

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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AMGEN INC.,  
Petitioner,

v.

BRISTOL-MYERS SQUIBB COMPANY,  
Patent Owner.

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Case No. IPR2025-00603  
Patent No. 11,332,529

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**PETITIONER'S OPPOSITION TO PATENT OWNER'S  
DISCRETIONARY DENIAL BRIEF**

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1001	U.S. Patent No. 11,332,529 (“529 Patent”)
1002	Prosecution History of U.S. Patent No. 11,332,529
1003	Declaration of Dr. Arta M. Monjaze
1004	Curriculum Vitae of Dr. Arta M. Monjaze
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1018	U.S. National Library of Medicine, National Institutes of Health, ClinicalTrials.gov, Glossary of Common Site Terms, <a href="https://clinicaltrials.gov/ct2/about-studies/glossary">https://clinicaltrials.gov/ct2/about-studies/glossary</a>
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## I. INTRODUCTION

Petitioner's challenges to the patentability of U.S. Patent No. 11,332,529 (the "'529 Patent") as being anticipated by and obvious over the prior art should be instituted as no reasonable basis exists for exercising discretion to deny the Petition. Rather, Patent Owner (PO) Bristol-Myers Squibb's request for discretionary denial should itself be denied.

PO markets Opdivo® (the brand name for nivolumab, an anti-PD-1 antibody) and has procured a large portfolio of granted US patents that cover Opdivo® and its use in combination with an anti-CTLA-4 antibody to treat various forms of cancer. PO's composition of matter patent expires in December 2028.

The '529 Patent at issue in this IPR expires in 2037 and does not claim the drug itself. Instead, the challenged claims simply recite the use of anti-PD-1 and anti-CTLA-4 antibodies for a specific indication that was long known in the art. Any differences between the claims of the '529 Patent and the prior art are trivial, are within the ordinary skill in the art of treating cancer, and do not justify extending patent protection on Opdivo® by another *nine years*. The Petition seeks to ameliorate the Patent Office error in allowing these unpatentable claims.

Petitioner's challenge to the '529 Patent raises legal and public policy factors that all weigh against discretionary denial. These include:

(1) clear and material Patent Office error as evidenced by the European Patent Office rejecting similar claims over similar prior art;

(2) timely filing of the Petition *before* any litigation has even commenced, let alone having a trial date set, and more than three *years before* the earliest date a biosimilar could launch in December 2028 (according to PO), and rejection of POs suggestion that a default rule exists prohibiting biosimilar developers from accessing IPR proceedings;

(3) a biosimilar manufacturer taking efficient and predictable steps to clear the path to commercialization, years before its anticipated launch, by filing an IPR petition against a mistakenly granted patent in a growing patent family both to negate the challenged patent and hopefully prevent the issuance of similarly unpatentable claims.

Each of these factors, described below and more fully throughout this brief compels a rejection of PO's request for discretionary denial.

*First*, outside of the US, PO's attempts to extend its patent protection have failed. Notably, the European equivalent to the '529 Patent was revoked in 2023 based on some of the very same references cited in the Petition. In fact, in Europe, PO conceded that it no longer approved of the granted text in its patent and *requested* revocation of the patent. IPR is designed to address precisely these errors and oversights in the US and to thereby avoid scenarios where otherwise

unpatentable “inventions” stand in the way of healthy competition and unnecessarily tax the American public. *Microsoft Corp. v. ParTec Cluster Competence Center, GmbH*, IPR2025-00318, Paper 9, at 3 (PTAB Jun. 12, 2025) (denying request for discretionary denial—“Petitioner appears to show a material error by the Office and it is an appropriate use of Office resources to review the potential error.”).

*Second, there is no parallel district court litigation.* No infringement action has been filed, nor is it likely one would be filed for at least another year, if at all. Petitioner has not yet filed its abbreviated Biologics License Application (aBLA) and expects to do so later this year. Under the Biologics Price Competition and Innovation Act (BPCIA), this aBLA filing triggers a potential identification of patents believed to be valid and infringed (hereinafter the “Patent Exchange”) for a first wave of litigation. This voluntary Patent Exchange can take approximately ten months to complete before an infringement action under the BPCIA is filed. Once filed, the average time for a decision on the merits by the district court in BPCIA cases is 2.5-3.5 years. By contrast, a Final Written Decision in this IPR would be issued by October of 2026—likely years earlier than any resolution via the BPCIA procedures.

