No. 20-1258

IN THE
Supreme Court of the United States

ONO PHARMACEUTICAL CO., LTD.,
TASUKU HONJO, E.R. SQUIBB & SONS, L.L.C.,
AND BRISTOL-MYERS SQUIBB COMPANY,
Petitioners,

v.

DANA-FARBER CANCER INSTITUTE, INC.,
Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF IN OPPOSITION

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QUESTION PRESENTED

Whether the court of appeals erred in affirming the district court's fact-bound determination that two omitted inventors made significant contributions to conception of the claimed inventions over the course of a cancer research collaboration spanning more than twelve months.

CORPORATE DISCLOSURE STATEMENT

Respondent Dana-Farber Cancer Institute, Inc. is a Massachusetts non-profit corporation. It has no parent corporation and no capital stock.

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INTRODUCTION

The Federal Circuit unanimously affirmed the district court's joint inventorship decision, holding that "[u]ltimately, the decision in this appeal rests on the extensive factual determinations made by the district court relating to the work performed together by Drs. Wood and Freeman, and Dr. Honjo." App. 17a. The district court's findings tell the story of a history-making collaboration, by which scientists from Massachusetts and Japan combined their resources and shared their ideas and experimental data to conceive a groundbreaking cancer treatment that has profoundly improved the lives of cancer patients everywhere. The district court's 111-page findings reflect the trial judge's mastery of the science, her meticulous review of the "flood of corroborating evidence," and her evaluation of the credibility of witnesses. App. 73a. In affirming, the Federal Circuit applied settled law, relying on the same decades-old precedents that BMS cites as the correct standard for joint inventorship.

BMS's petition claims that the district court and the Federal Circuit erred by giving insufficient weight to the fact that some of Dr. Freeman's and Dr. Wood's contributions had been published art as of the date Dr. Honjo filed his patent application. But there is no rule that a contribution is insignificant to conception simply because it is published *after* the contribution was made but before the invention is complete. In the Federal Circuit, BMS urged that the court adopt a categorical rule of disqualification in these circumstances, but the Federal Circuit correctly rejected its argument. In doing so, the court did not adopt any "bright-line" rule that publication before conception necessarily was irrelevant to

inventorship. It simply held that "publication of a portion of a complex invention *does not necessarily defeat joint inventorship of that invention, and it does not here*." App. 14a (emphasis added). BMS fails to acknowledge, let alone challenge, this articulation of the correct legal rule or its fact-bound application here.

To the extent BMS challenges the inventorship test applied by the Federal Circuit, it conflates two distinct concepts in patent law, inventorship and patentability. For inventorship, ideas may be found to have contributed significantly to conception if they were not publicly known *at the time they were shared with a collaborator*. If they later become publicly available before the filing of the patent application, that may impair patentability, because patentability is assessed in light of all prior art existing *at the time of the filing*. If the patent issues nonetheless, the question remains as to who should be credited as having contributed to the conception of the claimed invention.

Dr. Freeman's discoveries, experimental data, and insights, shared openly and in good faith with Dr. Honjo over an extended period of collaboration, paved the way not only to conception of the patented inventions but also to Dr. Honjo's 2018 Nobel Prize. BMS's petition belittles Dr. Freeman's contributions, but Dr. Honjo knows better, concluding his Nobel lecture by crediting Dr. Freeman as one of his "major collaborators" on "cancer immunotherapy by PD-1 blockade," the very subject matter of the patents at issue here.

The petition should be denied.

STATEMENT OF THE CASE

A. Overview

The petition acknowledges that "[i]f collaborators contribute significantly to an inventive concept, they deserve to be co-inventors of any resulting patent." Pet. 23. This is the question of fact the parties tried to the district court. In the course of a nine-day trial, the court (Saris, J.) heard live testimony from eight witnesses, including Dr. Freeman, Dr. Wood, and Dr. Honjo, and evaluated their credibility. It also considered deposition testimony from seven witnesses, contemporaneous correspondence, collaboration agreements, experimental data, meeting presentations and notes, and drafts of co-authored scientific papers. The court made detailed findings of fact based on this "flood of corroborating evidence." App. 73a.[1]

BMS does not challenge the district court's finding that the six patents-in suit are "all premised on blocking the inhibitory interaction of the PD-1/PD-L1 pathway to treat tumors that express PD-L1 or PD-L2." App. 23a. The evidence showed that Dr. Honjo, though he had discovered the PD-1 receptor in 1992, tried and failed to identify the molecule to which it binds (its "ligand"), only learning the identity of the ligand and its biological function in 1999 from Drs. Freeman and Wood. The district court found that Dr. Freeman and Dr. Wood together discovered PD-L1, characterized the PD-1/PD-L1

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[1] In its appendix to its petition, BMS omitted the district court's helpful Table of Contents. A complete copy of the decision is available at 379 F. Supp. 53 (D. Mass. 2019).

pathway as inhibitory, and discovered "that antibodies block the inhibitory effect of the pathway and stimulate the immune system." App. 94a.

The district court also found that Dr. Freeman made the critical discovery that PD-L1 in humans is expressed not only on normal cells—which use the PD-1/PD-L1 pathway to inhibit an autoimmune response —but also is expressed on a wide variety of tumor cells. Based on this, Dr. Freeman hypothesized that tumors could be using the pathway to inhibit the antitumor immune response. Blocking the interaction between PD-1 and PD-L1, he reasoned, could treat cancer by preventing the inhibitory signal and thereby enhancing the immune response. The district court determined that Dr. Freeman's discovery of PD-L1 expression on tumor cells was a "significant contribution": indeed, the court found that the mouse tumor experiments Dr. Honjo's lab in the latter half of 2000 "only triggered conception because Dr. Honjo knew from Dr. Freeman's work that, like the transfected [engineered] tumors in [those] experiments, human tumors express PD-L1." App. 95a-96a; App. 88a-90a.

