

**2026-1020, 2026-1021, 2026-1184, 2026-1185, 2026-1188,
2026-1189, 2026-1209, 2026-1210, 2026-1211**

**United States Court of Appeals
for the Federal Circuit**

THE JOHNS HOPKINS UNIVERSITY,
Appellant

v.

MERCK SHARP & DOHME LLC,
Appellee.

*Appeal from the United States Patent and Trademark Office,
Patent Trial and Appeal Board in Nos. IPR2024-00647, IPR2024-00240,
IPR2024-00622, IPR2024-00623, IPR2024-00624, IPR2024-00625,
IPR2024-00648, IPR2024-00649, and IPR2024-00650.*

NON-CONFIDENTIAL BRIEF OF APPELLEE

Naveen Modi
Benjamin W. Snyder
Daniel Zeilberger
Vladimir J. Semendyai
PAUL HASTINGS LLP
2050 M Street, NW
Washington, DC 20036
Tel.: (202) 551-1700

Preston K. Ratliff II
Principal Counsel
Bruce M. Wexler
Dana R. Weir
Jessica Stauring
Ben Gifford
PAUL HASTINGS LLP
200 Park Avenue
New York, NY 10166
Tel.: (212) 318-6000

Counsel for Appellee

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REPRESENTATIVE CLAIMS AT ISSUE

Claim 1 of U.S. Patent No. 11,649,287 (Appx600-632)

1. A method for treating colorectal cancer in a human patient, the method comprising:

in response to determining that the colorectal cancer is microsatellite instability high or DNA mismatch repair deficient, treating a human patient having colorectal cancer that is microsatellite instability high or DNA mismatch repair deficient with a therapeutically effective amount of pembrolizumab, wherein a biological sample from the patient had previously been tested to determine whether the colorectal cancer is microsatellite instability high or DNA mismatch repair deficient.

Claim 1 of U.S. Patent No. 10,934,356 (Appx667-697)

1. A method for treating cancer in a patient in need thereof, comprising:

determining that the patient has a tumor that exhibits a high microsatellite instability (MSI-high) or a mismatch repair (MMR) deficiency status;

administering an effective amount of pembrolizumab to the patient;

determining that 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; and

wherein the patient has received a prior cancer therapy drug.

Claim 1 of U.S. Patent No. 11,643,462 (Appx793-826)

1. A method for treating a patient having a solid tumor selected from the group consisting of endometrial cancer, small bowel cancer, gastric cancer,

ampullary cancer, cholangiocarcinoma, pancreatic cancer, prostate cancer, breast cancer, esophageal cancer, liver cancer, ovarian cancer, uterine cancer, cervical cancer, bladder cancer, testicular cancer and oral cancer that has progressed following at least one prior treatment, the method comprising:

testing or having tested a biological sample obtained from the patient to determine whether the solid tumor is microsatellite instability high or DNA mismatch repair deficient; and

in response to determining that the solid tumor is microsatellite instability high or DNA mismatch repair deficient, treating the patient determined to have a solid tumor that is microsatellite instability high or DNA mismatch repair deficient with a therapeutically effective amount of pembrolizumab.

CERTIFICATE OF INTEREST

Case Number: 2026-1020, -1021, -1184, -1185, -1188, -1189, -1209, -1210, -1211
Short Case Caption: Johns Hopkins University v. Merck Sharp & Dohme LLC
Filing Party/Entity: Merck Sharp & Dohme LLC

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: August 14, 2026

/s/ Preston K. Ratliff II
Preston K. Ratliff II

Counsel for Appellee
Merck Sharp & Dohme LLC

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	2. Real Party in Interest. Fed. Cir. R. 47.4(a)(2).	3. Parent Corporations and Stockholders. Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities.	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities.
Merck Sharp & Dohme LLC	Merck & Co., Inc.	None

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

Merck Sharp & Dohme LLC: Mark Stewart, Esq.

Paul Hastings: David J. Feigenbaum (no longer with the firm)

5. Related Cases. Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

Yes. *See* Merck Sharp & Dohme LLC's Amended Notice of Related Case Information, Dkt. No. 20 (Dec. 10, 2025).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

Not applicable.

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CONFIDENTIAL MATERIAL OMITTED

Pursuant to Federal Circuit Rule 25.1(e)(1)(B), Merck identifies the following omitted confidential material:

The material omitted on pages 49 and 50 of Merck’s Response Brief quotes information from JHU’s Investigational New Drug (“IND”) Application filing with the U.S. Food and Drug Administration (“FDA”) that is alleged to be confidential and is subject to a protective order entered by the Patent Trial and Appeal Board.

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STATEMENT OF RELATED CASES

This is a consolidated appeal from the Patent Trial and Appeal Board's final written decisions in nine related *inter partes* review proceedings. No appeal from the proceedings was previously before this or any other appellate court.

Merck is aware of only one case that could directly affect, or be directly affected by, this Court's decision in this consolidated appeal: *Merck Sharp & Dohme LLC v. The Johns Hopkins University*, No. 1-22-cv-03059 (D. Md.).

INTRODUCTION

This case involves efforts by Appellant Johns Hopkins University (“JHU”) to patent a treatment method already disclosed in the prior art, in which a known cancer drug developed by Appellee Merck is administered to a patient having a certain type of cancer. The Patent Trial and Appeal Board correctly rejected those efforts, finding that the claimed treatment method was anticipated by a study record published on www.ClinicalTrials.gov more than two years before the alleged priority date of JHU’s patents. The Board also correctly found that the dependent claims of JHU’s patents were either anticipated or obvious.

On appeal, JHU shifts focus from its unsuccessful positions below. Its primary argument before the Board was that the study record did not anticipate the claimed treatment method because it did not disclose the challenged limitations. The centerpiece of JHU’s appeal, by contrast, is its argument that the study record is not prior art *at all* because its prior-art status is negated by the experimental-use doctrine.

This Court should reject JHU’s retooled arguments and affirm the Board’s decisions. Every court to consider the question has held that the experimental-use doctrine does not negate the prior-art status of printed publications generally, including ClinicalTrials.gov postings specifically. JHU asks the Court to break with all precedent on the issue, but the exception from Section 102’s printed-publication

bar that JHU proposes is both atextual and inconsistent with policies underlying printed-publication prior art and the experimental-use doctrine.

JHU's fallback arguments likewise fail. The Board correctly declined to import an unclaimed negative limitation that would have required not treating other patients. And, unlike the Examiner during the original prosecution of JHU's patent applications, the Board properly applied this Court's inherency precedents to find that the study record anticipates even though it does not expressly disclose the results of the claimed treatment method. Finally, the Board was right to find, based on the testimony of Merck's experts, that the dependent claims of the challenged patents were either anticipated or obvious.

ISSUES PRESENTED

1. Whether the Board correctly found that the experimental-use doctrine does not negate the prior-art status of the study record at issue, where the statutory text contemplates no such negation and every court to address the question has held that the experimental-use doctrine does not apply to printed-publication prior art.

2. Whether the Board correctly found that the study record anticipates the challenged claims, where the Board: (1) construed the independent claims as requiring the recited method steps but declined to import an unclaimed negative limitation; (2) found that the study record anticipates the challenged claims by expressly disclosing the claimed method steps, which inherently produce the

claimed results; and (3) found, based on expert testimony, that a person of ordinary skill in the art would have understood the study record to disclose certain dependent claim limitations.

3. Whether the Board correctly found that certain dependent claims directed to trivial method details would have been obvious, where the prior art taught the additional limitations of those claims and where JHU did not tie any evidence of alleged secondary considerations to those dependent claims.

STATEMENT OF THE CASE

I. Merck's Cancer Drug Pembrolizumab

This case involves treatment using Merck's cancer drug pembrolizumab. Pembrolizumab is a Programmed Cell Death 1 ("PD-1") inhibitor that uses the body's own immune response system to fight cancer. Appx1654, ¶29. PD-1 inhibitors like pembrolizumab block receptors on cancer cells that essentially hide the cells from the immune system; with the receptors blocked, the cancer cells become susceptible to recognition and removal by the immune system. Appx1654-1656, ¶¶30-32.

Merck holds patents protecting pembrolizumab itself and its use for treating cancer. Appx15565, ¶146; Appx16606-16744; Appx17025-17071. Merck filed its first patent application on June 13, 2008. Appx17025. The patent, which issued on January 15, 2013, taught that pembrolizumab could be used broadly to treat cancer

and identified examples of preferred cancers for treatment, including colon cancer. *See, e.g.*, Appx17034, 2:22-25, Appx17037, 7:55-59, Appx17044, 21:65-22:14.

Merck began clinically developing pembrolizumab in 2010. Appx1656, ¶33; Appx1944. During development, Merck conducted many clinical studies to treat patients with a variety of cancers. Appx1656, ¶33; Appx1816, 1818; Appx1955; Appx1963; Appx5298. Merck's early studies—including the study at the center of this appeal—included colorectal and gastric cancer patients, among others, whose cancers had high microsatellite instability (referred to as “MSI-H”). Appx1656, ¶33; Appx5298. A person's cancer is considered MSI-H if the cancer cells' DNA contains small tracts of repeating DNA, called microsatellites, that are different in size from regularly occurring microsatellites. Appx1652-1654, ¶¶23-28; Appx1891-1892. MSI-H was known to occur commonly in several different types of cancer, including colorectal, endometrial, and gastric cancers, and to occur (albeit less frequently) in other solid-tumor cancer types as well. Appx1652-1653, ¶24; Appx139597, ¶25. Contemporaneously, another company, Bristol Myers Squibb (“BMS”), was clinically developing its own PD-1 inhibitor drug to treat cancer, including MSI-H colorectal cancer. Appx1654, ¶29; Appx5842; Appx5788.

Merck also developed the appropriate dosing regimens of pembrolizumab for treating cancer. Merck published studies in which patients were administered doses of pembrolizumab, including 10 mg/kg, for the treatment of cancer. *See, e.g.*,

Appx1899 (published June 2, 2013). Merck also timely filed a patent application—published on August 21, 2014—that described administering a 10 mg/kg dose of pembrolizumab every 14 days to treat cancer. *E.g.*, Appx16694, Appx16724, 22:14-19, Appx16744, 62:30-33.

Merck received accelerated approval for pembrolizumab from the Food and Drug Administration (“FDA”) on September 4, 2014. Appx15587, ¶14, Appx16228. Merck has continued to invest considerable resources in the development of pembrolizumab, resulting in more than 50 different approvals from the FDA for treating cancer. Appx15588, ¶16.

