Owner.

Upon considering the Petition, the Preliminary Response, and the evidence of record, we determine that Petitioner has demonstrated there is a reasonable likelihood that the Petitioner would prevail in showing that at

least one challenged claim is unpatentable and we institute *inter partes* review of all challenged claims on all asserted grounds. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1354, 1359–60 (2018); 37 C.F.R. § 42.108(a).

A. Real Parties-in-Interest and Related Matters

Petitioner identifies Merck Sharp & Dohme LLC and Merck & Co., Inc., as the real parties-in-interest. (*See* Pet. 55.) Patent Owner identifies The Johns Hopkins University as the real party-in-interest. (*See* Paper 3, 1)

Both Petitioner and Patent Owner report that the litigation *Merck Sharp & Dohme LLC v. The Johns Hopkins University*, 1:22-cv-03059-JRR (D. Md.), is a related matter. (*See* Pet. 55; *see* Paper 3, 1.) Patent Owner identifies eight other related petitions for *inter partes* review that Petitioner has filed. (*See* Paper 3, 1.) These other petitions are:

Petition for *Inter-Partes* Review	**Patent**
IPR2024-00240	11,591,393
IPR2024-00622	10,934,356
IPR2024-00623	11,325,974
IPR2024-00624	11,325,975
IPR2024-00647	11,649,287
IPR2024-00648	11,643,462
IPR2024-00649	11,629,187
IPR2024-00650	11,634,491

We note that *inter partes* review was instituted on June 13, 2024, in IPR2024-00240. (*See* IPR2024-00240, Paper 10.) Patent Owner requested

Director Review of the Decision on Institution (Paper 12), which was denied (Paper 24).

Decisions on the other petitions are pending.

Petitioner asserts, and Patent Owner does not dispute, that the co-pending Maryland litigation has been stayed in its entirety pending resolution of IPR2024-00240. (Pet. Reply 1 (citing Ex. 1100, 1 (June 29, 2024, Order in Maryland litigation)); *see* PO Sur-Reply 1 (acknowledging "the recent stay of the parties' co-pending litigation involving the '219 Patent").)

B. The '219 Patent and Challenged Claims

The '219 patent is directed to anti-cancer therapies that block immune system checkpoints, including the PD-1 receptor. (*See* Ex. 1001, Abstr.) More specifically, the '219 patent is directed to treating cancer patients with high mutational burdens, such as found in microsatellite instable (MSI) cancer, with anti-PD-1 antibodies. (*See* Ex. 1001, 3:35–38.) The Specification discloses that pembrolizumab is a humanized monoclonal anti-PD-1 antibody, attributed to Merck, which was administered to patients in a clinical trial. (*See* Ex. 1001, 8:43–54.)

Claim 1 of the '219 patent, the sole independent claim, recites:

> A method for treating cancer in a patient in need thereof comprising:
>
> selecting a patient who has an unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair (MMR) deficient tumor; and
>
> administering an effective amount of pembrolizumab to the patient;
>
> wherein the patient exhibits an outcome that is improved as compared to a corresponding outcome that would be

observed in a reference patient that has been administered pembrolizumab, wherein the reference patient has a tumor that does not exhibit a MSI-high or a MMR deficiency status.

(Ex. 1001, 25:32–26:8.)

C. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–8 of the '219 patent are unpatentable based on the following grounds (*see* Pet. 3–4):

	Claims Challenged	**Statutory Basis – 35 U.S.C.**[1]	**References**
1	1–4, 6–8	102	MSI-H Study Record[2] (Ex. 1005)
2	1–4, 6–8	103	MSI-H Study Record (Ex. 1005), Pernot[3] (Ex. 1006), and Benson[4] (Ex. 1009)

[1] The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) ("AIA"), included revisions to 35 U.S.C. §§ 102 and 103 that became effective on March 16, 2013, before the filing of the applications to which the '219 patent claims priority. Therefore, we apply the AIA versions of Sections 102 and 103.

[2] ClinicalTrials.gov, NCT01876511, "Study of MK-3475 in Patients with Microsatellite Unstable (MSI) Tumors (Cohorts A, B and C)," (June 10, 2013) available at https://clinicaltrials.gov/study/NCT01876511?tab=history&a=1 (Ex. 1005) ("MSI-H Study Record").

[3] Pernot et al, *Colorectal Cancer and Immunity: What We Know and Perspectives*, 20(14) WORLD J. GASTROENTEROLOGY 3738 (April 2014) (Ex. 1006) ("Pernot").

[4] Benson et al, *Colon Cancer*, Version 3.2014: Clinical Practice Guidelines in Oncology, 12(7) J. NAT'L COMPREHENSIVE CANCER NETWORK 1028 (July 2014) (Ex. 1009) ("Benson").

	Claims Challenged	Statutory Basis – 35 U.S.C.[1]	References
3	5	103	MSI-H Study Record (Ex. 1005), or the MSI-H Study Record (Ex. 1005), Pernot (Ex. 1006), Benson (Ex. 1009), and Chapelle[5] (Ex. 1007)
4	1–4, 6–8	103	MSI-H Study Record (Ex. 1005), Brown[6] (Ex. 1034), Duval[7] (Ex. 1087), and Benson (Ex. 1009)
5	5	103	MSI-H Study Record (Ex. 1005), Brown (Ex. 1034), Duval (Ex. 1087), Benson (Ex. 1009), and Chapelle (Ex. 1007)
6	8	103	MSI-H Study Record (Ex. 1005), or the MSI-H Study Record, Pernot (Ex. 1006) Benson (Ex. 1009), Chapelle (Ex. 1007), and Hamid[8] (Ex. 1011)
7	8	103	MSI-H Study Record (Ex. 1005), Brown (Ex. 1034), Duval (Ex. 1087), Benson (Ex. 1009), Chapelle (Ex. 1007), and Hamid (Ex. 1011)

[5] Chapelle et al, *Clinical Relevance of Microsatellite Instability in Colorectal Cancer*, 28(20) J. CLINICAL ONCOLOGY 3380 (2010) (Ex. 1007) ("Chappelle").
[6] Brown et al., *Neo-antigens predicted by tumor genome meta-analysis correlate with increased patient survival*, 24 GENOME RESEARCH 743 (May 2014) (Ex. 1034) ("Brown").
[7] Duval et al., *The mutator pathway is a feature of immunodeficiency-related lymphomas*, 101(14) PROC. NAT'L ACAD. SCI. 5002 (April 2004) (Ex. 1087) ("Duval").
[8] Hamid et al, Safety and Tumor Responses with Lambrolizumab (Anti-PD-1) in Melanoma, 369(2) NEW ENG. J. MEDICINE 134 (July 2013) (Ex. 1011) ("Hamid").