Dr. Freeman made additional contributions the district court found to be significant. Later in 1999, Dr. Freeman discovered a second PD-1 ligand, PD-L2, and shared its discovery with Dr. Honjo. App. 49a. Together, Drs. Freeman and Wood "generated the full-length sequence for the [PD-L2] molecule, showed that it binds to PD-1 and inhibits the immune response, and found that it is expressed on certain mouse tumor cells." App. 91a. The significance of these contributions is underscored by the district court's finding that "[e]verything [Dr. Honjo] knew

about PD-L2 came from Dr. Freeman and Dr. Wood." *Id.*

Drs. Freeman and Wood shared their many discoveries and ideas with Dr. Honjo "as part of a collaboration aimed at developing a treatment for cancer." App. 93a. In particular, the court found, "Dr. Freeman, Dr. Wood, and Dr. Honjo collaborated to discover and characterize the PD-1/PD-L1 pathway and to develop therapeutic applications based on blocking this inhibitory interaction with antibodies and enhancing the immune response for treatment of cancer and other diseases." App. 79a. After reviewing the district court's exhaustive findings, the Federal Circuit agreed that "Drs. Freeman and Wood's work linking PD-1 to its ligand and expression in tumors was a significant contribution to each of these patents' conception." App. 17a.

B. Factual Background

The patents claim methods of treating cancer using the body's own immune system to attack tumor cells, a pioneering addition to the arsenal of cancer treatments that is known as cancer immunotherapy. App. 27a. Tumor cells use the interaction between the PD-1 receptor on T cells and PD-L1 or PD-L2 ligands on tumor cells to evade attack by T cells. App. 26a. By blocking this signaling pathway, the claimed treatment methods "aim to stimulate the immune system to attack the tumor cells." *Id.*; *see* App. 3a.

Dr. Honjo identified the PD-1 receptor in 1992. But he did not fully understand PD-1's biological mechanism because he was unable to identify its ligand, despite years of trying. App. 31a. He believed that activation of PD-1 had an inhibitory effect, but

"he did not know that PD-L1 triggers this effect when it binds to PD-1 or how strong the inhibitory signal is." App. 86a.

In 1998, still unable to identify a PD-1 ligand, Dr. Honjo turned to Dr. Wood, a scientist at Genetics Institute ("GI"). Dr. Wood hypothesized that PD-1's ligand would be a member of the "B7" family of proteins, ligands that are expressed on certain white blood cells and bind to T cells. But a year went by and Dr. Wood's experiments likewise failed to identify the elusive PD-1 ligand. App. 33a-35a.

In October 1999, Dr. Honjo expanded his collaborative research to include Gordon Freeman, a cancer researcher at Dana-Farber Cancer Institute. Dr. Freeman had spent the past fifteen years studying B7 ligands. App. 35a. Dr. Freeman suspected there might be additional B7 ligands with immunological activity, and in 1998 he used his B7 expertise to devise a targeted search strategy. App. 35a-36a; *see* App. 4a-5a. He selected a specific sequence containing 208 amino acids that forms part of the binding portion of the B7-1 ligand and queried the massive "BLAST" database to look for similar molecules. App. 36a; *see* App. 27a-28a (BLAST database contains millions of sequences, many of them short fragments of genetic material whose identity and function are unknown).

Dr. Freeman's search identified 12 "extended sequence tags" (ESTs) that resembled portions of the B7-1 molecule, including one, denominated "292," that came from a human ovarian tumor. *Id.* Because all the then-known B7 proteins were found only in immune cells, not solid tumors, he decided to investigate the 292 EST further, determining its full-

length sequence and testing it for immunological properties. App. 35a-36a. (The 292 molecule was later renamed PD-L1.) As the district court's findings show, Dr. Freeman's discovery of 292 was the result of sophisticated scientific experimentation; he did not simply "locate" PD-L1 in a public database, as BMS disparagingly depicts his discovery.

After determining that 292 plays a role in immune regulation, Dr. Freeman utilized an existing collaboration with GI to further investigate 292's biological function, including the receptor to which it bound. He explained to GI that 292 was a B7 molecule and suggested that its receptor would resemble certain T cell receptors he identified. App. 37a.

When Dr. Wood learned that Dr. Freeman had discovered a new B7 protein, Dr. Wood tested whether PD-1 bound to it and found that it did. App. 38a. Dr. Wood shared the welcome news with Dr. Honjo and informed him of Dr. Freeman's role in the discovery. Dr. Honjo expressed great excitement and made plans to meet with them in Cambridge, Massachusetts on October 25, 1999. App. 38a.

At this meeting Dr. Freeman shared the amino acid sequence of PD-L1 with Dr. Honjo, and he and Dr. Wood shared their unpublished experimental data demonstrating that PD-L1's interaction with PD-1 inhibited the proliferation of T cells. Dr. Freeman also disclosed that PD-L1 was derived from a human ovarian tumor. App. 39a-42a. To the scientists at the meeting, these discoveries were revelatory—their mood was "jubilant." C.A.J.A. 1126. Dr. Honjo relied on the information he learned that day in his ensuing research. App. 97a. None of this

information was available to the scientific community until nearly twelve months later, when the three scientists published some of their early data.

Toward the end of 1999, Dr. Freeman discovered a second ligand that binds to PD-1, PD-L2. The interaction of PD-L2 with PD-1 similarly inhibits the immune response, and PD-L2, like PD-L1, is expressed on various tumor cells. App. 47a-48a. Dr. Freeman shared this discovery with Dr. Honjo in March 2000. *Id.* Treating a tumor that expresses PD-L2 is a claim element in three of the six patents obtained by Dr. Honjo, even though he did not discover PD-L2 and he never conducted any experiments involving PD-L2. *Id.*; App. 91a.

In November 1999, Drs. Freeman and Wood filed a provisional patent application describing research they conducted before beginning their three-way collaboration with Dr. Honjo. C.A.J.A. 3487-3640. The provisional described methods of modulating the immune response either by activating or blocking the PD-1/PD-L1 pathway and reported that the PD-1/PD-L1 interaction was inhibitory. App. 44a.[2] The provisional did not disclose Dr. Freeman's discovery of PD-L2, Dr. Freeman and Dr. Wood's discoveries that monoclonal antibodies could effectively block the PD-1/PD-L1 interaction, or Dr. Freeman's discovery that PD-L1 is highly expressed on human solid tumors, all of which came later. The USPTO issued three patents based

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[2] The provisional also hypothesized that PD-L1 might have a *stimulatory* effect if it bound to a second T cell receptor other than PD-1.

on the provisional beginning in 2004; only upon their issuance did the patents become prior art against the Honjo patents, under 35 U.S.C. § 102(e). App. 45a.