II. The Prior Art Recommended Using PD-1 Inhibitors Like Pembrolizumab To Treat MSI-H Cancers

The art has long been focused on investigating genetic biological markers associated with cancer. MSI-H was one such well-known biomarker. Appx1652-1653, ¶24. By the alleged priority date, it was routine to test tumors for MSI-H, because it could inform therapeutic choices, prognosis, and the likelihood of inherited cancer susceptibility. *Id.*

PD-1 inhibitors like pembrolizumab had shown natural efficacy in the treatment of cancers with characteristics also known to be exhibited by MSI-H tumors. For example, Merck’s declarant, Dr. Alfred I. Neugut, explained that the literature prior to JHU’s alleged priority date taught that: (1) PD-1 inhibitors naturally had more efficacy when treating tumors that have many mutations and are

already infiltrated by many immune cells; and (2) MSI-H tumors naturally displayed those characteristics. Appx1660-1667, ¶¶42-45. By late 2012, prior art reported that treatment with a different PD-1 inhibitor had led to a complete response in an MSI-H colorectal cancer patient. Appx1667, ¶46; Appx5842.

Further, consistent with publications from 2009 and 2011 connecting MSI-H colorectal cancer with immunotherapy, other publications specifically recommended that patients who had cancers with the MSI-H biomarker should be treated with immunotherapy drugs, including PD-1 inhibitors. Appx1667-1670, ¶¶47-49. For example, in January 2014, Champiat suggested treating MSI-H colorectal cancers with PD-1 inhibitors. Appx1668, ¶48; Appx5518, Appx5522. Similarly, in April 2014, Pernot recommended MSI-H colorectal cancers as “good candidates for immunotherapy” and discussed the “more than promising efficacy” of PD-1 inhibitors, including pembrolizumab. Appx1668, ¶48; Appx15543-15545, ¶¶106-108; Appx1823, Appx1826-1827. It was also known by February 2014 that BMS had begun a clinical study to treat MSI-H colorectal cancer patients with its PD-1 inhibitor, which it described in a posting on ClinicalTrials.gov. Appx1670, ¶49; *see* Appx5788.

In view of the efficacy that pembrolizumab was showing in treating tumors with characteristics similar to MSI-H tumors, and the prior successful treatment of an MSI-H colorectal cancer patient with a different PD-1 inhibitor, JHU approached

Merck in late 2012 about collaborating on a clinical study in which cancer patients who had MSI-H tumors would be treated with Merck's drug, pembrolizumab. *E.g.*, Appx15506-15509, ¶¶37-44 (discussing JHU 2013 FDA submission citing prior art for the scientific rationale and anticipated outcome for the parties' MSI-H clinical study). Merck agreed to support and collaborate on the study because it was "based on really good science." Appx7951. As part of that collaboration, Merck provided pembrolizumab free of cost, as well as other financial support and expertise regarding treating cancer patients with pembrolizumab, Appx1818; Appx8324-8325; Appx15509, ¶44; Appx14717, 73:3-6; Appx17216, 76:6-12. While JHU initially indicated that it had already secured funding for the study (Appx9450), Merck ultimately provided financial support throughout.¹

III. The Prior Art Study Record

On June 10, 2013, JHU submitted detailed information on the parties' collaborative clinical study to ClinicalTrials.gov. Appx1657, ¶35; Appx1816-1821. The study information was published the same day and was referred to in the proceedings below as the MSI-H Study Record ("Study Record"). *Id.*

¹ JHU asserts otherwise (at 7-8), but that unsupported assertion is inconsistent with the testimony of named inventor Dung Le, who admitted that Merck provided funding for the study, though she could not remember when. Appx14924-14925, 280:9-281:14.

The Study Record was aptly titled “Phase 2 Study of MK-3475 [pembrolizumab] in Patients With Microsatellite Unstable (MSI) Tumors.” Appx1816. It explained that the parties’ study would treat cancer patients with Merck’s drug pembrolizumab in three arms: (1) one arm included patients with MSI-H colorectal cancer; (2) one included patients with colorectal cancer that was not MSI-H; and (3) one included patients with MSI-H cancers other than colorectal cancer. Appx1819. The anticipated study enrollment was 71 patients. *Id.* The Study Record identifies Merck as a collaborator. Appx1818.

The Study Record required patients to be placed in the appropriate arm to receive treatment. It stated that the allocation of patients would be non-randomized and would require, for example, that patients with MSI-H colorectal cancer be placed only in Arm 1 of the study to receive treatment with pembrolizumab. Appx1819. As such, the Study Record required that patients agree to a biopsy of their cancer. Appx1820. The Study Record also discussed that patients would be treated with 10 mg/kg pembrolizumab every 14 days. Appx1819.

During prosecution of the application that matured into JHU’s first issued patent in this appeal (the ’356 patent), the Examiner recognized that the Study Record constituted relevant prior art and disclosed a mechanism for how pembrolizumab works in a patient whose cancer is MSI-H relative to a patient whose

cancer is not MSI-H.² Appx5207; *see* Appx5151-5183, Appx5205-5208. The Examiner also initially cited the Study Record as a basis for rejecting the '356 patent application under Section 102(a)(1) or, alternatively, under Section 103. Appx5177.

Later, however, the Examiner allowed the '356 patent over the Study Record on the rationale that the Study Record did not expressly disclose the results flowing from the disclosed treatment method steps. *See, e.g.*, Appx5207 (allowing the claims because “the [Study Record] does not establish why the person of ordinary skill in the art would have reasonably expected the claimed outcome”). In making that finding, the Examiner did not consider the principle of inherent anticipation or this Court’s controlling precedent in *Schering Corp. v. Geneva Pharmaceuticals*, 339 F.3d 1373 (Fed. Cir. 2003), and *In re Montgomery*, 677 F.3d 1375 (Fed. Cir. 2012).

IV. More Than One Year After Publication Of The Study Record, JHU Files Patent Applications Without Merck’s Knowledge

On November 13, 2014, more than 17 months after the Study Record published and without informing Merck, JHU filed a first provisional application directed to the treatment of several types of cancers that are MSI-H with immune checkpoint inhibitors. U.S. Patent App. No. 62/079,357 (“First Provisional”). Appx5469-5505. The purported written description support for the First Provisional application is the treatment method disclosed in the Study Record. For example, the

² JHU did not dispute during prosecution that the Study Record qualifies as relevant prior art.

First Provisional describes a clinical study involving three treatment arms identical to those in the Study Record. The disclosed method of treatment involves testing a cancer patient's tumor for MSI-H status to determine whether the tumor is MSI-H, and then administering, *inter alia*, a PD-1 inhibitor if the tumor is MSI-H. Appx5484-5487. The PD-1 inhibitor is pembrolizumab. Appx5496 (referring to pembrolizumab as MK-3475).

JHU filed the First Provisional without any data from the clinical study. *See* Appx5469-5505. Nearly eight months later, on July 10, 2015, JHU filed a second provisional application, U.S. Patent Application No. 62/190,977 (“Second Provisional”)—this time with data from the treatment disclosed in the Study Record more than two years earlier. *See* Appx5647-5703. JHU then proceeded to multiply its two provisional applications into the numerous overlapping and repetitive patents at issue in this appeal. During prosecution, JHU claimed priority to both provisional applications. *E.g.*, Appx600. After Merck raised challenges based on inherency, however, JHU dropped its priority claim to the First Provisional. *See* Opening Br. (AOB) 5 n.5.

JHU's patents all share the same specification and broadly claim a two-step treatment method in which a patient's cancer is tested for MSI status and, if the cancer is MSI-H, the patient is then treated with pembrolizumab. *E.g.*, Appx631, Claim 1. The claims are all directed to a method of treating *a* cancer patient (not a

group of some patients but not others). *Id.*; see Appx37608-37609, 66:22-25, 67:3-4. The patents also recite the efficacy resulting from treating a patient with the dose of pembrolizumab described in the Study Record. *E.g.*, Appx632, Claim 21. And, as relevant, some of the patents include claims that require treating a patient who has cancer that is metastatic, and who has received a prior cancer therapy and had their cancer progress. *E.g.*, Appx631, Claims 6-7.

In the proceedings below, JHU did not dispute that all nine patents presented identical issues of patentability. *See* Appx37702. JHU proposed grouping the patents based on the type of MSI-H cancer to be treated (Appx6479), as some of the patents concern the treatment of an MSI-H *colorectal* cancer patient ('287 and '393 patents), some concern the treatment of an MSI-H cancer patient not limited to a specific cancer type ('356, '974, '975, and '219 patents), and some concern the treatment of an MSI-H cancer patient having one of 16 listed *non-colorectal* cancers ('491, '187, and '462 patents). JHU did not argue, however, that such differences affected the patentability analysis.³

³ For ease of review, Merck—like JHU—cites the record from the lead case on appeal, the IPR proceeding concerning the '287 patent (IPR2024-00647). Where appropriate, Merck also cites the record from the IPR proceeding concerning the '393 patent (IPR2024-00240), including where corresponding documents do not appear in the '287 IPR record. Merck notes that the '393 record is the most comprehensive because the '393 IPR was filed first.

V. Procedural History

On November 30, 2023, two days after the '393 patent became IPR-eligible, Merck filed a petition for IPR of the '393 patent claims. Appx19219. Merck thereafter filed IPR petitions for JHU's eight other patents. Appx924; Appx37719; Appx62736; Appx88216; Appx113761; Appx138884; Appx155602; Appx172239. Merck explained that the Study Record anticipated the challenged claims by disclosing the steps of the claimed treatment method, and that the Examiner failed to apply *Schering* and *Montgomery* by allowing JHU's patents over the Study Record on the ground that the Study Record did not expressly include the results flowing from the disclosed treatment method. *See, e.g.*, Appx941; Appx5207.

JHU filed preliminary responses in five of the nine IPR proceedings. Appx24225-24229; Appx42466-42467; Appx67987-67988; Appx93262-93263; Appx119019-119020. JHU's preliminary responses focused only on claim construction and/or the *Fintiv* factors. *Id.* JHU never disputed in any of its preliminary responses that the Study Record qualified as prior art, and affirmatively described the Study Record as "[a] relevant prior art exhibit" in the '393 proceeding. Appx24236.

On June 13, 2024, the Board instituted review of the '393 patent. Appx25797. JHU sought Director Review of the institution decision, again without disputing the Study Record's status as a prior-art printed publication. *See* Appx25845-25863. The

Director denied review, Appx25879, and the Board subsequently instituted review of JHU's eight remaining patents. Appx6413; Appx43684; Appx69163; Appx94628; Appx120195; Appx144394; Appx161073; Appx177672.

Following the Board's institution decisions, in which it found a reasonable likelihood of inherent anticipation, JHU pivoted and argued for the first time in its Patent Owner's Responses that the Study Record should not qualify as a prior-art printed publication based on experimental use. *See, e.g.*, Appx26236-26243. JHU all but buried that argument in its voluminous Patent Owner's Responses, however (for example, devoting just eight of 91 pages to it in the '393 proceeding), even though experimental use is now the central focus of JHU's appeal. *See id.*

On June 9, 2025, after a lengthy oral hearing, the Board issued its final written decision for the '393 patent, finding all challenged claims unpatentable as anticipated by the Study Record and/or obvious. Appx196-247. JHU requested Director Review of the '393 final written decision, Appx37678-37696, but the Director denied review, Appx37708.