II. ANALYSIS

A. Legal Standards

"A person shall be entitled to a patent unless— (1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention . . . ." 35 U.S.C. § 102(a). To be anticipated, each and every element of the claim must be found, either expressly or inherently described, in a single prior art reference. *See Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006). When claim elements are inherently taught, the result must be a necessary consequence of what was deliberately intended, but the prior art need not demonstrate that the authors appreciated the results. *See Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999); *see Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) ("At the outset, this court rejects the contention that inherent anticipation requires recognition in the prior art.").

Under 35 U.S.C. § 103, a patent for a claimed invention may not be obtained,

> if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which said claimed invention pertains.

Obviousness is determined by looking to the scope and content of the prior art, differences between the prior art and the claims at issue, and the level of ordinary skill in the pertinent art. *See Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18 (1966). "[T]he analysis need not seek out precise

teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

B. Level of Skill and Declarants

Petitioner presents the testimony of Alfred I. Neugut, M.D., Ph.D., M.P.H., for opinion testimony regarding what one of ordinary skill in the art would have understood at the time of filing. (*See* Ex. 1003.) Dr. Neugut testifies that he is a medical oncologist with a particular focus on gastrointestinal tract cancers, including colorectal cancers. (*See id.* ¶ 4.) Dr. Neugut testifies further that he is the Director of the Center for Pharmacoepidemiology and Health Outcomes Research in Columbia's Department of Epidemiology and Director of Global Oncology Research for Columbia's Herbert Irving Comprehensive Cancer Center. (*See id.* ¶ 5.) Dr. Neugut testifies that he sees approximately 30 patients per week to treat gastrointestinal cancers, including colorectal cancer. (*See id.*)

Petitioner argues that one of ordinary skill in the art relevant to the claims of the '219 patent would be a medical doctor or a professional in a related field with at least five years of experience with treating cancer. (*See* Pet. 12 (citing Neugut Decl., Ex. 1003 ¶ 19).) Petitioner argues further that the ordinarily skilled artisan would have experience in or access to a person with knowledge of clinical studies for therapeutics and how they work and to a pathologist with comparable experience. (*See id.*) Petitioner also asserts that the grounds of challenge presented would not change if a "modestly lesser or greater level of experience" were to be determined. (*See*

id.) Dr. Neugut's testimony supports Petitioner's arguments regarding the level of skill that an ordinarily skilled artisan in the relevant field would have. (*See* Ex. 1003 ¶ 19.)

At this point in the proceeding, Patent Owner has not asserted any particular characteristics of one of ordinary skill in the art and does not contest that Dr. Neugut is qualified to testify about what one of ordinary skill would have understood at the time. Accordingly, in the analysis below, we apply the level of skill set forth by Petition and refer to Dr. Neugut's testimony of what one of ordinary skill in the art would have understood at the time the application that became the '219 patent was filed.

Patent Owner has not presented opinion testimony at this point in the proceeding. (*See* Prelim. Resp.)

C. Claim Construction

Petitioner argues that we need not construe any terms of the challenged claims to resolve the underlying controversy, as any reasonable construction reads on the prior art. (*See* Pet. 12.) At this point in the proceeding, Patent Owner does not argue for any specific claim construction. **(***See, generally*, Prelim. Resp.)

To the extent we deem it necessary to construe the terms of the challenged claims at this point in the proceeding, we do so in the analysis below. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019) ("The Board is required to construe 'only those terms . . . that are in controversy, and only to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

D. Ground 1: Anticipation of Claims 1–4 and 6–8 Based on the MSI-H Study Record

The parties agree that the MSI-H Study Record was publicly available by June 12, 2013. (*See* Pet. 8; *see* Prelim. Resp. 18 ("JHU submitted the MSI-H Study Record on June 10, 2013, and it was posted on clinicaltrials.gov on approximately June 12, 2013.").) Patent Owner does not dispute Petitioner's argument that the MSI-H Study Record is prior art under 35 U.S.C. § 102(a) and is not covered by any exceptions under 35 U.S.C. § 102(b). (*See* Pet. 8.)

The title of the MSI-H Study Record is "Phase 2 Study of MK-3475 in Patients with Microsatellite Unstable (MSI) Tumors." (Ex. 1005, 2.) Petitioner's witness, Dr. Neugut, testifies that MK-3475 is pembrolizumab, which Patent Owner does not dispute. (*See* Neugut Decl., Ex. 1003 ¶ 38.)

The MSI-H Study Record includes a "Brief Summary," explaining that

> [t]his study will be looking at whether MK-3475 (an antibody that blocks negative signals to T cells) is effective (anti-tumor activity) and safe in three different patient populations. These include: 1. patients with MSI positive colon cancer, 2. patients with MSI negative colon cancer, and 3. patients with other MSI positive cancers.

(Ex. 1005, 3.) Two of the outcome measures reported in the MSI-H Study Record are "Immune-related progression free survival (irPFS) rate in patients with MSI positive non-colorectal adenocarcinoma using immune related response criteria (irRC) at 20 weeks" and a determination of "[d]oes

MSI as a marker predict treatment response[?]" (Ex. 1005, 4–5.) The MSI-H Study Record provides "Arms and Interventions" as follows[9]

Arms	Assigned Interventions
Experimental: MSI Positive Colorectal Cancer	Drug: MK-3475 MK-3475 10 mg/kg every 14 days
Experimental: MSI Negative Colorectal Cancer	Drug: MK-3475 MK-3475 10 mg/kg every 14 days
Experimental: MSI Positive Non-Colorectal Cancer	Drug: MK-3475 MK-3475 10 mg/kg every 14 days

(Ex. 1005, 4.) The chart above identifies three patient populations and identifies the treatment for the patients in each population as 10mg/kg of pembrolizumab every 14 days.

Petitioner argues, in general, that the MSI-H Study Record inherently anticipates claims 1–4 and 6–8 of the '219 patent because the claims are directed to the methods disclosed in the MSI-H Study Record. (*See* Pet. 18.) Petitioner argues that the MSI-H Study Record teaches giving the claimed drug at the "only therapeutically effective dosage" described in the '219 patent and giving it to the claimed patient populations. (*See* Pet. 18 (citing Ex. 1005, 4 (Arms and Interventions), 2 (Study Identification), 3 (Study Description), 4–5 (Outcome Measures), 5–6 (Eligibility)).)