Ignoring this much faster timeline for resolution of an IPR, PO argues that because BPCIA litigation is expected in the future, IPRs should be discretionarily

denied. IPR was provided by Congress to serve as an alternative to litigation. PO's argument cannot be accepted by the agency to avoid its statutory mandate.

Moreover, if credited, PO's argument would preclude all biosimilar manufacturers from ever filing an IPR as all biosimilar products developed to date have faced the potential for BPCIA litigation. The mere possibility of future litigation should not deprive biosimilar developers of access to IPRs to efficiently challenge clearly unpatentable claims while still in the process of preparing to file aBLAs to secure FDA approval to sell their products in the United States.

*Third*, biosimilars are critical to the public's access to potentially less expensive options for treatment, and IPRs play a valuable role in enabling such access. More specifically, IPRs improve efficiency and reduce uncertainty in the development and advancement of biosimilars to commercialization by simplifying litigation and reducing the number of issues, and patents, if any, that need to be litigated before a biosimilar can launch. IPRs provide biosimilar developers the opportunity to identify erroneously granted patents and challenge their patentability prior to launch on a predictable timeline before an expert panel. And, as in this case, a successful challenge to unpatentable claims can help to prevent the issuance of similarly unpatentable patents. In addition, obtaining an IPR decision invalidating a method of treatment patent, like the '529 Patent, before aBLA approval may help inform the biosimilar applicant's strategy about whether

to obtain regulatory approval of an indication or dosing regimen that may be relevant to the patent or to omit that indication/dosing regimen from a carved-out label to reduce patent risk. In short, the continued availability of IPR proceedings to challenge improperly granted patents in advance of any BPCIA proceedings represents the “settled expectations” of biosimilar manufacturers. And it further advances the current Administration’s mandate to increase access to biosimilars overall.

Petitioner, which is headquartered in the U.S. and employs over 28,000 people, is a world leader in the manufacture of protein-based therapeutics, such as antibodies, and has brought multiple innovative new products to the market. In the interest of serving more patients with life-altering medicines, Petitioner also applies its manufacturing and clinical development capabilities to bring biosimilar products to the market. To this end, Petitioner seeks to market a biosimilar of Opdivo® and is preparing for a launch of its biosimilar product in the US by as early as the expiration of the composition of matter patent in December 2028, if not sooner. Pursuing an IPR against the obvious claims of the ’529 Patent is an important first step to clear the way for that product launch. As a leader in both innovative therapeutics and biosimilars, and as an active user of the patent system, Petitioner fully appreciates how the patent system can be utilized fairly and effectively to drive innovation in this country while encouraging competition at the

appropriate time. The '529 Patent was granted in error and improperly seeks to extend PO's exclusivity on Opdivo®. This is exactly the kind of patent that IPRs should address.

PO's request for discretionary denial of IPR2025-00603 against the '529 Patent should be denied.

## **II. BACKGROUND**

The claims of the '529 Patent are directed to methods of treating colorectal cancer by administering an anti-PD-1 antibody and an anti-CTLA-4 antibody. EX1001, cls. As the '529 Patent itself discusses, both these classes of antibodies are used in cancer immunotherapy and had been used to treat cancer long before PO filed the application giving rise to the '529 Patent. EX1001, 1:19-65.

Dependent claims in the '529 Patent specify that the anti-PD-1 antibody may be nivolumab (Opdivo®) and the anti-CTLA-4 antibody may be ipilimumab (Yervoy®). EX1001, cls. 17, 18. PO already obtained numerous patents covering Opdivo®, Yervoy®, and their methods of use in combination to treat cancer, including colorectal cancer, all of which were filed long before, and will expire long before, the '529 Patent.

**A. PO Requested Revocation of the European Equivalent to the '529 Patent When Challenged with The Same Prior Art Relied On in the Petition**

The March 26, 2025 Interim Processes for PTAB Workload Management (“Memorandum”) counsels that the PTAB will consider “[w]hether the PTAB or another forum has already adjudicated the validity or patentability of the challenged patent claims.” While there has been no prior adjudication of the challenged claims of the '529 Patent, counterpart claims to these have been opposed, and in one case revoked entirely, in Europe. The claims of the '529 Patent should not be allowed to erroneously stand where such claims are being duly rejected and withdrawn in Europe for the benefit of overseas patients.