In light of the '393 final written decision, and the relatedness of the arguments for the patent family, JHU proposed canceling the oral hearings in the remaining IPR proceedings. Appx19071. Merck agreed, and the Board granted the parties' joint request. Appx19069; Appx62706. The Board then issued its eight remaining final written decisions. In each, the Board found that all the challenged patent claims

were anticipated by the Study Record and/or obvious. Appx145-195; Appx248-296; Appx297-348; Appx349-392; Appx393-432, Appx433-493; Appx494-544; Appx545-599. Ultimately, the Board determined that all 230 challenged claims were unpatentable over the Study Record.

As exemplary, Merck discusses the Board's specific findings with respect to the '287 patent.

First, the Board construed a limitation in independent claims 1 and 11 requiring a patient to be treated “in response to” a determination that their colorectal cancer is MSI-H.⁴ The Board agreed that this limitation requires a causal relationship wherein the patient's colorectal cancer is tested for MSI status and, if the cancer is MSI-H, the patient is treated with 10 mg/kg of pembrolizumab every 14 days. Appx151-153. The Board, however, rejected JHU's argument that the claim also contains a negative limitation excluding treatment of other patients whose cancer is not MSI-H, or that it requires anything other than the two recited method steps. Appx154. As the Board explained, the limitation “does not mention any other patients or define patient populations to be excluded from treatment.” *Id.* The Board also explained that “[t]he use of the open-ended transitional phrase ‘comprising’ in

⁴ JHU challenges the construction of the “in response to” limitation in only the '287 and '393 patents.

claim 1 further suggest[ed]” that additional steps taken in conjunction with the recited method steps are “not excluded from the scope of the claim.” *Id.*

Next, the Board found that the Study Record anticipates the “in response to” limitation because it discloses “testing a colorectal cancer patient for MSI status” prior to enrollment and treatment, and “in response to determining that the colorectal cancer is MSI-H, treating the patient with a therapeutically effective amount of pembrolizumab.” Appx171. In making that finding, the Board reviewed both parties’ evidence, and it credited Merck’s experts, Dr. Neugut and Dr. Paul E. Oberstein—both board-certified medical oncologists. Appx166-171.

Relying on *Schering* and *Montgomery*, the Board also found that the Study Record inherently anticipated the claimed treatment methods, even though “the inventors were unaware of the results of the study described in the [Study Record] before it was concluded.” Appx172; Appx171-174, Appx183-184 (citation omitted). And the Board found that the inherency principles in *Schering* and *Montgomery* applied to dependent claims requiring certain method results, reasoning that because the Study Record disclosed the steps of the method recited in the independent claims, the results of carrying out such steps were inherent in the Study Record. *E.g.*, Appx183-184.

The Board rejected JHU’s fallback argument that the Study Record, despite being a relevant printed publication, does not qualify as prior art because it

purportedly described an experimental use. Appx174-176. The Board explained that clinical-trial protocols published on ClinicalTrials.gov have been successfully asserted as prior art in other cases, including before this Court. Appx175-176 (citing *Salix Pharms., Ltd. v. Norwich Pharms. Inc.*, 98 F.4th 1056, 1061 (Fed. Cir. 2024)). And it found unpersuasive the argument that JHU could not have sought to patent its invention without results from the MSI-H study, particularly given that JHU filed its First Provisional without disclosing any such results. Appx174-176; Appx5469-5505.

The Board next addressed dependent claims that require treating a patient who (1) has metastatic colorectal cancer or (2) has had their cancer progress after receiving a prior cancer therapy.⁵ The Board again credited the testimony of Drs. Neugut and Oberstein explaining how those limitations would be understood by a POSA reading the express disclosure of the Study Record. Appx177-181, 181-183. For example, the Board credited Dr. Oberstein's testimony that "because the eligibility criteria stated in the [Study Record] requires patients to have 'measurable disease,'" a POSA would have "expected a patient to have undergone prior cancer therapies and would have had their cancer progress after receiving those therapies prior to enrollment." Appx178. By contrast, the Board found that JHU's evidence

⁵ Merck also asserted obviousness challenges against those dependent claims, but the Board did not reach those arguments because it found the claims anticipated.

was “not [directed] to the specific understandings of one of ordinary skill in the art when reviewing the [Study Record],” and that JHU’s declarant, Dr. Lonberg, “fail[ed] to testify that [a POSA] would not have understood the [Study Record] in 2013 to teach treating patients who had received prior/different cancer therapies.” Appx179-180.

With respect to obviousness, the Board found certain dependent claims obvious over the Study Record and other prior-art references.⁶ Appx187-193. The Board determined that JHU responded to “all of [Merck’s] obviousness challenges together,” challenging only the “reasonable expectation of success in the methods recited in [the] independent claims . . . without arguing that any of the limitations recited in the dependent claims” specifically rendered those dependent claims non-obvious. Appx189-190. The Board also considered JHU’s evidence of secondary considerations and found that JHU did not provide any evidence of a nexus to the dependent claims challenged as obvious. Appx191-192. And the Board found that, even presuming a nexus, JHU’s secondary considerations evidence related only to the independent claims that the Board had found anticipated, and therefore was not persuasive of non-obviousness. Appx192-193.

⁶ The Board also found that the claims anticipated by the Study Record were obvious over the Study Record. Appx186-187.

SUMMARY OF ARGUMENT

I. The Board correctly found that the Study Record is prior art under Section 102(a).

A. The Study Record indisputably qualifies as a printed publication. “[T]he touchstone in determining whether a reference constitutes a ‘printed publication’” is “public accessibility,” *Jazz Pharms., Inc. v. Amneal Pharms., LLC*, 895 F.3d 1347, 1355 (Fed. Cir. 2018) (citation omitted), and there is no question that the Study Record was publicly accessible.

B. As every court to address the question has agreed, the experimental-use doctrine does not negate the prior-art status of printed publications. Under the experimental-use doctrine, the use of an invention for an experimental purpose is not a “public use” or “sale” within the meaning of Section 102 and thus does not trigger the bar on patentability associated with either type of prior art. A printed publication, by contrast, is a printed publication even if it is made for experimental purposes. Scientific journals regularly contain articles describing experimental work, for example, but no one would dispute that they still qualify as printed publications. Section 102 provides that a person generally cannot patent an invention “described in a printed publication . . . before the effective filing date of the claimed invention,” 35 U.S.C. § 102(a)(1), and there is no basis in statutory text or precedent for

disregarding that limitation whenever the subject matter discussed in a printed publication relates to alleged experimentation.

The rationale for the experimental-use doctrine also has no application to printed publications. The public-use and on-sale bars are concerned with “prohibiting the inventor from commercially exploiting the invention for a period greater than the statutorily prescribed time,” *Tone Bros. v. Sysco Corp.*, 28 F.3d 1192, 1198 (Fed. Cir. 1994), whereas the printed-publication bar “operates upon the theory that the invention in controversy is in the public domain,” *In re Bayer*, 568 F.2d 1357, 1361 (C.C.P.A. 1978). “Experimental use merely negatives the commercial exploitation necessary for public use.” *Pickering v. Holman*, 459 F.2d 403, 407 (9th Cir. 1972). “Such exploitation is irrelevant to whether a printing has been made accessible to a part of the public.” *Id.* Further reinforcing the rationale that the experimental-use doctrine does not apply to the printed-publication bar, many of the factors required by precedent for applying the experimental-use doctrine make no sense in the context of printed publications.

C. JHU makes no effort to reconcile its position with the text of Section 102(b), relying exclusively on “the policies underlying the experimental use doctrine.” AOB 25. Policy arguments cannot override statutory text, however, and even if they could, JHU’s arguments here are unpersuasive. JHU asserts (at 34) that “publishing an experimental proposal is a prerequisite to acquiring data necessary”

for a patent application, but it is well established that evidence from human clinical trials is not necessarily required for patentability. Even if such data were sometimes necessary, moreover, JHU identifies no sound basis for replacing the one-year grace period provided by Congress with a categorical, open-ended exemption. And while JHU expresses concern more generally with pharmaceutical researchers' ability to obtain protection for their inventions, real-world experience does not bear out those concerns.

II. The Board correctly found that the Study Record anticipates the challenged claims.

A. The Board correctly construed the limitation that a patient be treated “in response to” a determination that their colorectal cancer is MSI-H as requiring a causal relationship between the treatment and the MSI-H determination, rather than excluding treatment of a non-MSI-H cancer patient. That construction is consistent with the claim language, which says nothing about excluding patients, and the specification, which describes the same three-arm treatment method disclosed in the Study Record, under which some non-MSI-H cancer patients were administered pembrolizumab.

JHU seeks a construction that goes beyond a causal relationship and requires that pembrolizumab be administered to “*only* patients whose cancer is determined to be MSI-H.” AOB 47. Such a negative limitation is found nowhere in the

challenged patents. And it makes no sense given that the claims are directed to treating *a* patient, not a group of patients. JHU's position also leads to the absurd result that testing and then administering pembrolizumab to an MSI-H cancer patient would infringe the claims at issue, but that infringement would cease if another patient whose cancer is not MSI-H were also later treated with pembrolizumab.

Having properly construed the “in response to” limitation, the Board correctly found that it was anticipated by the Study Record. Substantial evidence, including expert testimony credited by the Board, amply demonstrated that a POSA would have understood the Study Record to disclose testing a colorectal cancer patient to determine if the patient's cancer is MSI-H, then—if the patient's cancer is found to be MSI-H—enrolling the patient in the MSI-H colorectal cancer arm of the study and treating him with 10 mg/kg pembrolizumab every 14 days.

B. The Board correctly found that the Study Record inherently discloses the efficacy of the claimed treatment method. This Court has held that where results naturally flow from practicing the express disclosure of prior art, that prior art anticipates. *See Schering*, 339 F.3d at 1377; *Montgomery*, 677 F.3d at 1381. JHU purports to distinguish this Court's cases, but in reality it asks the Court to hold that efficacy must be expressly disclosed for a prior art disclosure to anticipate. This Court has rejected that proposition.

C. The Board correctly found that the Study Record anticipates dependent claims that require treating a patient who has metastatic colorectal cancer and that require treating a patient who has had their cancer progress after receiving a prior cancer therapy. Substantial evidence supported the Board's factual determination that a POSA would have understood the Study Record to disclose both of those limitations. JHU suggests that the Study Record cannot anticipate because it did not expressly recite treating a patient who has "metastatic cancer" or who received "prior treatment." But that is not the standard; rather, "the dispositive question is whether a skilled artisan would 'reasonably understand or infer' from a prior art reference that every claim limitation is disclosed in that single reference." *Acoustic Tech., Inc. v. Itron Networked Sols., Inc.*, 949 F.3d 1366, 1373 (Fed. Cir. 2020) (citation omitted). On that question, Merck offered substantial evidence that JHU failed to meaningfully rebut.