By 2000, Dr. Freeman had hypothesized that cancer cells expressing PD-L1 could use the interaction between PD-L1 and PD-1 to inhibit the proliferation of T cells and protect themselves from immune attack. Blocking this interaction could enhance the immune response and thereby treat cancer. To test his hypothesis, Dr. Freeman undertook two important studies. First, his lab created monoclonal antibodies against human PD-L1 and established that they could effectively block the interaction between PD-1 and PD-L1 in human cells. App. 48a. (Dr. Honjo, less focused on developing human therapeutics, only studied the PD-1/PD-L1 interaction in mice).

Second, Dr. Freeman investigated PD-L1's pattern of expression in human cells through immunohistochemistry ("IHC") experiments that exposed *ex vivo* human tissues to PD-L1 antibodies. He showed that PD-L1 is highly expressed on a wide range of solid tumors, confirming that tumors could use the pathway to protect themselves from immune attack. App. 46a-47a; *see* App. 6a. These results had profound implications for cancer therapy. They were shared at a high level with Dr. Honjo at a private meeting in May 2000, App. 50a, and then in greater detail at a collaboration meeting in September. App. 53a. The IHC results were not made public until 2003. App. 6a, 47a.

On September 8, 2000, the three collaborators met to share their latest research on PD-1/PD-L1 cancer immunotherapy. Dr. Honjo reported the

results of an experiment indicating that mouse melanoma tumors engineered to express PD-L1 grew faster than tumors that did not express PD-L1. App. 52a-53a.[3] The experiment confirmed, in an animal model, Dr. Freeman's earlier hypothesis that cancer cells expressing PD-L1 could use the pathway to protect against immune attack. As noted, Dr. Freeman presented his IHC data showing that in humans PD-L1 is highly expressed on solid tumors. In addition, both Dr. Freeman and Dr. Wood reported their data showing that monoclonal antibodies could effectively block the PD-1/PD-L1 interaction. *Id.*

The results shared on September 8 quickly led to conception of the claimed inventions by no later than October. *See* App. 95a. Dr. Honjo testified that in his mind conception was complete by October 27, 2000. App. 54a. Although he claimed that the results of his lab's mouse tumor experiments were what persuaded him, the district court found that the mouse experiments "only triggered conception because Dr. Honjo knew from Dr. Freeman's work that, like the transfected tumors in [the mouse]

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[3] Contrary to the petition, Dr. Honjo's lab did not begin to run their mouse tumor experiments in "early 2000." Pet. 12. In March 2000, Dr. Honjo's lab outlined a plan for *future* PD-1/PD-L1 experiments, including mouse tumor experiments, but they were not conducted until late summer and not reported until September. C.A.J.A. 6226-6230; *see also* C.A.J.A. 4445. The Federal Circuit noted that the Honjo lab conducted the mouse tumor experiments only *after* Dr. Freeman had shown expression of PD-L1 in human tumors. App. 12a-13a.

experiments, human tumors express PD-L1." App. 95a-96a.

On October 2, 2000, shortly before the asserted date of conception, the three scientists and their colleagues published a paper in *Journal of Experimental Medicine* ("Freeman 2000"). C.A.J.A. 5796-5803. It reported research they conducted in 1999, including the discovery of PD-L1 as a PD-1 ligand and data from *in vitro* experiments showing that the PD-1/PD-L1 interaction inhibits the immune response. App. 45a-46a. The Freeman 2000 paper included a passage, written by Dr. Freeman, suggesting for the first time publicly that "tumors may use PD-L1 to inhibit the antitumor immune response." *Id.*; C.A.J.A. 2185-86, 5802. The paper did not disclose Dr. Freeman's and Dr. Wood's data showing that the pathway could be blocked using monoclonal antibodies, Dr. Freeman's discovery of PD-L2, or Dr. Freeman's data showing that PD-L1 is highly expressed on human solid tumors.

Dr. Honjo and Ono Pharmaceutical filed a provisional Japanese patent application on July 3, 2002 and a utility application a year later, leading to the six patents-in-suit. Each patent names as inventors only Dr. Honjo, two of his colleagues at Kyoto University, and a scientist at Ono.

Each patent recites a method of treating cancer or a tumor, decreasing tumor growth, and/or suppressing metastasis of tumor cells by administering a PD-1 or PD-L1 antibody. C.A.J.A. 145, 180, 213, 251, 289, 331-332. Five of the patents contain claim limitations requiring that the tumors express PD-L1 or PD-L2, and four of the patents limit the treatment method to particular types of tumors.

Nearly all of the recited tumors are ones Dr. Freeman identified to Dr. Honjo in 2000 as tumors that highly express PD-L1 or PD-L2. App. 102a-103a.

Dr. Honjo and Ono exclusively licensed their rights in the patents to global pharmaceutical giant Bristol-Myers Squibb. BMS obtained regulatory approval for its PD-1 antibody product Opdivo® in 2014 and has earned "billions of dollars in profits." App. 57a, 109a. In 2014 BMS sued its main competitor Merck for patent infringement by Merck's PD-1 antibody Keytruda®. In 2017, during the pendency of this litigation, BMS granted Merck a patent license in exchange for a $625 million licensing fee plus royalties. ECF No. 364 (Tr. 62).

C. The District Court Proceeding

Dana-Farber brought suit to correct inventorship in 2015 "to confirm its ability to grant non-exclusive licenses to companies interested in developing cancer immunotherapies directed to the PD-1/PD-L1 pathway, in order to ensure broad patient access to the cancer treatments claimed in the [p]atents." ECF No. 1, ¶ 56.

At trial, BMS raised three principal defenses, each now abandoned. First, it claimed that Dr. Freeman and Dr. Wood's contributions to conception were uncorroborated. The district court disagreed, pointing to the "flood of corroborating evidence" supporting joint inventorship. App. 72a-73a. The court credited Drs. Freeman and Wood with testifying truthfully about their experiments and their communications with Dr. Honjo. App. 72a-76a. The court also credited the scientific testimony of Dana-Farber's expert immunologist, who explained

that Dr. Freeman and Dr. Wood's contributions were critically important to the inventive process that led to conception of the claimed inventions. App. 61a.