In regard to the limitation of claim 1 of the '219 patent of "selecting a patient who has an unresectable or metastatic" tumor, Petitioner argues that

[9] Petitioner relies on the testimony of Dr. Neugut and several prior art references to assert that the terms "MSI positive," "MSI-high," "MSIH," and "MSI+" were used to mean "MSI-H" by those in the art at the time. (*See* Pet. 6 (citing, *e.g.*, (Ex. 1018, 293 ("MSIH (MSI high) was considered MSI positive and MSS (MS stable)"); Neugut Decl., Ex. 1003 ¶ 27).) Patent Owner does not contest the identifications in its Preliminary Response.

the MSI-H Study Record discloses that the patients treated have "tumors" and "measurable disease," which Dr. Neugut testifies would include metastatic and advanced colorectal cancers. (*See* Pet. 19 (citing Ex. 1005, 5 (Eligibility); Ex. 1003 ¶¶ 59–63).) Dr. Neugut testifies that advanced cancer refers to metastatic cancer or cancer that is so locally advanced it is unresectable for purposes of a cure. (*See* Pet. 19 (citing Ex. 1003 ¶ 59 (citing Ex. 1078,[10] 1278)).) Dr. Neugut testifies further that clinical trials that involve "measurable" disease would not include cancer that is resectable for the purposes of a cure because the patient could be cured by surgery. (*See* Neugut Decl. ¶ 60 (citing Ex. 1020, 7).) According to Dr. Neugut, it would be highly unusual if the MSI-H Study Record did not indicate inclusion of patients with metastatic and advanced cancer because the study was not directed to local treatments, such as radiation or surgery. (*See* Ex. 1003 ¶ 61.) Dr. Neugut also cites to a reference that indicates those of ordinary skill in the art considered the MSI-H Study Record to include patients with metastatic colorectal cancer. (*See* Ex. 1003 ¶ 62 (citing Ex. 1049,[11] 444 ("[P]embrolizumab is being tested in metastatic tumors with microsatellite instability, including colorectal cancer (NCT01876511 [the number of the MSH-I Study]).")))).)

Petitioner argues that the MSI-H Study Record teaches the element of claim 1 of the '219 patent requiring that the selected patients have a

[10] Young and Rea, *ABC of colorectal cancer: Treatment of advanced disease*, 321 BRITISH MED. J. 1278 (2000) (Ex. 1078).
[11] Mitaks, et al., *The Place of Targeted Agents in the Treatment of Elderly Patients with Metastatic Colorectal Cancer*, 7 CANCERS 439, 444 (2015) (Ex. 1049).

"microsatellite instability-high (MSI-H) or mismatch repair (MMR) deficient tumor" because the MSI-H Study Record discloses three study arms, including one of patients having MSI-H colorectal cancer and another of patients having MSI-H non-colorectal cancer. (*See* Pet. 21–23 (citing Ex. 1005, 4 (Arms and Interventions)).) Dr. Neugut's testimony supports this argument. (*See* Ex. 1003 ¶¶ 64–68.) In addition, Dr. Neugut testifies that the patients determined to have defective MMR (dMMR) status are biologically the same population as patients with MSI-H status. (*See* Ex. 1003 ¶ 66 (citing Ex. 1020,[12] 51 ("Patients determined to have defective MMR (dMMR) status are biologically the same population as those with MSI-H status.")).)

Petitioner continues the argument that the MSI-H Study Record anticipates claim 1 of the '219 patent, citing the "Arms and Interventions" section of the MSI-H Study Record, which teaches treating patient populations having both MSI-H colorectal cancer and MSI-H non-colorectal cancer with 10 mg/kg of pembrolizumab every 14 days. (*See* Pet. 23 (citing Ex. 1005, 4).) Petitioner cites Dr. Neugut's testimony that this teaching reads on the claim limitation "administering an effective amount of pembrolizumab to the patient" because the dose taught in the MSI-H Study Record is identical to the dose described as being effective in the '219 patent. (*See* Pet. 23 (citing Ex. 1003 ¶¶ 69–73); *see* Ex. 1001, 4:19–32, 8:48–54, 13:22–28, 16:1–8, 16:60–17:3, 19:55–21:20, Figures 2, 11.)

[12] National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Colon Cancer Version 3.2014 (January 27, 2014) (Ex. 1020).

Petitioner argues that the final limitation of claim 1 of the '219 patent is an inherent result of the method of treatment reported in the MSI-H Study Record. (*See* Pet. 25–26 (citing Ex. 1003 ¶¶ 40–41, 69–76).) Specifically, Petitioner argues that the limitation "wherein the patient exhibits an outcome that is improved as compared to a corresponding outcome that would be observed in a reference patient that has been administered pembrolizumab, wherein the reference patient has a tumor that does not exhibit a MSI-high or a MMR deficiency status," is an inherent result of the methods taught. (*See id.*) Petitioner argues that the MSI-H Study Record teaches actively measuring specific outcomes in patients having MSI-H cancer and cancer that is not MSI-H. (*See* Pet. 25 (citing Ex. 1003 ¶ 75).) In support, Dr. Neugut testifies that the examples, tables, and figures of the '219 patent discuss the design and results of the MSI-H Study, as explained in the affidavit by the inventors on February 4, 2022. (*See* Ex. 1003 ¶¶ 40–41, 74–76, (citing Ex. 1001, 3:16–18, 6:48–22:15, Figures 1–13; Ex. 1005; Ex. 1002, 295–96 (February 4, 2022 Affidavit ¶¶ 22–23)).)

Petitioner cites to an affidavit executed by Andrew Pardoll, M.D., an inventor named on the '219 patent, as supporting Dr. Neugut's testimony. (*See* Pet. 8 (citing Ex. 1002, 295–96).) Dr. Pardoll's affidavit was submitted during prosecution of the '219 patent and cites Exhibit D, which is identified with the same ClinicalTrials.gov Identifier (NCT01876511) as the MSI-H Study Record. (*See* Ex. 1002, 361; *see* Ex. 1005.) Dr. Pardoll testifies:

> 22. Our research group eventually approached Merck. Merck agreed in early 2013 to supply its then-unapproved anti-PD-1 antibody, MK-3475 (pembrolizumab) for use in the study. It was, however, the research team at Hopkins who secured IRB approval, conducted, and paid for the study. On June 12, 2013,

> the solicitation for patients was first posted on clinicaltrials.gov **(Exhibit D).** In my mind, the four arms allowed us to try to get at an answer to a question to which we did not know the answer-specifically whether or not patients with MSI-high or MMR deficient tumors would exhibit an improved response when treated with MK-3475, compared with the more common MSS [microsatellite stable] or MMR proficient colon cancers. Thus, the trial covered all patients with colon cancer, MSI and MSS, but separated into two groups.
>
> 23. The preliminary results of this study demonstrated clinical responses at an unexpectedly high rate (>50% objective response rate) in the MSI-high (MMR deficient) arm but not in the MSS (MMR proficient) arm.