III. The Board correctly found that dependent claims directed to trivial method details would have been obvious. That determination was particularly well founded given that JHU argued against all of Merck's obviousness challenges together, without arguing that any of the limitations recited in the dependent claims rendered the claimed treatment method as a whole non-obvious. And the Board appropriately found JHU's secondary considerations evidence unpersuasive because

it was directed to the independent claims, which were anticipated, rather than the methods recited in the dependent claims, where obviousness was shown.

STANDARD OF REVIEW

This Court “review[s] the Board’s legal determinations de novo and its fact findings for substantial evidence.” *Provisur Techs., Inc. v. Weber, Inc.*, 50 F.4th 117, 124 (Fed. Cir. 2022). The Court “defer[s] to the Board’s findings concerning the credibility of expert witnesses.” *Incept LLC v. Palette Life Scis., Inc.*, 77 F.4th 1366, 1377 (Fed. Cir. 2023).

Whether the experimental-use doctrine negates the prior-art status of a printed publication is a legal question. *See Samsung Elecs. Co. v. Infobridge Pte. Ltd.*, 929 F.3d 1363, 1369 (Fed. Cir. 2019) (“The ultimate question of whether a reference is prior art . . . is a legal question we review de novo.”). So too is claim construction, though the Court “review[s] the Board’s factual findings underlying this inquiry for substantial evidence.” *MTD Prods. Inc. v. Iancu*, 933 F.3d 1336, 1341 (Fed. Cir. 2019). “Anticipation is a question of fact reviewed for substantial evidence.” *In re Antor Media Corp.*, 689 F.3d 1282, 1287 (Fed. Cir. 2012). Obviousness is a “question[] of law, based on underlying factual findings.” *Id.*

ARGUMENT

Having failed to rebut Merck’s evidence below that the Study Record discloses the limitations of the challenged claims, JHU focuses on appeal on its

argument that the Study Record is not prior art at all. That argument lacks merit. The Study Record is a printed publication, and—as every court to address the question has held—the experimental-use doctrine does not negate the prior-art status of a printed publication.

JHU’s other arguments also fail. As the Board correctly found, the Study Record anticipates the independent claims, and it inherently discloses the efficacy of the claimed treatment method. It also anticipates dependent claims that require treating a patient who has colorectal cancer that is metastatic and that require treating a patient who has had their cancer progress after receiving a prior treatment. Finally, the Board correctly found that the remaining dependent claims, adding certain trivial method details, were obvious.

I. The Board Correctly Found That The Study Record Is Prior Art Under Section 102(a)

In its preliminary responses, JHU did not dispute that the Study Record qualifies as prior art. Indeed, JHU acknowledged that the Study Record was a “relevant prior art exhibit.” Appx24236. It was not until the Board instituted review finding likely inherent anticipation that JHU first invoked the experimental-use doctrine to argue that the Study Record should not be considered prior art at all. *See, e.g.,* Appx26236-26243. Even then, JHU relegated the argument to a fallback position. *See, e.g.,* Appx26208-26298.

JHU now pivots and devotes more than half its argument on appeal to experimental use. *See* AOB 25-45. That pivot cannot save its case. The experimental-use doctrine does not apply to printed publications like the Study Record. The doctrine simply recognizes that the use of an invention for an experimental purpose is not a “public use” or “sale” at all. A printed publication allegedly describing an experiment, by contrast, is still a “printed publication,” and neither statutory text nor the rationale underlying the experimental-use doctrine supports disregarding its status as prior art under Section 102.

A. There Is No Dispute The Study Record Is A Printed Publication

Section 102 of the Patent Act provides that a person is not entitled to a patent if the claimed invention was “described in a printed publication . . . before the effective filing date of the claimed invention.” 35 U.S.C. § 102(a)(1). Congress has established a limited exception to that statutory bar, under which a prior printed publication (or other prior disclosure of the invention) by the inventor will not foreclose issuance of a patent if it was disclosed “1 year or less before the effective filing date.” 35 U.S.C. § 102(b)(1)(A). But if the invention was disclosed in a printed publication more than one year before the effective filing date of the claimed invention, then the invention is statutorily ineligible for patent protection regardless of who authored the publication.

That statutory bar is decisive here. Even JHU concedes that the Study Record is a printed publication. *See, e.g.*, AOB 31 (arguing that the Study Record “is protected by the experimental use doctrine despite *it being a printed publication*” (emphasis added)). It could hardly argue otherwise. As this Court has explained, “the touchstone in determining whether a reference constitutes a ‘printed publication’” is “public accessibility.” *Jazz Pharms., Inc. v. Amneal Pharms., LLC*, 895 F.3d 1347, 1355 (Fed. Cir. 2018) (citation omitted). And whether a document is publicly accessible depends on whether it “has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it.” *Id.* (citation omitted). The Study Record indisputably satisfied those criteria.

Confirming the point, judicial decisions have repeatedly treated similar publications posted to the ClinicalTrials.gov website as prior art. In *Salix Pharmaceuticals, Ltd. v. Norwich Pharmaceuticals Inc.*, 98 F.4th 1056 (Fed. Cir. 2024), for example, this Court affirmed the district court’s determination that the claimed invention would have been obvious in view of a ClinicalTrials.gov posting and a journal article. *Id.* at 1064. That decision would make little sense if the ClinicalTrials.gov posting was not prior art. Likewise, in *Janssen Pharmaceuticals, Inc. v. Tolmar, Inc.*, 718 F. Supp. 3d 394 (D. Del. 2024), Judge Bryson, sitting by designation, engaged in an extended analysis regarding whether the claimed

invention was obvious over a ClinicalTrials.gov posting. *See id.* at 424-31. Although he ultimately held that the claimed invention was not obvious, the need to engage in the analysis shows that the ClinicalTrials.gov posting was printed-publication prior art.

B. The Experimental-Use Doctrine Does Not Apply To “Negate” The Prior-Art Status Of A Printed Publication

Because it is undisputed that the Study Record is a “printed publication” within the meaning of Section 102, the question for the Court is whether the experimental-use doctrine can negate the prior-art status of that publication. The answer is no.

The Supreme Court provided the canonical articulation of the experimental-use doctrine in *City of Elizabeth v. American Nicholson Pavement Co.*, 97 U.S. 126 (1877). The plaintiff there had invented “a new and improved wooden pavement,” which he tested publicly for six years before applying for a patent. *Id.* at 127, 129. He subsequently sued the defendants for infringement, and the defendants argued in relevant part that the patent was invalid because the plaintiff’s experimental use was prior art. *See id.* at 133. The Court framed the question before it as whether the pavement “was in public use or on sale” within the meaning of the patent statute. *Id.* And the Court held that it was not. Rather, the Court explained, “[t]he use of an invention by the inventor himself, or of any other person under his direction, by way of experiment, and in order to bring the invention to perfection, has never been

regarded as such a use.” *Id.* at 134; *see id.* at 135 (“So long as he does not voluntarily allow others to make it and use it, and so long as it is not on sale for general use, he keeps the invention under his own control, and does not lose his title to a patent.”).

Since *City of Elizabeth*, the Supreme Court and this Court have repeatedly affirmed that an experimental use is not a “public use” or “sale.” *See Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 64 (1998) (“The law has long recognized the distinction between inventions put to experimental use and products sold commercially.”); *TP Labs., Inc. v. Pro. Positioners, Inc.*, 724 F.2d 965, 971 (Fed. Cir. 1984) (“[I]f a use is experimental, even though not secret, ‘public use’ is negated.”). No court has ever held, however, that experimental use negates the prior-art status of a printed publication. JHU asks this Court to become the first, but the Court should reject that invitation for several reasons.

To start (and, really, to finish), the text of Section 102 forecloses JHU’s position. As discussed, while an experimental use is not a “public use” or “sale” within the meaning of the statute, there is no dispute here that the Study Record is a “printed publication.” *See* Section I.A, *supra*. And Section 102 provides that a person is not entitled to patent an invention “described in a printed publication . . . before the effective filing date of the claimed invention.” 35 U.S.C. § 102(a)(1). While Congress expressly excepted printed publications by the inventor that were published “1 year or less before the effective filing date,” 35 U.S.C. § 102(b)(1)(A),

JHU does not qualify for that statutory exception because it did not file within one year of the publication of the Study Record. JHU therefore asks this Court to carve out an additional exception (of apparently unlimited duration) for publications that allegedly relate to experimentation. “When Congress provides exceptions in a statute,” however, “it does not follow that courts have authority to create others.” *United States v. Johnson*, 529 U.S. 53, 58 (2000). Rather, “[t]he proper inference . . . is that Congress considered the issue of exceptions and, in the end, limited the statute to the ones set forth.” *Id.*

In any event, even if Congress *had* given courts authority to establish additional exceptions to Section 102(a), the experimental-use doctrine’s rationale for negating certain uses and sales does not apply to printed publications. As this Court (and Congress) has recognized, printed-publication prior art is materially different from public uses or sales. *See Lynk Labs, Inc. v. Samsung Elecs. Co.*, 125 F.4th 1120, 1131-32 (Fed. Cir. 2025). The public use and on-sale bars are concerned with “prohibiting the inventor from commercially exploiting the invention for a period greater than the statutorily prescribed time.” *Tone Bros. v. Sysco Corp.*, 28 F.3d 1192, 1198 (Fed. Cir. 1994). The experimental-use doctrine responds to that concern by recognizing that commercial exploitation is not implicated where a use or sale is made for experimental purposes. *See Allen Eng’g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1354 (Fed. Cir. 2002). It is a negation of the “public use” or “sale” itself.

The printed-publication bar, by contrast, “operates upon the theory that the invention in controversy is in the public domain, and once there, is no longer patentable by anyone.” *In re Bayer*, 568 F.2d 1357, 1361 (C.C.P.A. 1978).⁷ The experimental-use doctrine is unresponsive to that concern, because a publication made for allegedly experimental purposes is as much a part of the public domain as a publication made for commercial purposes. As the Ninth Circuit explained over 50 years ago in a decision squarely holding that the experimental-use doctrine does not apply to printed publications, “[a]ny publication, regardless of the purposes behind it, violates the policies behind the publication bar,” and “[p]ublication pursuant to experiment is no exception.” *Pickering v. Holman*, 459 F.2d 403, 407 (9th Cir. 1972); *see id.* (“Experimental use merely negatives the commercial exploitation necessary for public use. Such exploitation is irrelevant to whether a printing has been made accessible to a part of the public.”).⁸

Given that mismatch in rationales, it should come as no surprise that the test for determining whether a use is experimental cannot sensibly be applied to printed

⁷ This Court adopted the precedent of the Court of Customs and Patent Appeals as its own in *South Corp. v. United States*, 690 F.2d 1368 (Fed. Cir. 1982) (en banc).