Second, BMS denied that Drs. Freeman and Wood collaborated with Dr. Honjo on methods of treating cancer, claiming that their collaboration was limited to identifying PD-1's ligand and characterizing its function. ECF No. 375 at 1-2. The centerpiece of BMS's defense was Dr. Honjo's testimony that the purpose of the collaboration was only to "find the ligand," ECF. No. 362 (Tr. 185), and his denial that he had collaborated with Drs. Freeman and Wood on cancer immunology. *Id.* (Tr. 111-12). This defense fell flat when the evidence revealed that in his Nobel lecture two months before trial, Dr. Honjo credited Dr. Freeman as a "major collaborator" on "*Cancer immunotherapy by PD-1 blockade*," the very subject matter of the claimed inventions. C.A.J.A. 7396-7397 (emphasis added); App. 60a, 77a; *see* App. 8a.[4] The district court did not credit Dr. Honjo's self-serving denial, finding that the three scientists collaborated "to develop therapeutic applications based on blocking this inhibitory interaction with antibodies and enhancing the immune response *for treatment of cancer* and other diseases." App. 79a; *see* App. 77a (emphasis added).

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[4] Dr. Honjo listed Dr. Freeman first among his four "major collaborators." The second, Dr. Minato, was a named inventor. The others were clinicians whose involvement with Dr. Honjo came long after the research that led to the patents. C.A.J.A. 7396-7397; C.A.J.A. 2024-2025.

BMS's third defense was that Dr. Freeman's discovery of the PD-L1 and PD-L2 ligands amounted to nothing more than explaining the current state of the art. BMS claimed that because the partial or full-length sequences of the two molecules appeared in public databases, Dr. Freeman's contributions did not meet the Federal Circuit's test for significance. The district court rejected this defense as well. As to PD-L1, the court found that its identity and function as a PD-1 ligand were unknown at the time Dr. Freeman shared his discovery with Dr. Honjo, and hence it was not a "well-known concept[]" or the "current state of the art." App. 83a. The court also noted Dr. Honjo's inability to find the ligand over a seven-year period of investigation, demonstrating that Dr. Freeman's discovery "required more than 'the basic exercise of ordinary skill in the art.'" App. 84a. As to PD-L2, the court found that while its sequence appeared in a public database, its identity as a PD-1 ligand and its biological function were unknown until Drs. Freeman and Wood made these discoveries and shared them with Dr. Honjo. App. 91a.

After reviewing the patents claim-by-claim, the district court found that "conception of the inventions in the Honjo patents was the result of the collaboration of all three scientists." App. 93a. Dr. Freeman and Dr. Wood "made significant contributions to conception" of the claimed inventions "through their discovery of PD-L1 and PD-L2, their discoveries of blocking antibodies, Dr. Wood's discovery of the inhibitory interaction between PD-1 and PD-L1, and Dr. Freeman's discovery of the expression of PD-L1 on tumor cells." App. 103a-104a; *see* App. 14a-17a. These contributions were "fundamental and essential building blocks for

conception" of the claimed cancer treatment methods. App. 98a, 95a.[5]

D. The Federal Circuit Appeal

On appeal, BMS did not, and could not, challenge the district court's findings of fact. Instead, BMS argued that the judgment should be reversed on the ground that it was flawed by "conceptual errors." BMS Br. 27. This contention turned on questions of fact, but BMS tried to present them as legal issues by urging categorical rules to disqualify Dr. Freeman's and Dr. Wood's contributions as a matter of law.

The Federal Circuit applied settled inventorship law to dispose of BMS's proposed categorical rules. BMS's first argument was that Dr. Freeman and Dr. Wood's contributions were "too far removed" from treating cancer because they did not participate in the Honjo lab's mouse tumor experiments in late 2000. App. 10a, 12a. Citing joint inventorship cases dating to the 1990s, the court noted that BMS was asking it to adopt a new and "unnecessarily heightened inventorship standard." App. 11a. The court explained that "the statute and our case law make clear that joint inventors need not contribute to all aspects of a conception," and that "*in vivo* verification" is not required for conception. App. 12a. The court added that in any case Dr. Honjo's

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[5] Although the district court was unable to determine which of the three scientists was first to propose the idea of blocking the pathway to treat cancer, it found that they were simultaneously focused on this idea in early 2000 and "working toward a shared goal." App. 92a-93a.

mouse tumor experiments were performed only "*after* Dr. Freeman had shown expression of PD-L1 in human tumors" and thus "as a factual matter, PD-L1's potential utility in treating human cancers was developed jointly with Dr. Freeman." App. 12a-13a.

BMS's second argument was that certain of Dr. Freeman and Dr. Wood's contributions, though not in the prior art when shared with Dr. Honjo, became prior art by the time Dr. Honjo filed his patent application and on that ground should be disqualified as a matter of law. App. 10a. Citing the disclosures in the 1999 provisional and the co-authored Freeman 2000 paper, BMS argued that if a patent "issues over" a prior art reference disclosing alleged contributions, they cannot be considered in determining joint inventorship.

The Federal Circuit noted that BMS was urging the Federal Circuit, contrary to settled law, "to adopt a legal rule that once a contribution is made public, it "no longer qualifies as a significant contribution to conception." App. 10a. The court declined to adopt BMS's proposed bright-line rule and made clear that whether contributions are significant for joint inventorship purposes is case-specific and fact-bound. Thus, it held, "publication of a portion of a complex invention *does not necessarily defeat joint inventorship of that invention, and it does not here*." App. 14a (emphasis added).

E. BMS's Petition for Rehearing En Banc

After the Federal Circuit issued its unanimous decision, BMS petitioned for panel rehearing and rehearing en banc. Its request for panel rehearing was based on the panel's alleged "factual errors,"

repeating its now-abandoned contention that Dr. Freeman and Dr. Wood's contributions to conception should have been found to be insignificant because they were "too far removed" from the Honjo's lab's *in vivo* mouse studies. Its request for en banc rehearing previewed its petition to this Court, asserting that the panel's decision conflicted with the same Federal Circuit precedents that BMS now cites in its petition.