(Ex. 1002, 295–96.) The affidavit supports the argument that the improved outcome of treating a patient with a tumor exhibiting an MSI-high or an MMR deficiency status with pembrolizumab, compared to similarly treating a patient without an MSI-high or an MMR deficiency status, as recited in claim 1, is an inherent result because the treatment would necessarily provide the result. *See Mehl/Biophile*, 192 F.3d at 1366 ("Where, as here, the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."). Patent Owner does not dispute this result in the Preliminary Response. (*See* Prelim. Resp. 7 ("The '219 Patent reports that mismatch repair-deficient colorectal cancers (i.e., MSI-H CRC) had an immune-related objective response rate and immune-related progression-free survival rate of 40% and 78%, respectively—a huge improvement compared to the 0% and 11% rates found in mismatch repair-proficient colorectal cancers (i.e., MSI negative CRC).").)

Furthermore, the ’219 patent states: “The data from the small phase 2 trial of pembrolizumab to treat tumors with and without deficiency of MMR supports the hypothesis that MMR-deficient tumors are more responsive to PD-1 blockade than are MMR-proficient tumors.” (Ex. 1001, 6:48–52.)

Patent Owner does not put forth substantive arguments in the Preliminary Response against Petitioner’s Ground 1 for the unpatentability of claims 1–4 and 6–8 as being anticipated by the MSI-H Study Record.

At this point in the proceeding, Petitioner sufficiently demonstrates that it has shown a reasonable likelihood it will prevail in showing that the MSI-H Study Record teaches a method for selecting a patient who has an unresectable or metastatic microsatellite instability-high tumor and administering an effective amount of pembrolizumab to the patient, as recited in claim 1 of the ’219 patent. (*See* MSI-H Study Record, Ex, 1005, 4 (Arms and Interventions); *see also id*., 2 (Study Identification), 3 (Study Description), 4–5 (Outcome Measures), 5–6 (Eligibility); *see* Neugut Decl., Ex. 1003 ¶¶ 58–73.) At this point in the proceeding, we also find that there is sufficient evidence that there is a reasonable likelihood that Petitioner will prevail in showing that one of ordinary skill in the art would have understood the inherent results of the MSI-H Study Record to be an improved outcome of treating a patient with a tumor that is MSI-H or dMMR with pembrolizumab as compared to similarly treating a reference patient having a tumor that is not MSI-high or MMR deficient. (*See* Neugut Decl., Ex. 1003 ¶¶ 74–76.)

Accordingly, we determine that there is sufficient evidence to warrant institution of review on claim 1 based on Ground 1 of the Petition.

We have reviewed Petitioner's allegations regarding the MSI-H Study Record's disclosure of the additional limitations of dependent claims, and find that Petitioner has sufficiently demonstrated, on this record as supported by the testimony of Dr. Neugut, that the MSI-H Study Record discloses those additional limitations. *See* Pet. 26–30; Ex. 1003 ¶¶ 77–86. Accordingly, we determine that Petitioner has established that there is a reasonable likelihood that it will prevail in showing that the dependent claims are also unpatentable.

E. Grounds 2–7: Obviousness of Claims 1–8

Petitioner presents alternative grounds of challenge against the patentability of the claims of the '219 patent based on obviousness. (*See* Pet. 30–52.)

In regard to Ground 2, challenging the patentability of claims 1–4 and 6–8, Petitioner cites to Pernot and Benson, in addition to the MSI-H Study Record. (*See* Pet. 34–41.) Petitioner asserts that these references disclose elements that Patent Owner might argue are not taught in the MSH-I Study Record, specifically the improved outcome and efficacy recited in claim 1, testing for MSI-H or dMMR tumors, and treating patients that have progressive or metastatic disease. (*See* Pet. 34–41.)

Petitioner argues that Pernot teaches treating colorectal cancer and that, therefore, because the MSI-H Study Record is directed to a clinical study treating colorectal cancer in a patient whose cancers are MSI-H with pembrolizumab, which is an anti-PD-1 antibody, one of ordinary skill in the art knowing the teachings of the MSI-H Study Record would have considered the teachings of Pernot. (*See* Pet. 36.) Petitioner argues that

Pernot teaches that colorectal cancer patients that are MSI-H are "good candidates for immunotherapy," such as PD-1 inhibitors. (*See* Pet. 36 (quoting Ex. 1006, 3741 ("[Colorectal cancer] associated with MSI could lead to a more intense immune response, but also to specific immunoregulatory phenomena, making [patients with colorectal cancer] good candidates for immunotherapy.")).)

Petitioner cites further to Dr. Neugut's testimony to argue that one of ordinary skill in the art would have been motivated to combine the disclosure of Pernot with the methods taught in the MSI-H Study Record in order to obtain the results of the MSI-H Study Record's study. (*See* Pet. 36 (citing Ex. 1003 ¶ 93).)

Petitioner also argues that the state of the art indicates one of ordinary skill would have had a reasonable expectation of success in the claimed method because successful treatment with a PD-1 inhibitor of a colorectal cancer patient having an MSI-H tumor was reported in the prior art. (*See* Pet. 36–37.) For example, Petitioner refers to Lipson[13] for its reporting of the successful treatment of a colorectal cancer patient having MSI-H status with a PD-1 inhibitor, albeit a different inhibitor from pembrolizumab:

> A 71-year-old male with [colorectal cancer] underwent a right hemicolectomy in October 2003, revealing a moderately differentiated adenocarcinoma with metastases to 4 of 16 pericolonic lymph nodes and vascular and perineural invasion [G2, pT3N2; microsatellite instability (MSI)-high genotype]. He received adjuvant 5-fluorouracil (5-FU) and leucovorin; however, a CT scan the following year revealed metastatic

[13] Lipson et al, *Durable Cancer Regression Off-Treatment and Effective Reinduction Therapy with an Anti-PD-1 Antibody*, 19(2) CLINICAL CANCER RESEARCH 462 (January 2015) (Ex. 1057) ("Lipson").

> disease. Over the subsequent 3 years, the patient received multiple chemotherapeutic regimens with temporary response but then progression at multiple lymph node sites (gastrohepatic, portacaval, and peripancreatic); therapies included FOLFOX, irinotecan, bevacizumab, and cetuximab. Chemotherapy was last administered in April 2007. *The patient began therapy with anti-PD-1 at 3 mg/kg per dose in July 2007 after documentation of disease progression, and received 5 doses over the next 9 months. CT scans conducted 8 and 12 weeks after a single dose of anti-PD-1 showed a partial response (Fig. 1A). A [complete remission] was achieved in January 2008, and periodic CT and PET scans have revealed no evidence of recurrence since then*. The patient was most recently evaluated in April 2011, at which time he had not received any antineoplastic therapy for 3 years and had no evidence of disease recurrence.