⁸ Given the distinct purposes behind the public use and on-sale bars, on the one hand, and the printed-publication bar, on the other, it is not illogical, as JHU asserts, that a legally required pre-study posting can preclude attempts to patent the disclosure of the publication more than a year later, even if the underlying alleged experimental work would not be a public use. AOB 33. The disclosure of a publication enters the public domain permanently and irretrievably. An experimental use does not.

publications. In *Allen Engineering Corp. v. Bartell Industries, Inc.*, this Court identified 13 factors that bear on whether a use qualifies as experimental rather than public. Many of those factors are wholly inapposite in the context of printed publications. *Allen* asks courts to consider, for example, “the amount of control . . . retained by the inventor,” or “whether there was a secrecy obligation.” 299 F.3d at 1353 (citation omitted). But a printed publication, by its nature, is neither secret nor within the inventor’s control. So, while JHU criticizes the Board for “ignoring the 13-factor experimental use analysis,” AOB 37 (emphasis and capitalization omitted), the reality is that the test for assessing experimental uses—established in the context of public uses and sales—simply has no relevance in the distinct context of printed publications. *See, e.g., Appx175-176.*⁹

Adopting JHU’s rule would also fly in the face of decades of precedent. To Merck’s knowledge, every court to address the question has held that the experimental-use doctrine does not apply to printed-publication prior art. As noted above, the Ninth Circuit squarely rejected JHU’s position more than 50 years ago in

⁹ Applying a 13-factor experimental-use test whenever a publication arguably describes experimentation would also be highly destabilizing. Myriad publications routinely relied on in patent validity determinations, from journal articles to conference presentations, describe alleged experimental work of researchers. *See, e.g., Telefonaktiebolaget LM Ericsson v. TCL Corp.*, 941 F.3d 1341, 1344, 1347 (Fed. Cir. 2019); *In re Klopfenstein*, 380 F.3d 1345, 1347, 1352 (Fed. Cir. 2004). If the prior-art status of publications could be attacked based on after-the-fact assertions of experimental purpose, the public would have no predictability as to what is or is not printed-publication prior art.

Pickering v. Holman. And *Pickering* is just one in a long line of cases reaching the same conclusion. In *Thacher v. Inhabitants of Town of Falmouth*, 235 F. 151 (D. Me. 1916), the court explained with respect to experimental use that “[w]hat the courts have said upon this subject bears upon the question of public use, and does not apply to a case where the court is seeking to find whether an alleged improvement has been discovered in a printed publication.” *Id.* at 158; *see Binckley v. United States*, 83 Ct. Cl. 444, 473 (1936) (quoting this language from *Thacher*). In *Regents of University of California v. Howmedica, Inc.*, 530 F. Supp. 846 (D.N.J. 1981), the court similarly stated that “[t]he publication bar is based upon the theory that an idea once published is in the public domain,” and that, “[f]or this reason, and for the protection of the reasonable expectations of the public, the ‘experimental use’ doctrine does not apply to overcome the printed publication bar.” *Id.* at 859. And in *Bausch Health Ireland Ltd. v. Padagis Israel Pharmaceuticals Ltd.*, No. 20-cv-5426, 2022 WL 17352334 (D.N.J. Dec. 1, 2022), the court declined to apply the experimental-use doctrine to a ClinicalTrials.gov posting, finding “no authority for the proposition that the experimental use exception can apply to a printed publication.” *Id.* at *31.

Decisions from this Court and the Court of Customs and Patent Appeals are of a piece. As discussed, this Court’s decision in *Salix* treated a ClinicalTrials.gov posting as printed-publication prior art. *See* p. 26, *supra*. JHU observes that “the

parties in *Salix* did not argue whether the posting at issue there was subject to the experimental use doctrine.” *See* AOB 35 (emphasis omitted). But it fails to mention that an amicus argued at length that “[g]overnment-mandated disclosure of an ongoing clinical trial falls within the experimental use exception.” Corrected Brief of Vanda Pharmaceuticals Inc. as Amicus Curiae at 14, *Salix*, 98 F.4th 1056; *see generally id.* at 14-25. The question of experimental use therefore did not “lurk in the record”; it was unambiguously “brought to the attention of the court.” AOB 35 (citation omitted). Likewise, in *In re Hassler*, 347 F.2d 911 (CCPA 1965), the court held that a newspaper article reporting on the progress of an experiment was prior art that rendered obvious the invention resulting from the experiment. *Id.* at 912-13. JHU has no meaningful response.

C. JHU’s Contrary Policy Arguments Are Unpersuasive

JHU implicitly concedes that its proposed exception to the printed-publication bar has been rejected by every court to consider it. *See* AOB 34 (arguing that while “[o]ther courts have addressed this issue,” those decisions are all “either inapposite or erroneous”). And JHU makes no effort to reconcile its proposed exception with the text of Section 102. Instead, JHU tries to invoke (at 25) “the policies underlying the experimental use doctrine.” In particular, JHU argues (at 33-34) that failing to apply the experimental-use doctrine to ClinicalTrials.gov postings would be “inconsistent with the objectives embodied by 35 U.S.C. § 112,” because

“publishing an experimental proposal is a prerequisite to acquiring data necessary to support an adequate disclosure.” That policy argument cannot justify disregarding the plain text of Section 102, however, and it is unpersuasive on its own terms for multiple reasons.

First, nothing in Section 112 *per se* requires that evidence from human clinical trials be provided for patentability. *See* Appx31773; *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009) (“human trials are not required for a therapeutic invention to be patentable”). Pharmaceutical inventors typically file patent applications promptly based on in vitro and/or in vivo data correlated to an expectation of human utility. *See* MPEP 2107.03. Here, for example, where the prior art taught the correlation of MSI-H and PD-1 inhibitor use, JHU filed its first provisional application without clinical data at all (though still after the one-year grace period). *See* p. 10, *supra*. There is thus no reason to conclude that this particular study was necessary to support JHU’s patent applications, let alone that JHU could not have collected any necessary data within the one-year period from publication provided by Congress in Section 102(b)(1). *See* AOB 8-9 (reciting testimony that “patients felt better almost immediately after beginning therapy” and that “patients’ tumors [were] shrinking rapidly”).

Second, even if human clinical trials *were* necessary to support a particular patent application, that would provide no sound basis for refusing to consider

ClinicalTrials.gov postings (or similar clinical-protocol publications) as prior art. In arguing otherwise, JHU seems to assume that “stripping the whole category of clinical trial postings from the protections provided by the experimental [use] doctrine” would lead to the anticipation of any invention that results from such trials. AOB 33. But that assumption is incorrect. For one thing, a clinical-trial posting need not necessarily include all the limitations in a later-filed patent application. JHU, for example, was under no obligation to include dosage information. *See* 42 C.F.R. § 11.10(b)(12) (providing that the intervention description “*may* include dosage form, dosage, frequency, and duration” (emphasis added)). Moreover, it is possible for a patentee to argue that a clinical-trial posting is not enabling of a particular treatment method, a requirement already existing in the law for anticipation. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1374 (Fed. Cir. 2001). Here, however, JHU did not argue that the Study Record was non-enabling because it plainly was, as it disclosed the steps for treating a patient whose cancer is MSI-H with a specific dose of pembrolizumab.

Third, real-world experience belies JHU’s alleged concern that pharmaceutical researchers (to whom Merck is understandably sympathetic) will be unable to obtain protection for their inventions unless this Court creates a new exception to the printed-publication bar. *See, e.g.*, AOB 38-39. As discussed above, every court to address the question has held that the experimental-use doctrine does

not apply to printed publications. Yet in the more than 25 years since Congress established ClinicalTrials.gov, there has been no pattern of decreased innovation in pharmaceutical research because of regulatorily compelled disclosure. Indeed, the fact that JHU can describe the question of whether publications containing clinical protocols should be “negated as prior art” as “an issue of first impression” for this Court, AOB 25, just confirms that Section 102 and ClinicalTrials.gov can coexist without the need for judge-made exceptions to the printed-publication bar.

At bottom, JHU asks this Court (at 22) to “balance[] the need to experiment publicly against the policy favoring prompt patenting.” But Congress already struck that balance by giving inventors one year to file a patent application after disclosing their invention in a printed publication.¹⁰ *See* 35 U.S.C. § 102(b)(1)(A). Congress did not carve out additional exceptions for ClinicalTrials.gov postings specifically or publications that relate to experimentation more generally. This Court should accordingly affirm the Board’s consideration of the Study Record as a relevant prior-art printed publication.

¹⁰ Merck is unaware of any country in the world that has a grace period longer than one year for printed-publication prior art, let alone the effectively unlimited grace period that JHU proposes. Indeed, many countries, including in Europe, do not provide a grace period at all.

II. The Board Correctly Found That The Study Record Anticipates The Challenged Claims

This Court should likewise affirm the Board’s findings that the Study Record anticipates all of the independent claims and most of the dependent claims. Substantial evidence supports those findings, and JHU identifies no sound reason to set them aside.

A. The Board Correctly Found That The Study Record Discloses The Two-Step Treatment Method Recited By The Independent Claims Of The ’287 And ’393 Patents

The Board correctly construed the “in response to” limitation recited by the independent claims of the ’287 and ’393 patents, then properly applied that construction to find that the Study Record anticipates them. On appeal, JHU argues that “‘in response to’ requires that *only* patients whose cancer is determined to be MSI-H are treated with the claimed method.” AOB 47. But the “in response to” limitation imposes no such constraint on the treatment of other patients, and JHU’s objections fall apart without one.

1. The Board Correctly Construed “In Response To”

The Board correctly “beg[a]n claim construction by looking to the language of the claim itself.” *Immunex Corp. v. Sanofi-Aventis U.S. LLC*, 977 F.3d 1212, 1218 (Fed. Cir. 2020). In doing so, it “agree[d] with [JHU] that the phrase ‘in response to’ . . . requires a causal relationship wherein the patient must be tested for MSI-H and, if he or she is determined to be MSI-H . . . , then the patient is treated

with 10 mg/kg of pembrolizumab every 14 days.” Appx153. The Board was “not persuaded that [the independent claims] require[] or exclude[] anything else” beyond the articulated causal relationship, however, “because nothing else is recited in the claim[s].” *Id.* In particular, the Board emphasized that the claims “d[o] not mention any other patients or define patient populations to be excluded from treatment.” Appx154.