The Federal Circuit unanimously denied both panel and en banc rehearing. App. 19a-20a.

REASONS FOR DENYING THE PETITION

BMS's petition presents no issues warranting review. The Federal Circuit held that the district court committed no error in its factual determination that Dr. Freeman and Dr. Wood, individually and together, made significant contributions to conception of the claimed subject matter. BMS does not and cannot challenge this determination as a factual matter. Contrary to BMS's contrived arguments, the Federal Circuit's decision did not, and did not purport to, make new law or impose any bright-line rule for assessing inventorship evidence. A fact-bound determination of joint inventorship presents no occasion for this Court to revisit settled law, on which patent owners and inventors have relied for decades.

A. The Federal Circuit's Decision Did Not Deviate from Precedent or Create a "Bright-Line" Rule Precluding a District Court's Consideration of Relevant Inventorship Evidence

BMS's petition should be denied, first, because the legal issue it seeks to raise is not presented at all.

BMS contends that the Federal Circuit adopted a "bright line" rule that precludes a district court from considering evidence that an alleged inventive contribution was published prior to the date of conception in determining whether that contribution was significant to conception. But the district court excluded no such evidence and the Federal Circuit adopted no such rule. On the contrary, the Federal Circuit simply rejected BMS's now-abandoned argument that if the ideas contributed enter the prior art before the date of conception, they are disqualified, *as a matter of law,* from consideration in the inventorship determination.

Applying settled precedent and evaluating the district court's findings under the clearly erroneous standard of review, the Federal Circuit found that "publication of a portion of a complex invention *does not necessarily* defeat joint inventorship of that invention, *and it does not here*." App. 14a (emphasis added). This articulation of the legal standard, which BMS tellingly fails even to acknowledge, and its application to the facts of this case, belie any preclusive, bright-line rule. The Federal Circuit left joint-inventorship law where it found it, and where BMS concedes (for purposes of its petition) it should be: later publication may or may not bear on the significance of a particular contribution, depending on the facts and circumstances that led to conception in a particular case.

1. The Federal Circuit's Decision Applied Settled Law

The Federal Circuit's affirmance of the district court's determination that the contributions of Drs. Freeman and Wood were significant—

notwithstanding that some of their 1999 contributions either were published, or were not published but technically constituted prior art—properly applied settled inventorship law that BMS does not challenge.

a. "[A] joint invention is simply the product of a collaboration between two or more persons working together to solve the problem addressed." *Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997); App. 11a. To encourage "modern team research," Congress amended the patent statute in 1984 to provide that joint inventors need not work in physical proximity or at the same time, or make the same type or amount of contribution. 35 U.S.C. 116(a); 130 Cong. Rec. 28,069-71 (1984) (statement of Rep. Kastenmeier). Joint inventors thus may contribute at different stages of the inventive process. *See Ethicon, Inc. v. United States Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir. 1998) (each inventor "needs to perform only a part of the task which produces the invention"); *Vanderbilt Univ. v. ICOS Corp.*, 601 F.3d 1297, 1303 (Fed. Cir. 2010) ("each contributor need not have their own contemporaneous picture of the final claimed invention in order to qualify as joint inventors"); App. 12a.

There is no "explicit lower limit on the quantum or quality of inventive contribution required for a person to qualify as a joint inventor." *Fina Oil*, 123 F.3d at 1473. All that is required is that each joint inventor "make a contribution to the conception of the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention." *Id.*; *see CODA Dev. s.r.o. v. Goodyear Tire*

& Rubber Co., 916 F.3d 1350, 1359 (Fed. Cir. 2019) (joint inventor must make "a more-than-insignificant contribution to the conception of at least one claim").

A contribution is not necessarily insignificant merely because it is made public prior to conception. In *Pannu v. Iolab Corp.*, 155 F.3d 1344 (Fed. Cir. 1998), the omitted inventor (Pannu) had disclosed his contributions publicly more than a year before collaborating with the named inventor. The Federal Circuit reversed the district court's grant of JMOL dismissing Pannu's correction-of-inventorship claim, holding that despite his prior art disclosures, a factfinder could find Pannu to be a co-inventor because he was "contributing his ideas . . . to a total inventive concept." 155 F.3d at 1351. To be sure, an alleged contribution that amounts merely to explaining "well-known concepts and/or the current state of the art" does not make one a joint inventor. *Id.* at 1351; *see Hess v. Advanced Cardiovascular Sys., Inc.*, 106 F.3d 976, 981 (Fed. Cir. 1997); App. 13a-14a. But under the standard articulated more than twenty years ago in *Pannu*, the mere fact that some aspect of a co-inventor's overall contribution enters the prior art does not mean that that the contribution necessarily should be disregarded.

The Federal Circuit reiterated this principle in 2017, noting the absence of any precedent in which the court had "barred co-inventorship, as a matter of law, just because the contribution later appeared in the public domain, where the ideas contributed were not contemporaneously available to an ordinary skilled artisan and were otherwise significant in producing the inventive conception at the time it was completed." *CardiAQ Valve Techs., Inc. v. Neovasc Inc.*, 708 F. App'x 654, 660 (Fed. Cir. 2017)

(unpublished) ("*CardiAQ*"). As the court explained, "[w]e have been presented no sound reason for adopting such a legal bar now." *Id.*[6]

Pannu and *CardiAQ* illustrate the settled law that, for a contribution to be significant, the ideas contributed must not have been *contemporaneously* available to an ordinary skilled artisan *at the time of the contribution*. But this is not the same as asking whether an invention is novel and nonobvious over a contribution that later entered the prior art, the test BMS proposed. App. 13a. The test for joint inventorship does not "depend on" the novelty and nonobvious of the invention over a particular researcher's contribution; rather, it depends on whether the researcher's ideas made a significant contribution to the process that led to conception of the claimed invention. App. 13a.

b. In its decision, the Federal Circuit applied settled law and charted no new territory. It reaffirmed the principle that to be a joint inventor one must make a not insignificant contribution to the claimed invention and do more than merely inform another about the current state of the art, citing both *Pannu* and *Hess*. App. 11a, 13a. BMS did not challenge the district court's finding, affirmed by the Federal Circuit, that when Drs. Freeman and Wood shared their discoveries with Dr. Honjo in October 1999—twelve months before publication of their co-authored paper—they were sharing "confidential,

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[6] *CardiAQ*, like this case, involved § 102(e) prior art that was not publicly available at the time of the omitted inventor's contribution and became prior art only retroactively. *CardiAQ,* 708 F. App'x at 659.

unpublished experimental results." App. 87a. Because the PD-L1 discoveries Drs. Freeman and Wood shared with Dr. Honjo in 1999 contributed significantly to the inventive process and were not "contemporaneously available to an ordinary skilled artisan," there was no bar to co-inventorship "just because the contribution later appeared in the public domain." *CardiAQ*, 708 F. App'x at 660.