(Ex. 1057, 463–64 (emphasis added).) Dr. Neugut's testimony supports the Petitioner's characterization of Lipson as a publication showing that a colorectal cancer patient, whose cancer was MSI-H, had been successfully treated with a PD-1 inhibitor. (*See* Ex. 1003 ¶ 94.)

Petitioner cites to other references, for example Champiat,[14] which teaches:

> Moreover, if high levels of mutational heterogeneity increase the tumor immunogenicity, it will be interesting to evaluate the clinical activity of PD-1/PD-L1 agents in DNA mismatch repair (MM)- deficient tumors, such as microsatellite instability (MSI)+ colorectal carcinoma as well as BRCA1 and 2 neoplasms (breast cancer 1 and 2, early onset), all of which display severe genomic instability.

[14] Champiat et al, *Exomics and Immunogenics Bridging Mutational Load and Immune Checkpoints Efficacy*, 3(1) ONCOIMMUNOLOGY e27817-1(January 2014) (Ex. 1032) ("Champiat").

(Ex. 1032, e27817-5.) Dr. Neugut testifies that Champiat, as well as other references, "independently urged the person of ordinary skill to treat MSI-H cancer with PD-1 inhibitors, like pembrolizumab, or other immunotherapy." (Ex. 1003 ¶ 95.) Citing to Dr. Neugut's testimony, Petitioner argues further that the prior art teaches that PD-1 inhibitors naturally have more efficacy when treating tumors comprised of cancer cells that are easy for immune cells to recognize and that are already infiltrated by immune cells. (*See* Pet. 37 (citing Ex. 1003 ¶¶ 43–46, 96).)

In light of this evidence of the state of the art at the time of the invention, Dr. Neugut testifies that one of ordinary skill in the art would have wanted to obtain data from the MSI-H Study Record and would have reasonably expected success in arriving at the claimed method, given that pembrolizumab was already approved for another oncology indication. (*See* Ex. 1003 ¶ 97; *see* Pet. 37.) Dr. Neugut concludes that "[a]s a result of carrying out the methods in the MSI-H Study Record of treating MSI-H colorectal patients with pembrolizumab at the dosage that was applied in the clinical study, the person of ordinary skill would have seen the results that naturally flow from those methods . . . ." (*See* Ex. 1003 ¶ 97.)

Petitioner also argues that the MSI-H Study Record would have motivated one of ordinary skill in the art to test patients' tumors for MSI-H because the MSI-H Study Record requires patients be placed into the proper study arm. (*See* Pet. 38–39 (citing Ex. 1003 ¶ 98 ("Testing was the way in which it was possible for the person of ordinary skill determine if the patient had the MSI-H colorectal cancer required for placement in that arm.")).)

Petitioner argues further that one of ordinary skill in the art would have considered it obvious that the MSI-H Study Record discloses treating patients with metastatic or unresectable cancer in light of the teachings of Benson. (*See* Pet. 39–41.) Petitioner argues that Benson is directed to ways in which clinical studies involving colorectal cancer are conducted, which is in the same field as the MSI-H Study Record. (*See id.* (citing Neugut Decl., Ex. 1003 ¶ 99).) Benson teaches that, under the standard of care, the patient population with tumors and measurable disease that would take part in a clinical study are patients having metastatic and advanced disease. (*See* Ex. 1009, 1034; *see* Neugut Decl., Ex. 1003 ¶ 100.) Dr. Neugut testifies further that the term "advanced cancer" refers to metastatic cancer or cancer that is so locally advanced that it is unresectable for purposes of a cure, and he concludes that a person of ordinary skill would have been motivated to carry out that the method of the MSI-H Study Record on colorectal cancer that was metastatic, with a reasonable expectation of success. (*See* Neugut Decl., Ex. 1003 ¶¶ 100, 101.)

In summary, Petitioner relies on Pernot to demonstrate that one of ordinary skill in the art would have considered patients with MSI-H tumors to be good candidates for immunotherapy, such as PD-1 inhibitors, and thus, that the ordinarily skilled artisan would have been motivated to obtain the results of the MSI-H Study Record. (*See* Pet. 35–36 (citing Ex. 1006, 3741).) Petitioner relies on Benson to demonstrate that one of ordinary skill in the art would have understood the MSI-H Study Record to be directed to patients with an unresectable or metastatic tumor. (*See* Pet. 39–40 (citing Ex. 1009, 1034).) At this point in the proceeding, Patent Owner does not

dispute Petitioner's characterization of or prior art status of either Pernot or Benson or the other references that Petitioner cites.

In regard to Ground 4, challenging the patentability of claims 1–4 and 6–8, Petitioner cites to Brown, Duval, and Benson, in addition to the MSI-H Study Record. (*See* Pet. 41–43.) Petitioner argues that Brown teaches that PD-1 inhibitors were inherently more effective when treating tumors comprised of cells that are easy for immune cells to recognize (*See* Pet. 44 (citing Ex. 1034, 747).). Petitioner argues further that Duval teaches that MSI-H cancers have cells that are easy for immune cells to recognize. (*See* Pet. 44 (citing Ex. 1087, 5002).) Dr. Neugut's testimony supports Petitioner's argument that Brown and Duval would have motivated a person of ordinary skill in the art to obtain the results of the MSI-H Study Record. (*See* Ex. 1003 ¶ 114; *see* Pet. 44.)

In regard to Grounds 3 and 5, which challenge the patentability of claim 5, Petitioner cites to Chappelle in addition to the MSI-H Study Record and the other references cited in Grounds 2 and 4. (*See* Pet. 41–43, 49.) Claim 5 depends from claim 1 and includes the limitations:

> wherein the unresectable or metastatic, microsatellite instability-high (MSI-H) or mis-match repair (MMR) deficient tumor exhibits instability in a microsatellite marker, wherein the microsatellite marker is BAT-25, BAT-26, MONO-27, NR-21 or NR-24, or wherein the unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair (MMR) deficient tumor exhibits a deficiency of a mismatch repair marker, wherein the mismatch repair marker is POLE, POLD1, or MYH.