The Board also observed that the claims’ “use of the open-ended transitional phrase ‘comprising’ . . . further suggests . . . that any additional steps taken in conjunction with expressly recited method steps, such as the treatment of patients who are not MSI-H . . . , are not excluded from the scope of the claim[s].” *Id.* That is because “comprising” “is generally interpreted to not exclude additional, unrecited elements.” *Id.* (quoting *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368 (Fed. Cir. 2003)). Accordingly, the Board refused to limit the claims to “administering the claimed treatment *only* as a reaction to the determination that the patient’s cancer is MSI-H,” because nothing in those claims “exclude[s]” additional “treatment of *other* patients who are not MSI-H.” *Id.*

The Board’s reasoning is consistent with the sole treatment embodiment in the specification, which describes a clinical study (the same study disclosed in the Study Record) as providing for treatment of patients in three arms: (1) “patients with [MSI-H] colorectal” cancer; (2) “patients with [non-MSI-H] colorectal” cancer; and

(3) “patients with [MSI-H] cancers of types other than colorectal.” Appx623 (’287 patent), 8:29-36. The specification explains that “[a]ll patients underwent [MSI-H] status testing prior to enrollment.” Appx624 (’287 patent), 9:48-49. And it further provides that the study “consisted of the three parallel cohorts described above,” and that “[t]he study agent, pembrolizumab (Merck), was administered at 10 mg/kg intravenously every 14 days.” Appx623 (’287 patent), 8:50-53; *accord* Appx626, 13:31-14:2. In other words, the written description support for the claims is the very study underlying the Study Record, in which pembrolizumab was administered to both MSI-H and non-MSI-H cancer patients in separate arms of the study.

The Board’s construction is therefore in accord with the intrinsic record, and JHU offers no persuasive grounds to disturb it. JHU argues (at 46-47) that the Board’s construction reads out the required “causal relationship” between MSI-H identification and treatment. But the Board agreed (as did both parties) that the “in response to” limitation implies “a causal relationship.” Appx153. Indeed, JHU’s own declarant acknowledged that the Board, in its institution decision, did not disregard the causal relationship required by the “in response to” limitation. Appx14506, 125:5-14.

What JHU actually seeks is a construction that goes beyond a causal relationship and requires that pembrolizumab universally be administered “*only* [to] patients whose cancer is determined to be MSI-H.” AOB 47. The challenged patents

contain no such negative limitation, however, and inserting one would be inconsistent with the claims' focus on treating *a* patient—rather than a group of patients—and the clinical study in the specification. *See* Appx154; Appx631, 24:42-52 ('287 patent, claim 1); Appx37608-37609, 66:22-25, 67:3-4 (JHU's counsel conceding that the claim is not directed to treatment on a clinical level, but rather is “directed to treating a patient”). Even JHU acknowledges (at 47) that “[t]he claims say nothing about giving treatment in response to determining that the CRC is *not MSI-H*.” That silence dooms JHU's attempt to import a negative limitation into the claims. *See Steuben Foods, Inc. v. Shibuya Hoppmann Corp.*, 127 F.4th 348, 359 (Fed. Cir. 2025) (declining to import negative limitation where “[t]he patent is silent as to whether” that limitation was present).

JHU is also incorrect to assert (at 48) that “[n]owhere does the specification teach treating patients whose cancer is *not* MSI-H.” As noted, the specification describes the clinical study underlying the Study Record—the only clinical study it discusses—as administering pembrolizumab not only to patients with MSI-H cancer, but also to patients whose cancer was not MSI-H. This Court “do[es] not construe claims in a manner that would exclude the preferred embodiment, especially where it is the only disclosed embodiment.” *GE Lighting Sols., LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1311 (Fed. Cir. 2014).

For similar reasons, JHU’s attack (at 51-53) on the Board’s reasoning with respect to the word “comprising,” Appx154, misses the mark. JHU argues that the Board used that term “to abrogate” the “in response to” limitation, which it contends is not “consistent with” the “intrinsic record” and “remove[s] the limitations that are present” in the claims. AOB at 51-53 (capitalization omitted) (quoting *Power Mosfet Techs., LLC. v. Siemens AG*, 378 F.3d 1396, 1409 (Fed. Cir. 2004)). As explained above, though, the specification expressly describes administering pembrolizumab to patients whose cancer is MSI-H *and* to patients whose cancer is not MSI-H, and the claims require treatment of a patient with MSI-H cancer, not the exclusion of every patient whose cancer is not MSI-H. *See* Appx623-626 (’287 patent), 8:29-36, 8:50-53, 9:48-49, 13:31-14:2. The Board’s construction accordingly does not “remove [any] limitations that are present.” *Power Mosfet Techs.*, 378 F.3d at 1409.

JHU’s recourse to a passing statement in the “Summary of the Invention” section of the specification, which refers to non-MSI-H tumors as “bad candidate[s]” for treatment, likewise fails. AOB 48. Such a “fleeting referenc[e] cannot overcome the overwhelming evidence in the specification” that the claims do not require excluding treatment of other people without MSI-H cancers, “especially given the specification did not ‘even refer with any detailed particularity’” to the supposed bad-candidate embodiment. *Trs. of Columbia Univ. in City of New York v. Symantec*

Corp., 811 F.3d 1359, 1368 (Fed. Cir. 2016) (citation omitted). If the bad-candidate embodiment were fully described, moreover, JHU’s argument would still be wrong, because “[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using ‘words or expressions of manifest exclusion or restriction.’” *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (citation omitted). JHU has demonstrated no such intention here, let alone a “clear intention.”

JHU’s reliance on the prosecution history is similarly misplaced. As the Board explained, during prosecution of the ’393 patent, JHU overcame a prior-art reference because that reference did not disclose treating the patient “based on a determination of [MSI-H] . . . as claimed.” Appx155 (quoting Appx19765). In that prior art, the patient was determined to be MSI-H *after* the patient had already been treated for cancer—it was purely retrospective. Appx4624, ¶20. Thus, the Examiner concluded that the prior-art reference did not disclose a causal relationship as the claims require. In the Study Record, by contrast, patients in two arms of the study were admitted and treated with pembrolizumab only if testing first confirmed that their cancer was MSI-H. Appx169-171; Appx1819; Appx1676-1677, ¶68; Appx15520-15521, ¶¶65-67.

The cases on which JHU relies (at 47-49, 52) also do not suggest that the Court should import a negative limitation here. In *Rodime PLC v. Seagate Technology, Inc.*, 174 F.3d 1294 (Fed. Cir. 1999), the Court simply declined to import affirmative limitations that were recited in some claims into other claims that omitted them. *See id.* at 1304-05. The Court explained that had the patentee “intended or desired to claim” the additional limitations, “it could have done it explicitly, as [it had done] in [the first claims].” *Id.* at 1305. Because the patentee did not, the Court held that “[t]he absence of any such explicit language” showed that the claims at issue did not include the additional limitations. *Id.* It does not follow that where a patentee seeks to import a negative limitation, the Court must do so absent “explicit language” to the contrary; indeed, this Court’s cases hold the opposite. *See pp. 39-40, supra.*

Nor does *American Calcar, Inc. v. American Honda Motor Company*, 651 F.3d 1318 (Fed. Cir. 2011), help JHU. In that case, the Court held that an “in response to” limitation was properly construed “to require a cause-and-effect relationship.” *Id.* at 1339-40. But, again, there is no dispute here that “the claim term ‘in response to’ requires a causal relationship between a first action and a second action.” Appx157. And nothing in *American Calcar* concerns “excluding one condition over another,” *id.*, so it has no application to the claim language here.

Finally, *Trading Technologies International, Inc. v. eSpeed, Inc.*, 595 F.3d 1340 (Fed. Cir. 2010), is inapposite. There, the Court held that “comprising” could

not be used to import limitations expressly excluded by “inventors [that] acted as their own lexicographers.” *Id.* at 1353-54. Here, the inventors did not act as their own lexicographers for “in response to” and, as explained above, the term “comprising” does not import any limitations, but rather suggests—consistent with the claim language, the specification, and the prosecution history—that the challenged claims do not require anything beyond a specified treatment of an MSI-H cancer patient.

2. The Study Record Anticipates The Independent Claims

Substantial evidence—including testimony from Merck’s experts—supports the Board’s findings that the Study Record discloses the treatment of a patient with colorectal cancer where (1) the patient’s cancer is tested to determine whether it is MSI-H, and (2) if the patient’s cancer is MSI-H, the patient is treated with a therapeutically effective dose of pembrolizumab (i.e., 10 mg/kg every 14 days). Appx170.

With respect to the first step, the disclosures in the Study Record tell a POSA to test the patient’s cancer to determine whether it is MSI-H. Indeed, the title of the study is “Phase 2 Study of MK-3475 [pembrolizumab] in Patients *With Microsatellite Unstable (MSI) Tumors*.” Appx1816 (emphasis added). Moreover, one treatment arm consisted entirely of colorectal cancer patients whose tumors were tested and determined to be MSI-H. Appx1819. And the eligibility criteria reflected

in the Study Record required that patients agree to a biopsy of their tumor, Appx1820, which Merck's expert explained is the medical procedure for determining whether the patient's cancer is MSI-H, Appx1676-1677, ¶68; *see also* Appx961-962; Appx15521-15522. As such, the Board correctly found that the Study Record discloses testing a colorectal cancer patient to determine if the patient's cancer is MSI-H. Appx169. JHU does not dispute that finding. *See* AOB 53.

With respect to the second step, the Study Record describes a treatment arm specifically composed of MSI-H colorectal cancer patients. Appx1819. The Study Record discloses that a patient determined to have MSI-H colorectal cancer will be placed into the MSI-H colorectal cancer arm of the study and treated with 10 mg/kg pembrolizumab every 14 days. *See* Appx162 (quoting Appx1819). The Board credited Dr. Neugut's explanation that "in order to place the patients into the proper arm" in accordance with the eligibility criteria, "the [Study Record] required a biological sample from the patient that had *previously been tested* to determine whether the colorectal cancer is [MSI-H]." Appx167 (emphasis added) (quoting Appx962; Appx1676-1677, ¶68). The Board also credited Dr. Oberstein's testimony that, "[g]iven the low incidence of MSI-H in the colorectal cancer population that would be treated in the MSI-H Study, a POSA would understand that the MSI-H Study Record requires that a patient is tested to determine whether the patient is

MSI-H before being enrolled and treated in the study.” Appx168 (quoting Appx15520-15521, ¶67). “Otherwise, with an anticipated enrollment of 71 total patients, the POSA would understand that there would not be enough MSI-H colorectal cancer patients treated in the study.” *Id.* (quoting Appx15521). As the Board recognized, a POSA would thus understand the Study Record to disclose that colorectal cancer patients would be enrolled in the study and treated with pembrolizumab because of a determination that their cancer was MSI-H. *See* Appx169-170.