The Federal Circuit applied this principle in its decision, stating that the preclusive rule BMS sought "would ignore the realities of collaboration, especially that collaboration generally spans a period of time and may involve multiple contributions." App. 13a. Here, "the collaborators had worked together for around one year prior to the disclosure, and the disclosure occurred just a few weeks prior to conception." App. 14a. Echoing its comment in *CardiAQ,* the court stated, "there is no principled reason to discount genuine contributions made by collaborators" to conception over time just "because portions of that work were published prior to conception for the benefit of the public." The court cautioned that earlier publication may, by putting a collaborator's disclosures into the prior art, create "a potential hazard to patentability." *Id.* Despite that, the court held, "publication of a portion of a complex invention does not necessarily defeat joint inventorship of that invention, and it does not here." *Id.*

2. The Petition Mischaracterizes the Federal Circuit's Opinion

In seeking review, BMS does not challenge either the legal test the Federal Circuit applied or its application in this case. Instead it attacks a straw

man—a new categorical rule of inventorship the Federal Circuit never articulated. BMS asserts that "the Federal Circuit adopted a bright-line rule" that "alleged contributions that were already in the prior art" can never be "probative of whether those alleged contributions were significant to conception." Pet. i. This mischaracterizes the decision.

When the opinion is read in light of the district court's findings of fact and the case law discussed above, it is apparent that the decision made no new law and announced no bright-line rule dictating how a district court should evaluate evidence of inventorship contributions. BMS criticizes the court's statement that joint inventorship does not "depend on" whether the claimed invention is "novel or non-obvious" over a particular researcher's contribution. App. 13a. But under settled law, that is not the test for joint inventorship, and the court rightly rejected BMS's attempt to change the law.

The petition seizes on the court's statement that Dr. Freeman and Dr. Wood's 1999 provisional was not "probative" of whether it was the "collaborative research efforts" of all three scientists that "led to the inventions claimed here." App. 13a. BMS mischaracterizes this statement as intending to promulgate a bright-line rule that a patent's issuance over prior art disclosing a scientist's contributions can never be relevant to joint inventorship. But the court's statement was made in the context of *the evidence in this case*: the 1999 provisional disclosing only the earliest of the many discoveries Drs. Freeman and Wood shared with Dr. Honjo; the collaborative research efforts of the three scientists over a twelve-month period; the specific "inventions claimed here"; and the particular contributions each

of the scientists made to conception of those inventions. Tellingly, BMS's so-called "clean legal issue" cannot be stated without reciting these case-specific facts. Pet. 29.

The petition ignores the Federal Circuit's actual *holding* in the case, set out in the final sentence of Part A of the opinion. In holding that publication of a portion of the claimed invention did not "necessarily" defeat joint inventorship and it did not "here," the Federal Circuit rested its decision on the district court's unchallenged findings of fact, not on the application of a categorical rule. BMS has not presented a "clean" or "bright-line" legal issue for this Court to review.

B. The Decision Does Not Conflict with this Court's Precedent

BMS reaches back to 1853 to find a Supreme Court case that allegedly conflicts with the Federal Circuit's decision. But the case on which it relies, *O'Reilly v. Morse*, 56 U.S. 62 (15 How.) (1853), concerned the validity of Morse's patent, not a claim of joint inventorship. One of the accused infringer's defenses was that Morse was not a "true inventor" of the telegraph, because in the course of his research he received advice from "men of science." The Court disagreed, pointing out that it made no difference whether he derived information "from books" or from conversations with men "skilled in the science." 56 U.S. at 111. Because the information in books was publicly available, the "men of science" with whom Morse conversed did nothing more than what the Federal Circuit described in *Pannu* as explaining "well-known concepts and/or the current state of the

art," not enough to make one a joint inventor. 155 F.3d at 1351; *see* App. 11a.

BMS's contention that under the Federal Circuit's decision, Morse would have had to share credit for his invention with the "men of science" with whom he consulted distorts the decision, which says the opposite. BMS does not challenge the district court's findings that Drs. Freeman and Wood did much more than explain well-known concepts or the current state of the art to Dr. Honjo. App. 83a-84a, 87a.

The petition cites *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), and *Bilski v. Kappos*, 561 U.S. 593 (2010), but they have no bearing on this case except to underscore the absence of a question appropriate for review. In *KSR*, the Court granted certiorari to review the Federal Circuit's long-standing and consistently articulated "teaching-suggestion-motivation test" for determining obviousness of a claimed invention. This was the epitome of a bright-line rule, created by the Federal Circuit's predecessor court to resolve obviousness questions with "uniformity and consistency." *KSR*, 550 U.S. at 407.

In *Bilski*, the Court granted certiorari to review the Federal Circuit's "machine-or-transformation test" for determining patent eligibility of a process under § 101. *In re Bilski*, 545 F.3d 943, 949, 956 (Fed. Cir. 2008). When the case came to this Court, there was no dispute that the question presented was a bright-line rule.

In this case, by contrast, the Federal Circuit did not purport to create a bright-line rule. BMS's

repeating that phrase twenty-eight times in the space of a twenty-nine page petition does not make it so.