(Ex. 1001, 26:19–29.) Petitioner argues that Chapelle teaches standard methods of testing whether a tumor is MSI-H, including determining

whether the patient's tumor exhibits instability in a microsatellite marker, such as BAT-25 or BAT-26. (*See* Pet. 42 (citing Ex. 1007, 3380, 3383).) Dr. Neugut supports this characterization of Chapelle. (*See* Ex. 1003 ¶ 107.)

In regard to Grounds 6 and 7, which challenge the patentability of claim 8, Petitioner cites to Hamid, in addition to the MSI-H Study Record and the other references cited in Ground 4. (*See* Pet. 50–52.) Claim 8 recites the method of claim 1, "wherein pembrolizumab is administered by intravenous infusion." (Ex. 1001, 26:34–35.) Petitioner argues, and Dr. Neugut agrees, that Hamid teaches infusion of pembrolizumab[15] by intravenous infusion. (*See* Pet. 51 (citing Ex. 1011, 134); *see* Ex. 1003 ¶¶ 129, 131.)

Patent Owner does not dispute Petitioner's characterization of or prior art status of any of the references cited in the obviousness challenges. Patent Owner raises only procedural issues, without addressing the substantive merits of Petitioner's challenges. Specifically, Patent Owner argues that Petitioner fails to meet the particularity requirement of 35 U.S.C. § 312(a)(3) in all of its challenges under 35 U.S.C. § 103. (*See* Prelim. Resp. 23–32.) According to Patent Owner, the Petition fails to set forth, with particularity, a sufficient mapping of each challenged claim to the cited prior art in each of the obviousness-based grounds of unpatentability. (*See* Prelim. Resp. 24.) Patent Owner argues that,

> [f]or example, in one ground (Ground 2), as explained below, the Petition identifies the claim limitation at issue (limitation [1.2]) but not the cited prior art that allegedly teaches or

[15] Hamid refers to "lambrolizumab," which Dr. Neugut testifies is the same as pembrolizumab. (*See* Ex. 1003 ¶ 129.)

> suggests that limitation. In that same ground, the Petition goes on to identify prior art but then fails to set forth the claim limitation allegedly taught or suggested by that prior art. In other words, in each situation, the Petition fails to properly relate the prior art to the claims.

(*See* Prelim. Resp. 24.)

We do not agree with Patent Owner that there is insufficient mapping. Patent Owner does not provide a citation to the Petition where "limitation [1.2]" is addressed in Petitioner's challenges under 35 U.S.C. § 103 and does not identify which limitation Patent Owner believes is "limitation [1.2]," although Patent Owner appears to consider Petitioner's identification of the limitation [1.1], "selecting a patient who has an unresectable or metastatic [tumor]," to be properly called "limitation [1.2]." (*See* Prelim. Resp. 26, n.7; *see* Pet. 19.) Patent Owner fails to address or identify any deficiency in Petitioner's arguments regarding the teachings of Benson that, under the standard of care, the patient population with tumors and measurable disease who would take part in a clinical study are patients having metastatic and advanced disease and that the term "advanced cancer" would indicate their cancers are unresectable. (*See* Pet. 39–41 (citing Ex1009, 1034; Ex. 1003 ¶¶ 99–101).)

Patent Owner argues further that Petitioner's obviousness grounds of the challenged claims do not clearly identify particular limitations that are allegedly taught by which references. (*See* Prelim. Resp. 25–28.) We disagree. Petitioner explains that the challenges under 35 U.S.C. § 103 put forth in Grounds 2–7 are presented to address the potential arguments by Patent Owner that the MSI-H Study Record cannot anticipate because it did

not disclose an improved outcome as required in the claims or because one of ordinary skill in the art would not have reasonably expected the efficacy recited in the claims. (*See* Pet. 34–35.) Petitioner further asserts that Ground 2 is presented to address potential arguments that the MSI-H Study Record does not disclose testing or the claim limitations to metastatic disease. (*See* Pet. 35.)

In light of our analysis above, we are not persuaded by Patent Owner's arguments that we should deny institution because the petition advances ambiguous or unclear grounds of unpatentability for obviousness. (Prelim. Resp. 24.) Moreover, Petitioner relies on the MSI-H Study Record in each of Grounds 2–7, which, as discussed above with regard to Ground 1, provides sufficient evidence for us to determine there is a reasonable likelihood Petitioner will prevail on the anticipation challenge to at least claim 1. That is, we are persuaded by Petitioner's arguments regarding the MSI-H Study Record that there is sufficient reason to institute review based on Petitioner's mappings of the elements of at least claim 1 to the teachings of the MSI-H Study Record. We are not persuaded that the additional teachings of the prior art cited in Grounds 2–7 somehow erase that sufficiency.

Patent Owner argues further that the cross-references to arguments in the Petition are "ill-defined and confusing," although Patent Owner admits they are not "*per se* improper." (Prelim. Resp. 28–30.) As explained above, we are persuaded that the MSI-H Study Record accompanied by Petitioner's declarant's testimony provides sufficient evidence that Petitioner would

prevail regarding the unpatentability of at least claim 1. On this record, we do not view Petitioner's cross-references as inappropriate.

Patent Owner argues that Petitioner relies on "a voluminous number of additional exhibits without sufficient analysis and explanation about the relevant contents of each exhibit." (Prelim. Resp. 30–32.) Patent Owner's argument does not substantively overcome Petitioner's case. We are not persuaded that the mere number of references cited to support and argument is necessarily detrimental to the argument. If Patent Owner had cited to teachings of the cited references that contradict the arguments Petitioner makes in the grounds of challenge to the claims of the '219 patent, we might be persuaded that the claims are not obvious. But Patent Owner argues only that too many references were cited. We are not persuaded by this argument that we should decline to institute *inter partes* review of the challenged claims.

After weighing the parties' arguments and reviewing the evidence relied on in the Petition, as discussed above, we determine that there is sufficient evidence to indicate a reasonable likelihood Petitioner will prevail on at least one claim challenged under 35 U.S.C. § 103 in each of Grounds 2–7 in the Petition. Specifically, Petitioner presents sufficient evidence to demonstrate that it is reasonably likely that at least claim 1 is obvious over the MSI-H Study Record, Pernot, and Benson (Ground 2; *see* Ex. 1005, Ex. 1006, 3741, Ex. 1009, 1034; *see* Ex. 1003 ¶¶ 93–102) and over the MSI-H Study Record, Brown, Duval, and Benson (Ground 4; *see* Ex. 1005, Ex. 1087, 5002, Ex. 1034, 747, Ex. 1009, 1034; *see* Ex. 1003 ¶¶ 109–126), that claim 5 is obvious over the MSI-H Study Record, Pernot, Benson, and