JHU argues (at 53) that the Study Record “describes treating patients *not* as a result of the patient having MSI-H cancer, but instead simply as a result of the patient being enrolled in the study.” That argument implicitly treats enrollment and having MSI-H cancer as independent variables. As Dr. Oberstein’s testimony (credited by the Board) made plain, however, a POSA would not have understood them as independent. Appx15519-15521, ¶¶64-67. Rather, based on the disclosure in the Study Record, a POSA would have understood that a patient with MSI-H colorectal cancer is enrolled in the study as a result of their cancer’s MSI-H status, and thus would have understood that their subsequent treatment with pembrolizumab as a study participant also was a result of their cancer’s MSI-H status. JHU’s effort to pull apart that tightly connected causal chain fails, and provides no basis for setting

aside the Board’s factual findings that the Study Record anticipates the “in response to” limitation.

B. The Board Correctly Found That The Study Record Inherently Discloses The Claimed Efficacy Results

The Board also correctly rejected JHU’s argument that the Study Record cannot anticipate because it does not disclose the results of the claimed treatment method. *See* AOB 54-58. As the Board recognized, the Study Record discloses those results inherently because they naturally follow from the steps of the specific treatment method disclosed in the Study Record. Appx172-173.

This Court has explained that “[a] reference may anticipate inherently if a claim limitation that is not expressly disclosed ‘is necessarily present, or inherent, in the single anticipating reference.’” *In re Montgomery*, 677 F.3d 1375, 1379-80 (Fed. Cir. 2012) (citation omitted). Addressing the specific context of pharmaceutical treatment methods, the Court held in *Montgomery* that if “efficacy is inherent in carrying out the claim steps,” the prior art anticipates a claim to the treatment method even if the prior art does not expressly describe the efficacy results of the disclosed steps. *Id.* at 1381. *Montgomery* followed from this Court’s decision in *Schering* and rejected the argument that a prior-art disclosure cannot anticipate unless there is express recognition at the time of disclosure of the results of following the prior art. *Montgomery*, 677 F.3d at 1382-83.

Applying that law here, the Board found as a matter of fact that the result of treating an MSI-H cancer patient with pembrolizumab “inherently follows its administration” as described in the Study Record. Appx 173; *see* Appx184 (finding that “the results of such [claimed] steps would be inherent even if they had not yet been reported”). And because the Study Record discloses the same treatment steps described in the patents’ specification, that is not surprising. Here, “there is no question . . . that treating” MSI-H cancer patients with pembrolizumab in the manner described in the Study Record “does in fact inevitably treat” that cancer as claimed in the challenged patents. *Montgomery*, 677 F.3d at 1382.

JHU argues (at 55-56) that because “the inventors could not have known the results of the study before it was performed,” the Study Record was simply an “invitation to investigate” and therefore cannot anticipate. But this Court rejected that same argument in *Montgomery*. *See* 677 F.3d at 1379. There, too, the results of the study were not known at the time of the prior-art publication, but the publication nonetheless inherently anticipated. *See id.* at 1378. The Court explained that for inherent anticipation, “it matters not that those of ordinary skill heretofore may not have recognized the inherent characteristics of the prior art.” *Id.* at 1381 (alterations omitted); *accord Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (“[I]nherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure.”).

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Rather, the dispositive point is that the results are “inherent in carrying out” the steps disclosed by the prior art. *Montgomery*, 677 F.3d at 1381. And JHU cannot “dispute that [pembrolizumab] is in fact effective at . . . treating [MSI-H colorectal cancer], which is the entire premise of [its] patent.” *Id.* Indeed, here, pembrolizumab was already known to treat various cancers, and JHU itself cited a raft of prior art to the FDA to show that pembrolizumab was likely to be effective in treating MSI-H cancers. *See* Appx15506, ¶38; Appx12744; Appx12722; Appx12738.¹¹

JHU argues (at 56) that the Study Record “is very different from the anticipating [study] in *Montgomery*” and is instead “similar to the non-anticipatory example” that the Court offered of a hypothetical “document that recited administration of all known compounds for treatment of all known diseases, with no evidence that any of these treatments would be effective.” 677 F.3d at 1382 n.13. The Study Record, however, “does not merely suggest that pembrolizumab may be useful in some unidentified subset of colorectal cancer patients or suggest that some unidentified drug may be useful for MSI-H colorectal cancer patients.” Appx173. Rather, it specifically discloses testing a cancer patient for MSI-H and, if that patient’s cancer is determined to be MSI-H, treating that patient with pembrolizumab

¹¹ JHU’s assertion that the Study Record’s “efficacy or survival outcomes” were not “expected,” AOB 57, is further belied by its representations to the FDA that the study’s **IND Statement** was a **IND Statement** for patients with MSI-H cancer, Appx12744.

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at a specified dose. *Id.* In short, the Study Record is not “so vague it does not teach the steps expressly recited in” the challenged claims. Appx172.

JHU’s other attempts to distinguish *Montgomery* also fail. JHU argues (at 56) that when the Study Record “became public, the study had not started.” That is immaterial, though, because inherent anticipation does not require “the claimed method [to] have been actually performed”; rather, “even if [the prior art study] merely proposed the administration of [the drug] for treatment . . . (without actually doing so), it would still anticipate.” 677 F.3d at 1382. Likewise, JHU’s reliance (at 56-57) on the differences in the phases of *Montgomery*’s study and the Study Record (Phases III and II, respectively) is misplaced, because those differences do not negate the substantial evidence that the Study Record discloses a treatment that naturally produces the claimed efficacy. That is particularly so where pembrolizumab was known prior to the publication of the Study Record and was already in use for the treatment of cancer, and the Study Record clearly identified the patients being treated and the dosing of the drug. *See* Appx1818-1819. Moreover, JHU’s assertion that the underlying study was “designed to determine efficacy—not confirm it,” AOB 57, is belied by its own statement to the FDA that the design of the study [REDACTED]

IND Statement

for pembrolizumab treatment,

Appx12721 (emphasis added).

C. The Board Correctly Found That The Study Record Discloses The Metastatic And Prior-Treatment Limitations

The Board also analyzed dependent claims that require treating a patient who (1) has colorectal cancer that is metastatic and (2) has received a prior cancer therapy and had their cancer progress. Based on substantial evidence, including the testimony of Merck’s experts, the Board found that the Study Record also anticipates those dependent claims. JHU identifies no basis for setting aside its factual findings.

1. Dependent Claims Including The Metastatic Limitation

With respect to the claims requiring that the patient have metastatic cancer, JHU’s only arguments below, which it repeats on appeal (at 59), were premised on a contorted reading of Dr. Neugut’s testimony as saying that the Study Record’s disclosure of treating patients with “measurable disease” and “tumors” is “synonymous with ‘metastatic.’” That was not Dr. Neugut’s testimony, and is not reflective of Merck’s arguments. To the contrary, Dr. Neugut (and Dr. Oberstein) testified that a POSA would understand the Study Record’s disclosures—in the context of a disclosed phase 2 clinical study involving the treatment of colorectal cancer patients with an immunotherapy drug—to refer to a patient having metastatic cancer. *E.g.*, Appx1678-1679, ¶¶76-80; Appx15522-15524, ¶¶70-74. That reflects the fact, understood by a POSA, that patients with “colon cancer appropriate for resection (non-metastatic)” were recommended to undergo surgery to remove their cancer, whereas patients with metastatic colorectal cancer were recommended to be

treated in a clinical trial (after undergoing at least two prior treatments and having their cancer progress). Appx1679, ¶77; Appx15523-15524, ¶72; *see* Appx2003; Appx2021.

Consistent with the disclosures of the Study Record and the standard of care at the time, all 41 patients treated in the study described by the Study Record did have metastatic colorectal cancer. Appx623, 8:29-31; Appx5506-5507. JHU's declarant, Dr. Lonberg, conceded that metastatic colorectal cancer patients are included in the Study Record's treatment method, clarifying his position to be that the "[Study Record] is not limited or does not require treatment of *only* patients who have metastatic disease." Appx17448, 58:3-10 (emphasis added). As with the "in response to" limitation, however, none of JHU's patent claims requires treating *only* a patient who has metastatic disease.

Moreover, the Board found that entirely apart from Dr. Neugut's testimony, the Study Record's disclosure of the metastatic limitation was evident from two academic papers published in 2015 that also "referr[ed] to the Study Record" in a way that "indicates that physicians understood the [Study Record] to be for patients with metastatic tumors." Appx182 (citation omitted). One paper, published before the alleged priority date, referred to the Study Record and stated that "pembrolizumab is being tested in *metastatic* tumors with [MSI-H], including colorectal cancer." *Id.* (emphasis added) (quoting Appx5766). The second paper

also referred to the Study Record as “investigating immunotherapy in MSI-H . . . *metastatic* colorectal cancer.” *Id.* (emphasis added) (quoting Appx5772, Appx5774).

JHU argues (at 59-60) that those papers “show, at most, a later-revealed understanding or characterization” of the Study Record. But the Board reasonably found, based on the evidence before it, that the papers corroborated the understanding of a POSA, *as of the priority date*, that the Study Record “disclose[d] treating patients with metastatic colorectal cancer.” Appx182. JHU identifies no error in the Board’s reasoning, and never even addresses the fact that one of the publications predated the alleged priority date. In any event, JHU forfeited its “later-revealed understanding” argument by failing to raise it before the Board. *See Implicit, LLC v. Sonos, Inc.*, 169 F.4th 1107, 1111 (Fed. Cir. 2026) (“A party forfeits an argument that it failed to present to the Board”).¹²

JHU also challenges the Board’s reliance on the two publications on the ground that they constitute “later-in-time . . . extrinsic commentary.” AOB 59. JHU never raised that argument before the Board, either. And even if the argument were preserved, JHU “confuses prior art with extrinsic evidence used to support what is

¹² JHU did not address the two publications at all in the ’393 patent proceeding. In the ’287 patent proceeding, it argued that the publications “d[o] not imply any equivalence between metastatic cancer and the term ‘measurable disease,’” Appx6539, but it did not dispute that the studies provided evidence of how POSAs would have understood the Study Record as of the alleged priority date.

‘necessarily present’ in a prior art’s teaching.” *Monsanto Tech. LLC v. E.I. DuPont de Nemours & Co.*, 878 F.3d 1336, 1345 (Fed. Cir. 2018). As this Court has explained, such “[e]xtrinsic evidence may be used to interpret the allegedly anticipating reference and to shed light on what it would have meant to a POSA.” *Id.* (internal quotation marks, alteration, and citations omitted). JHU acknowledges that the two publications “refer to the [Study Record] by its ClinicalTrials.gov identifier.” AOB 59. And the Board found that the publications demonstrate that a POSA would have understood the Study Record to disclose treating a patient who has metastatic colorectal cancer. This Court “may not reweigh this evidence on appeal.” *In re Warsaw Orthopedic, Inc.*, 832 F.3d 1327, 1333 (Fed. Cir. 2016).