C. The Decision Does Not Conflict with Federal Circuit Precedent, Fourth Circuit Precedent, or "Black Letter Patent Law"

BMS identifies no inconsistency between the decision below and any other decision of the Federal Circuit or other court of appeals. The inventorship cases BMS cites have nothing to do with the facts of this case. They involve situations where the contribution of "information in the prior art," Pet. 26, was deemed insignificant because the information was *already* in the prior art at the time it was contributed. That is, it was "*contemporaneously* available to an ordinary skilled artisan." *See CardiAQ,* 708 F. App'x at 660.

a. The petition argues the Federal Circuit's decision creates a split in the circuits over "basic principles of patent law." Pet. 19. Inventorship is an area of substantive law assigned to the exclusive jurisdiction of the Federal Circuit. BMS's implausible claim rests on a 19-year-old nonprecedential Fourth Circuit decision. *See Levin v. Septodont, Inc.*, 34 F. App'x 65 (4th Cir. 2002).

There is no conflict. *Levin* is just another in the line of cases denying joint inventorship where the putative inventor's idea was known in the prior art at the time he contributed it. *See* 34 F. App'x at 73-74 (mouthwash ingredients suggested by Levin were well-known in the literature; he "did no more than explain the existing state of the art"). In determining that the plaintiff's alleged contributions did not "help[]

to make the invention patentable," the court explicitly relied on the same *Pannu* standard discussed above. *Id.* at 70-74. The alleged contributions did not help to make the invention patentable for the simple reason that Levin's ideas were already known publicly at the time he shared them.

b. Nor is there any conflict with Federal Circuit precedent. The decisions BMS cites, like the Fourth Circuit's *Levin* decision, recite or apply the *Pannu* standard, holding that merely informing another about the state of the art does not make one a joint inventor.[7] The petition's contention that the decision conflicts with Federal Circuit precedent misleadingly implies that the PD-L1 discoveries Drs. Freeman and Wood shared with Dr. Honjo in October 1999 were already in the prior art *at that time.* But BMS did not challenge the district court's factual

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[7] *See, e.g.*, *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1362 (Fed. Cir. 2004) (if chemical properties of claimed compound were already in the public domain, alleged contribution would not give rise to joint inventorship); *Garrett Corp. v. United States*, 422 F.2d 874, 879-81 (Ct. Cl. 1970) (putative inventor's contribution of a water ballast pocket feature was already disclosed in nine-year-old prior art); *Nartron Corp. v. Schukra U.S.A., Inc.*, 558 F.3d 1352, 1357-58 (Fed. Cir. 2009) (putative inventor's alleged contribution was admittedly known in the art at the time). *Maatuk v. Emerson Elec., Inc.*, 781 F. App'x 1002 (Fed. Cir. 2019) (per curiam) (nonprecedential), *affirming Maatuk v. Emerson Elec., Inc.*, 2019 U.S. Dist. LEXIS 17403 at *29 (N.D. Ohio Feb. 4, 2019) (technology disclosed by putative inventor "was already known in the prior art").

determination that Dr. Honjo had the benefit of their "confidential, unpublished experimental results," App. 87a, for some twelve months before the three scientists published portions of their 1999 research in October 2000.

c. The decision likewise does not conflict with *Board of Education ex rel. Board of Trustees of Florida State University. v. American Bioscience, Inc.*, 333 F.3d 1330 (Fed. Cir. 2003), where the information allegedly contributed similarly was in the prior art at the time of the alleged contribution.[8]

American Bioscience underscores the weakness of BMS's arguments for additional reasons. While initially brought as a correction of inventorship case, *American Bioscience* ultimately turned on which of two competing groups of scientists were the "true inventors"—i.e., first to invent—three chemical compounds claimed in American Bioscience's (ABI's) patent. *See Vanderbilt University v. ICOS Corp.*, 601 F.3d 1297, 1307 (Fed. Cir. 2010) (explaining that *American Bioscience* was a priority contest, not a joint inventorship case). The patent's prosecution history showed that ABI originally claimed a genus of chemical compounds, but it later substituted narrow claims limited to three specific compounds in order to overcome prior art of plaintiff Florida State University (FSU) that disclosed compounds invented by FSU's scientists. 333 F.3d at 1335; *Bd. of Educ. ex rel. Bd. of Trs. of Fla. State Univ. v. Am. Bioscience,*

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[8] BMS's suggestion of a conflict with *American Bioscience* is implausible: Judge Lourie, the author of the decision in this case, also authored *American Bioscience*.

Inc., 2001 U.S. Dist. LEXIS 19480 at *32 (N.D. Fla. Oct. 31, 2001). The Federal Circuit determined that the FSU scientists were not co-inventors, because there was no evidence they communicated with ABI about the three specifically-claimed compounds. Only after so ruling did the court suggest that issuance of ABI's patent over FSU's prior art provided added "support" for—not that it *required*—finding that the claimed compounds were "not the invention of the FSU scientists." *Id.* at 1340.

The decision in *American Bioscience* turned on the disputed patent's prosecution history and testimony from the prosecuting attorney explaining it. Here, by contrast, BMS did not offer the patents' prosecution histories into evidence. The record contains no evidence that the applicants narrowed their claims in such a way as to reduce the significance of any of Dr. Freeman and Wood's contributions, or that the examiner viewed any of the provisional's disclosures as bearing on the "novelty and nonobviousness" of the allowed claims. As a result, the factual premise for BMS's flawed argument—that the issuance of the Honjo patents necessarily diminished the significance of contributions disclosed in the provisional—lacks an evidentiary basis.[9]

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[9] The petition cites a U.K. opinion regarding the validity of a European counterpart patent. But a foreign judge's analysis of a different patent cannot serve as a proxy for the U.S. prosecution histories that BMS failed to put into evidence. Moreover, in finding the U.K. patent nonobvious, the judge cited the scientific debate, *e.g.*, C.A.J.A. 5802, over whether PD-L1 also bound to a *stimulatory* receptor. This led

D. The Federal Circuit Determined that Drs. Freeman and Wood Made Significant Contributions to Conception of the Claimed Inventions that Were Not Disclosed in Prior Art