Chapelle (Ground 3; *see* Ex. 1005, Ex. 1006, 3741, Ex. 1009, 1034, Ex. 1007, 3380, 3383; *see* Ex. 1003 ¶¶ 103–108) and over the MSI-H Study Record, Brown, Duval, Benson, and Chapelle (Ground 5; *see* Ex. 1005, Ex. 1087, 5002, Ex. 1034, 747, Ex. 1007, 3380, 3383, Ex. 1003 ¶ 127), and that claim 8 is obvious over the MSI-H Study Record, Pernot, Benson, Chapelle, and Hamid (Ground 6; *see* Ex. 1005, Ex. 1006, 3741, Ex. 1009, 1034, Ex. 1007, 3380, 3383, Ex. 1011, 134; *see* Ex. 1003 ¶¶ 128–134) and over the MSI-H Study Record, Brown, Duval, Benson Chapelle, and Hamid (Ground 7; *see* Ex. 1005, Ex. 1087, 5002, Ex. 1034, 747, Ex. 1007, 3380, 3383, Ex. 1011, 134; *see* Ex. 1003 ¶ 135).

F. Discretionary Denial

1. 35 U.S.C. § 325(d)

Under 35 U.S.C. § 325(d):

> In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, 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.

Thus, we have the discretion to deny institution when the prior art cited in Petitioner's challenges was previously presented to the Office. To determine whether denial under § 325(d) is appropriate, we look to the parties' evidence of

> (a) the similarities and material differences between the asserted art and the prior art involved during examination; (b) the cumulative nature of the asserted art and the prior art evaluated during examination; (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection; (d) the extent of the overlap between

> the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art; (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph). We apply a two-part test to analyze these factors, as articulated in *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GMBH*, IPR2019-01469, Paper 6 (Feb. 13, 2020) (precedential), wherein we ask

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

(*Id.* at 8.)

Petitioner argues that discretionary denial is inappropriate because of how the Examiner considered the information in the MSI-H Study Record. (*See* Pet. 53–55.) Petitioner acknowledges that the Examiner considered the MSI-H Study Record during prosecution of prior application 16/144,549 ("the '549 application"), which issued as U.S. Patent No. 10,934,356 ("the '356 patent") and is in the chain of priority of the '219 patent. (*See id.* (citing Exs. 1002, 1022).) Petitioner argues that the Examiner erroneously allowed the claims of the '356 patent on the reasoning that the MSI-H Study Record did not affirmatively disclose the results flowing from treatment with

pembrolizumab. (*See* Pet. 54 (citing Ex. 1022, December 14, 2020 Notice of Allowability, 3 (Part 11, 3073)).) The Examiner stated:

> Clinical Trial Announcement NCT01876511 does not teach the mental step of determining that the patient with a MSI-high or MMR deficiency status who has been treated with pembrolizumab exhibits an improved outcome compared to a patient who has been treated with pembrolizumab but does not have such a status. The announcement contemplates evaluating this parameter as primary and secondary outcome measures of the proposed clinical trial. (Page 3/8.) On its own, however, the announcement does not establish why the person of ordinary skill in the art would have reasonably expected the claimed outcome. In particular, the announcement does not establish a reasonable expectation of observing claim 41's objective response rate of about 12%-96% in MSI-high or MMR-deficiency patients treated with pembrolizumab.

(December 14, 2020, Notice of Allowability, EX1022 (part 11), 3073.)

Petitioner argues that the Examiner's requirement for an express disclosure of an inherent result "was incorrect as a matter of law, particularly given the evidence that the methods in the MSI-H Study Record were, in fact, shown to be effective, as explained above." (Pet. 54.) Specifically, Petitioner argues that the Examiner allowed the claims of the '356 patent over the MSI-H Study Record on the rationale that it did not affirmatively disclose an improved outcome and that the POSA would purportedly not have expected such efficacy. (*See* Pet. 54.) Petitioner argues that, because one carrying out the techniques reported in the MSI-H Study Record (administering pembrolizumab to MSI-H positive colorectal cancer patients) could be accused of infringement of the '356 patent, the reference should have been asserted as anticipating the then-pending claims. (*See* Pet. 54

(citing *Schering Corp.*, 339 F.3d at 1379 ("that which would literally infringe if later in time anticipates if earlier.")).) Petitioner argues that the Examiner did not consider whether the MSI-H Study Record inherently anticipates the methods claimed in the '356 patent and, thus, discretionary denial is inappropriate for the challenges presented in the Petition. (*See* Pet. 9, 55.)

Patent Owner responds by arguing that we should exercise discretion to deny instituting a trial under 35 U.S.C. § 325(d) because the Examiner repeatedly considered the MSI-H Study Record and updates to it during prosecution of the '219 patent and at least nine other related applications examined before the '219 patent was allowed. (*See* Prelim. Resp. 18–22 (citing Ex. 1002 (part 1), 257, 261, 515; Ex 1001, 4 Ex 2009, 1; Ex. 2010, 1; Ex. 2012, 1; Ex. 2014, 1; Ex. 2015, 1; Ex. 2018, 9–12, Ex. 2019, 10–13, Ex. 1022, 3009–12, 3039–49, 3072–74; Ex. 2054, 1).) Patent Owner notes the Examiner's considerations, as indicated by signatures on Information Disclosure Statements, reliance on in rejections, discussions in interviews, and explanation in the "reasons for allowance" notification in at least some of these applications. (*See id*.) Patent Owner points specifically to the Examiner's consideration of the MSI-H Study Record in the prosecution of related '549 application and application 15/611,017 prior to allowance of the claims in the '356 patent. (*See* Prelim. Resp. 20–21.)

Turning to the *Becton, Dickinson* factors, even if we consider the MSI-H Study Record to have been fully considered during prosecution of the application that became the '219 patent and, even if we consider that it would have been the basis for a rejection had it not been discounted in the

prosecution of prior applications (factors (a) through (c)), we are persuaded that these considerations do not indicate we should deny institution in this case. As discussed above, at this point in the proceeding, we agree with Petitioner that the MSI-H Study Record teaches the steps of at least claim 1 of the '219 patent — selecting a patient who has an unresectable tumor or metastatic MSI-H or MMR deficient tumor and administering an effective amount of pembrolizumab. Thus, at this point, we agree with Petitioner that the Examiner erred by failing to appreciate the teachings of the prior art when the claims were allowed over the MSI-H Study Record on the rationale that the art did not affirmatively disclose an improved outcome or that one or ordinary skill would not have expected such efficacy. (*See* Pet. 54.) We are persuaded that a reference need not show the efficacy of treatment if the steps were taught in the prior art. *See Mehl/Biophile*, 192 F.3d at 1366 (Fed. Cir. 1999) ("MEHL/Biophile does not dispute on appeal that the laser operating parameters disclosed in the article substantially coincide with those disclosed in the patent. Accordingly, to the extent that the embodiment in the patent achieves hair depilation, so does the Polla method. Where, as here, the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results.").