2. Dependent Claims Including The Prior-Treatment Limitation

With respect to the limitation requiring that a patient have received a prior cancer treatment, the Board considered both parties’ evidence and found Merck’s “more persuasive of what [a POSA] would have understood from the” Study Record. Appx180. On appeal, JHU argues (at 61-62) that “nothing in the [Study Record] itself indicates” that the prior-treatment limitation is disclosed. “In an anticipation analysis,” though, “the dispositive question is whether a skilled artisan would ‘reasonably understand or infer’ from a prior art reference that every claim limitation is disclosed in that single reference.” *Acoustic Tech., Inc. v. Itron Networked Sols., Inc.*, 949 F.3d 1366, 1373 (Fed. Cir. 2020) (citation omitted). And “[e]xpert

testimony may shed light on what a skilled artisan would reasonably understand or infer from a prior art reference.” *Id.* (citation omitted).

Here, the Board pointed to Dr. Neugut’s testimony that a POSA would have understood from the Study Record’s reference to “measurable cancer” in the context of the disclosed cancer treatment that patients enrolled in the study had “advanced cancer” and “would have generally received at least two other prior drug therapies.” Appx177 (quoting Appx1680, ¶¶82-83). And the Board observed that Dr. Oberstein “agree[d] with Dr. Neugut” and “testifie[d] that because the eligibility criteria stated in the [Study Record] requires patients to have ‘measurable disease,’” a POSA “would have expected a patient to have undergone prior cancer therapies and would have had their cancer progress after receiving those therapies prior to enrollment in the” study. Appx178 (quoting Appx15525, ¶76). Indeed, JHU’s declarant, Dr. Lonberg, admitted that the treatment method in the Study Record applies to a patient whose cancer has progressed following a prior cancer therapy, thus clarifying his opinion to be that the Study Record “does not require treatment of *only* patients who have received at least one prior cancer therapy.” Appx17447-17448, 57:5-58:2.

The Board acknowledged that Dr. Lonberg disputed the testimony of Drs. Neugut and Oberstein, but found that Dr. Lonberg “d[id] not directly contradict Dr. Neugut’s or Dr. Oberstein’s testimony about the [Study Record] as it was published in 2013.” Appx179. Rather, Dr. Lonberg offered only “evidence . . . directed to the

general knowledge in the field, not to the specific understandings of [a POSA] when reviewing the [Study Record].” *Id.*

In addition, as Dr. Neugut explained, a poster presented by the parties at the American Society of Clinical Oncology more than a year before the alleged priority date indicated that the study underlying the Study Record required that patients have “progressive disease,” that colorectal cancer patients have “at least 2 prior therapies,” and that non-colorectal cancer patients have “at least 1 prior therapy.” Appx1681, ¶86; Appx6047. JHU did not dispute that the poster is prior art that is consistent with the understanding of a POSA. *See* Appx6535-Appx6537. And, notably, all patients treated in the study prior to 2016 did in fact receive one or more prior cancer treatments and have their cancer progress. Appx15526-15528, ¶¶79-80; Appx627, 16:1-8; Appx5508.

JHU asserts (at 61) that Merck’s experts testified only as to a POSA’s expectation that patients would have received prior treatment. That is incorrect. In the very testimony JHU cites, Dr. Neugut stated that “measurable . . . is a term that’s used for assessing the progress of treatment for patients.” Appx8698, 14:16-21. And contrary to JHU’s assertion that “Dr. Oberstein admitted that the [Study Record] does not include enough information to rule out patients who did not have prior therapy,” AOB 61 (emphasis omitted), Dr. Oberstein testified that “a POSA reading [the Study Record] would understand that a patient with metastatic colorectal cancer

is only appropriate for clinical trial . . . if they had failed first and second line chemotherapy options,” Appx18847, 278:19-25. Dr. Oberstein also testified that doctors “would not have placed a person on a clinical trial such as this if they didn’t fit that criteria.” Appx18848, 279:1-4. Indeed, he explained that if the study had been limited to only patients who did *not* receive prior treatment (i.e., “first line” patients), prior treatment would have been expressly listed in the exclusion criteria. Appx15525-15526, ¶77. It was not. That is substantial evidence supporting the Board’s decision, because it “explains in detail how [the prior-treatment] claim element is disclosed in the” Study Record. *Acoustic Tech.*, 949 F.3d at 1373 (citation omitted).

III. Substantial Evidence Supports The Board’s Finding That The Remaining Dependent Claims Directed To Trivial Method Details Would Have Been Obvious

In creating an estate of similar and overlapping patents, JHU crafted dependent claims with various trivial details already disclosed in the prior art that do not materially affect the treatment method. For example, claims 9 and 19 of the ’287 patent require biological-sample testing to be performed using “immunohistochemistry testing, next generation sequencing[,], or PCR testing.” Appx632, 25:1-3, 25:35-38. And claims 3 and 13 of the ’287 patent require the biological sample to be “a body fluid from the patient.” Appx631, 24:55-56; Appx632, 25:22-23. As the Board correctly recognized, the dependent claims

adding such details were obvious in view of the Study Record and other prior art references. *See, e.g.*, Appx187-193.

At the outset, the Board correctly found that the independent claims from which the dependent claims descend were obvious because they were anticipated, and “anticipation is the epitome of obviousness.” *See* Appx186-187 (quoting *In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002)). JHU does not claim any error in that determination. Given that finding of anticipation, the Board properly recognized that any differences between the prior art and these dependent claims as a whole resided in certain trivial details that did not affect the obviousness of the claimed treatment method, such as the obvious fact that a doctor would administer pembrolizumab to the patient intravenously. Appx187; *see, e.g., Hibler v. Krasne Corp.*, 824 F.2d 977, 1987 WL 37458, at *1 (Fed. Cir. 1987) (table) (affirming obviousness finding based on anticipatory prior art and the district court’s finding that certain claims with “additional limitation[s]” were obvious to a POSA).

Addressing each dependent claim’s sole additional differentiating limitation in turn, the Board found that the prior art as a whole rendered that claim obvious. Appx187-189. In doing so, the Board found that the record supported a determination that a POSA would have had a motivation to combine the relevant prior art and a reasonable expectation of success. *See id.* The Board’s obviousness determination was particularly well founded given that JHU “d[id] not raise specific

arguments against any of the [obviousness] challenges.” Appx189; *see* Appx6569-6570. Instead, JHU “argue[d] against all of the obviousness challenges together, without arguing that any of the limitations recited in the dependent claims renders the method . . . nonobvious.” Appx190 (citation omitted).

The Board also addressed JHU’s evidence of secondary considerations, including nexus to the dependent claims. The Board first explained that, with respect to the independent claims that were found to be anticipated, JHU’s secondary considerations evidence “is not persuasive of the patentability.” Appx191; *see Cohesive Tech., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cir. 2008) (“[S]econdary considerations are not an element of a claim of anticipation.”). As for the dependent claims, the Board found that JHU presented secondary considerations evidence that “addresses the methods of [the anticipated] independent claims . . . , not the limitations of the [challenged dependent] claims.” Appx192. Thus, the Board was “not persuaded that this evidence is persuasive of the non-obviousness of the specific methods recited in the dependent claims.” Appx193.

JHU’s argument (at 63) that the Board incorrectly required it to present secondary considerations evidence on a limitation-by-limitation basis—and did not consider its purported evidence—is meritless. As the Board explained, JHU “d[id] not direct [the Board] to evidence of a nexus to limitations recited in the dependent claims.” Appx192. That was a critical omission by JHU because evidence of

secondary considerations must have a nexus to the features of the claim. *See Yita LLC v. MacNeil IP LLC*, 69 F.4th 1356, 1364 (Fed. Cir. 2023); *Ethicon Endo-Surgery, Inc. v. Covidien LP*, 812 F.3d 1023, 1034 (Fed. Cir. 2016) (“[I]f the feature that creates the commercial success was known in the prior art, the success is not pertinent.”).

Moreover, given that secondary considerations “evidence was principally directed to features of the [anticipated] independent claims,” it was reasonable for the Board to treat such evidence as having “lesser probative value.” *Vicor Corp. v. SynQor, Inc.*, 869 F.3d 1309, 1326 (Fed. Cir. 2017); *see Low Temp Indus., Inc. v. Duke Mfg. Co.*, No. 2021-2137, 2021 WL 6124455, at *6 (Fed. Cir. Dec. 28, 2021) (evidence of nexus insufficient where patentee “did not tie any objective indicia to” limitations disclosed in dependent claims, but “instead tied its objective indicia evidence to” limitations of anticipated independent claim).

Finally, JHU fails to overcome the impact of Merck’s own blocking patents—for the pembrolizumab drug itself and its uses to treat cancers—which further undermine JHU’s purported evidence of secondary considerations. *See* Appx15565, ¶146; Appx15596-15598, ¶¶31-34; *see also Acorda Theras., Inc. v. Roxane Labs., Inc.*, 903 F.3d 1310, 1338-42 (Fed. Cir. 2018) (discounting weight of commercial success, failure of others, and long-felt unmet need in view of blocking patent in the record); *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364 (Fed. Cir. 2005).

The Board's obviousness determination was accordingly correct and supported by substantial evidence.

CONCLUSION

The Board's final written decisions should be affirmed.

August 14, 2026

/s/ Preston K. Ratliff II

Preston K. Ratliff II
Bruce M. Wexler
Dana R. Weir
Jessica Stauring
Ben Gifford
PAUL HASTINGS LLP
200 Park Avenue
New York, NY 10166
Tel.: (212) 318-6000

Naveen Modi
Benjamin W. Snyder
Daniel Zeilberger
Vladimir J. Semendyai
PAUL HASTINGS LLP
2050 M Street, NW
Washington, DC 20036
Tel.: (202) 551-1700

Counsel for Appellee

CERTIFICATE OF SERVICE

I certify that I filed the foregoing motion with the Clerk of the United States Court of Appeals for the Federal Circuit via the CM/ECF system and also served a copy on counsel of record via the CM/ECF system.

Date: August 14, 2026

By: /s/ Preston K. Ratliff II
Preston K. Ratliff II
PAUL HASTINGS LLP
200 Park Avenue
New York, NY 10166
(212) 318-6000

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BY: /s/ Preston K. Ratliff II
Preston K. Ratliff II
Paul Hastings LLP
200 Park Avenue
New York, NY 10166
(212) 318-6000

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Form 31
July 2020

**UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT**

CERTIFICATE OF CONFIDENTIAL MATERIAL

Case Number: 2026-1020, -1021, -1184, -1185, -1188, -1189, -1209, -1210, -1211 

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Name: Preston K. Ratliff II