BMS's legal theory would not lead to reversal of the judgment, a further reason to deny review. The district court found, and the Federal Circuit agreed, that Dr. Freeman and Dr. Wood made significant contributions to each patent's conception that were *not* disclosed in either the 1999 provisional or the Freeman 2000 paper. Among these were their joint discovery that PD-1 and PD-L1 monoclonal antibodies can block the pathway's inhibitory signal and Dr. Freeman's discovery that human tumors highly express PD-L1. App. 94a-103a; App. 14a-17a. BMS does not contend, nor could it, that any of these discoveries was in the prior art as of the filing of Dr. Honjo's patent application. *See* App. 47a, 87a. As a

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him to conclude that, as of the priority date of the patent, the idea of blocking PD-1 to treat a tumor was nonobvious because it lacked "a fair expectation of success." *See Merck Sharp & Dohme Ltd. v. Ono Pharmaceutical Co. Ltd.*, [2015] EWHC 2973 (Pat), ¶ 243(v). That conclusion, based on assessment of the prior art as a whole, does not diminish in any way the importance of Dr. Freeman and Dr. Wood's discovery of PD-L1 and the PD-1/PD-L1 inhibitory pathway in leading to conception of the patented inventions. The U.K opinion—which BMS did not offer as evidence or even cite to the district court—does not support its argument that the district court committed legal error by failing to find that "the invention lay elsewhere." Pet. 17.

consequence, this case does not present the question whether one can be a joint inventor if *all* of his or her contributions have entered the public domain by the time a patent application is filed.

BMS is flatly wrong in asserting that the district court or Federal Circuit found that no contributions of Drs. Freeman and Wood other than their discovery of PD-L1 and the PD-1/PD-L1 pathway were significant. Pet. 28-29. The Federal Circuit described Dr. Freeman's discovery of PD-L1 expression by human tumors as a "significant building block[] upon which the '474 patent is built," App. 16a, and held that it represented a "significant contribution to *each of [the] patents' conception*." App. 17a (emphasis added); *see* App. 95a-96a, 99a-104a. BMS selectively quotes the district court's statement questioning whether a contribution to a *dependent claim* "by itself" would support joint inventorship. App. 103a. Under settled law, it would. *See Eli Lilly*, 376 F.3d at 1362 (contribution to sole limitation added in dependent claim 6 would suffice for co-inventorship). The district court rightly viewed this question as academic, having found that Dr. Freeman's PD-L1 tumor expression discovery contributed significantly to the conception of *independent claims* as well. App. 101a, fn. 18.

E. The Decision Will Not Trigger a "Flood of Litigation," "Chill Collaboration," or "Deliver Windfalls"

BMS's dire predictions as to the consequences of the Federal Circuit's decision lack any support by amici or otherwise. As explained above, the Federal Circuit held, more than two decades ago in *Pannu*, that a researcher's public disclosure of his

contributions does not automatically disqualify him as a joint inventor, even though the patent issued over his prior art disclosures. BMS identifies no "flood" of inventorship litigation that followed that decision, Pet. 27, and it has no basis to claim that this decision applying the same principle will produce a different result.

Overall, inventorship litigation is rare. In their appellate briefs, the parties identified a total of twenty-nine reported inventorship cases since 1990, including this one, approximately one per year. This paucity of cases suggests that inventorship law is not a burning issue for inventors, companies, universities, or practitioners. Notably, although the district court's decision was issued more than two years ago and the Federal Circuit's decision nearly one year ago, BMS fails to identify any subsequent inventorship case allegedly prompted by this case. In the only two reported decisions citing to the Federal Circuit's inventorship discussion in this case, the courts cited it merely for the principle that informing another about the state of the prior art is not enough to make one a joint inventor. *Astellas Inst. for Regenerative Med. v. ImStem Biotechnology, Inc.*, 2021 U.S. Dist. LEXIS 21900 at *61 (D. Mass. Feb. 5, 2021); *Plate, LLC v. Elite Tactical Sys., LLC*, 2020 U.S. Dist. LEXIS 159083 at *40-41 (E.D. Tenn. Sept. 1, 2020).

Nor is there any reason to accept BMS's speculation that the Federal Circuit's decision will discourage scientists from participating in research collaborations. In this case, Dr. Honjo began collaborating because he needed help. App. 16a. He continued to collaborate because it gave him access to Dr. Freeman and Dr. Wood's "confidential,

unpublished experimental results," App. 87a, on which "Dr. Honjo relied in his ensuing research" over a twelve-month period when the rest of the scientific community had no knowledge of their groundbreaking discoveries. App. 97a-98a. By collaborating with them, Dr. Honjo obtained a valuable head-start over other researchers, a powerful incentive for collaborative research.

The district court found that failing to credit a researcher's experiments such as those of Dr. Freeman and Dr. Wood would "disincentivize scientists from participating in this type of innovative research collaboration." App. 84a-85a. As the Federal Circuit observed, BMS's proposed rule disqualifying contributions because they later become public "would ignore the realities of collaboration," which "generally spans a period of time and may involve multiple contributions." App. 13a. BMS's argument has it backwards. It is reversal of the decision in this case that would discourage future research collaborations and impede the progress of science.

BMS's petition asserts that the Federal Circuit's affirmance of the judgment correcting inventorship "will deliver a windfall" to individuals like Dr. Freeman, because it gives him (and his assignee Dana-Farber) the full right to license the patents to third parties. Pet. 23-24. In truth, it is BMS that enjoyed a windfall, by refusing to correct inventorship and by exploiting its purported exclusive rights in the patents to negotiate lucrative licensing deals for itself.

As the district court's findings reflect, Dr. Freeman dedicated a year-and-a-half of his

professional life as a cancer researcher, plus substantial Dana-Farber laboratory resources, to his collaboration with Dr. Honjo. He openly shared his experimental data, expertise, and insights, which the court found to be important contributions to the inventive process that led to conception. The court's order correcting inventorship simply allows Dana-Farber to offer licenses to third party manufacturers in the few years that remain before the patents expire, helping to ensure broad patient access to the patented cancer treatments. Upholding the judgment of joint inventorship hardly amounts to delivering a windfall to an undeserving "purported co-inventor[]" claiming patent rights that "turn out to be valuable." Pet. 23.

CONCLUSION

The petition should be denied.

sRespectfully submitted,

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