We disagree with Patent Owner that merely because the Examiner considered the MSI-H Study Record during prosecution, we should exercise discretion to deny institution of *inter partes* review because we are persuaded that Petitioner has pointed out sufficiently that the Examiner failed to appreciate the inherent disclosures in the asserted prior art.

2. 35 U.S.C. § 314(a)

Patent Owner argues that we should exercise our discretion to deny institution of *inter partes* review in light of the parallel district court litigation. (*See* Prelim. Resp. 8–18 (citing *Merck Sharp & Dohme LLC v. The Johns Hopkins University*, 1:22-cv-03059-JRR (D. Md.) ("the Maryland litigation")); *see also* PO Sur-Reply, Paper 10.) Petitioner opposes Patent Owner's assertions. (*See* Pet. 52–53; *see also* Pet. Reply, Paper 8.) We look to the following factors in evaluating whether to do so:

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

Apple Inc. v. Fintiv, Inc., IPR2020-00019, Paper 11 at 5–6 (PTAB Mar. 20, 2020) (precedential). We are also guided by the Director's Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation, issued on June 21, 2022 ("Memorandum") (Ex. 1065).

Petitioner asserts, and Patent Owner does not dispute, that the co-pending Maryland litigation has been stayed in its entirety pending resolution of IPR2024-00240, which involves a related patent that is also involved in the litigation. (Pet. Reply 1 (citing Order in *Merck Sharp &*

Dohme LLC v. The Johns Hopkins University, 1:22-cv-03059-JRR (D. Md.), dated June 29, 2024, Ex. 1100, 1); *see* PO Sur-Reply 1 (acknowledging "the recent stay of the parties' co-pending litigation involving the '219 Patent.").) In its Memorandum Opinion, the court acknowledged that *inter partes* reviews of additional patents involved in the litigation could be instituted. (*See* Ex. 1101, 3.)

"A district court stay of the litigation pending resolution of the PTAB trial allays concerns about inefficiency and duplication of efforts. This fact has strongly weighed against exercising the authority to deny institution under NHK." *Fintiv*, at 6. Accordingly, the first *Fintiv* factor weighs heavily against exercising discretion to deny institution of *inter partes* review.

The stay indicates that the court's trial date will not be close to the Board's projected statutory deadline for a final written decision and that neither the court nor the parties will invest further in the parallel proceeding. (*See also* Ex. 1101, 2 (noting that the litigation is in a "relatively early stage," before depositions have been taken or paper discovery is complete, and before the parties have "invested time and attention to developing the record and evidence for the *Markman* hearing and trial"); *contra* Prelim. Resp. 11–15.) Thus, because of the stay, the second and third *Fintiv* factors also weigh heavily against exercising discretion to deny institution of *inter partes* review.

As to *Fintiv* factors 4 and 5, although the same claims, the same prior art, and the same parties are involved in the district court proceeding, these facts do not outweigh the effect of the court's stay or the court's desire to

simplify and streamline the material issues before it by waiting for the Board's decision on the patentability of the involved patents. (*See* Ex. 1101, 3–4; *see* Prelim. Resp. 15–17, 33.)

Patent Owner argues that *Fintiv* factor 6, particularly the merits of Petitioner's arguments, indicates that institution should be denied. (*See* Prelim. Resp. 17–33; *See* PO Sur-Reply, Paper 10, 1.) Patent Owner repeats many of the arguments presented in the Preliminary Response to argue that the merits of Petitioner's challenges are weak. (*See id.* at 2.)

Because we determine that *Fintiv* factors 1–5 collectively do not favor discretionary denial, we need not determine whether compelling merits weigh in favor of institution. *See CommScope Techs. LLC v. Dali Wireless, Inc*, IPR2022-01242, Paper 23 at 4–5 (Feb. 27, 2023) (precedential) ("[I]n circumstances where the Board determines that the other *Fintiv* factors 1–5 do not favor discretionary denial, the Board shall decline to discretionarily deny under *Fintiv* without reaching the compelling merits analysis.").

Patent Owner argues further that the claims challenged and issues raised in the current petition are different from the claims challenged and issues raised in IPR2024-00240, which was the basis of court's stay in the Maryland litigation, and that the Board's determination in IPR2024-00240 does not "compel a similar result here." (PO Sur-Reply 3.) Patent Owner argues that Petitioner has engaged in "strategic delay" and "gamesmanship" that prejudice Patent Owner by creating staggered trial dates, thereby allowing

Petitioner to unfairly rely on Patent Owner's arguments in previous proceedings. (*See id.*; *see* Prelim. Resp. 32–33.)

None of these arguments persuades us that we should exercise our discretion to deny institution of *inter partes* review where the District Court has stayed litigation addressing patentability of a related patent, indicating that the proximity of a trial date and the investment of the parties and the court in the parallel proceeding do not merit discretionary denial.

Accordingly, we decline to exercise discretion to deny institution of a trial under 35 U.S.C. § 314(a).

III. CONCLUSION

After reviewing the merits of the Petition and Patent Owner's arguments in opposition, we are persuaded that Petitioner has met the burden to show a reasonable likelihood of prevailing on at least one challenge to claim 1. *See* 35 U.S.C. § 314(a). We are not persuaded there is a reason to exercise the discretion provided by either 35 U.S.C. § 314(a) or § 325(d) to deny institution of trial. Accordingly, we institute trial on all grounds of challenge presented in the Petition.

We have not made a final determination as to the patentability of any challenged claim or as to the construction of any claim term. Any final determination will be based on the record developed during trial.

IV. ORDER

It is hereby ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–8 of U.S. Patent 11,339,219 B2 is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), *inter-partes* review of the ’219 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

FOR PETITIONER:

Naveen Modi
Bruce M. Wexler
Preston K. Ratliff II
Daniel Zeilberger
David J. Feigenbaum
PAUL HASTINGS LLP
PH-MSD-JHU-IPR@paulhastings.com

Mark Stewart
MERCK SHARP & DOHME LLC
mark.stewart@merck.com

FOR PATENT OWNER:

Nicholas Stephens
Grace J. Kim
Todd G. Miller
Anita L. Meiklejohn
Matthew L. Chun
FISH & RICHARDSON P.C.
IPR52261-0009IP1@fr.com
nstephens@fr.com
gkim@fr.com
miller@fr.com
meiklejohn@fr.com
mchun@fr.com