The European equivalent to the '529 patent—European Patent No. EP3464373B1 (EX1074)—was revoked in a Decision mailed by the European Patent Office on April 19, 2023. EX1075. The broadest claim in EP3464373B1 before revocation corresponded to a narrower version of claim 1 in the '529 Patent, incorporating features from dependent claims 11, 17, and 18 in the '529 Patent, as shown in the table below.

<b>Claims in '529 Patent</b>	<b>Claims in EP3464373B1 Before Revocation</b>
1. A <b>method of treating</b> a subject afflicted with a tumor derived from a <b>colorectal</b>	

<p><b>cancer</b>, comprising administering to the subject:</p> <p><b>(i) an anti-PD-1 antibody,</b></p> <p><b>and</b></p> <p><b>(ii) an anti-CTLA-4 antibody;</b></p> <p>wherein the tumor is a colon cancer or a rectal cancer; and</p> <p>wherein the tumor exhibits a <b>high degree of microsatellite instability (MSI-H).</b></p>	<p>1. <b>Nivolumab<sup>1</sup></b> for use in a <b>method of treating a colorectal cancer</b> tumor in a subject, wherein the tumor exhibits a <b>high degree of microsatellite instability ("MSI-H")</b>, wherein the subject is administered <b>nivolumab</b> at a dose of about <b>3 mg/kg</b> body weight in combination with <b>ipilimumab</b> at a dose of about <b>1 mg/kg</b> body weight <b>once about every three weeks.</b></p>
<p>11. The method of claim 1, wherein the anti-PD-1 antibody is administered at a dose of about <b>3 mg/kg</b> body weight and the anti-CTLA-4 antibody is administered at a dose of about <b>1 mg/kg</b> body weight <b>once about every 3 weeks</b> for a total of 12 weeks.</p>	
<p>17. The method of claim 16, wherein the anti-PD-1 antibody is <b>nivolumab.</b></p>	

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<sup>1</sup> “Nivolumab,” marketed as “Opdivo®”, is an anti-PD-1 antibody.

18. The method of claim 17, wherein the anti-CTLA-4 antibody is <b>ipilimumab</b> .	
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After EP3464373B1 granted, six Notices of Opposition were filed against it. EX1076. Rather than substantively respond to these six Notices of Opposition, PO filed a request for revocation on April 13, 2023 in which it indicated that it “no longer approves the text in which European Patent No. 3464373 was granted.” EX1077. Notably, five of the Notices of Opposition cited **NCT-188**, the primary reference in all of **Grounds 1A-C** and **2A-C** in the Petition (referred to as D4-D4b in the Consolidated list of cited references from the oppositions; EX1078), and four of the oppositions cited **Le**, the primary reference in **Grounds 3A-C** in the Petition (referred to as D13 in the Consolidated list of cited references from the oppositions; EX1078).

Thus, when facing the primary references relied on in the Petition cited against very similar claims in Europe, PO conceded that it “no longer approved of the granted text” in its patent and requested revocation of the patent. EX1077.

## **B. Resolving Patent Disputes Under The BPCIA**

Unlike for small molecule drugs, where generic approval is linked to a mechanism for resolving patent disputes, approval of an aBLA for a biosimilar is only linked to an *optional* litigation mechanism (BPCIA Patent Exchange and

ensuing litigation) for resolving patent disputes. *Sandoz, Inc. v. Amgen, Inc.*, 582 U.S. 1, 18-19 (2017). For parties who do participate in the BPCIA Patent Exchange, litigation generally does not commence until approximately ten months after the aBLA is filed and generally runs for at least 2.5-3.5 years.<sup>2</sup>

Here, as PO acknowledged, Petitioner has not yet even filed an aBLA for its Opdivo® biosimilar which is still in development. Therefore, all PO can do is speculate about: (1) the timing of possible future events of aBLA filing, (2) the possible participation in the BPCIA Patent Exchange process, and (3) the possible filing of a lawsuit and time to a decision which would be expected to take at least 2.5-3.5 years after the complaint is filed. *See supra* note 2. By contrast, a Final Written Decision in this case would be issued far sooner and more predictably,

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<sup>2</sup> Case schedules and timelines pulled from five BPCIA litigations that were terminated after trial and final judgment demonstrate that average time from Complaint filing through trial to termination is 828 days, with a maximum of 1320 days. *See Regeneron v. Mylan*, 1:22-cv-00061 (N.D. W. Va.); *Amgen v. Hospira*, 1:15-cv-00839-RGA (D. Del.); *Immunex v. Sandoz*, No. 2:16-cv-01118 (D.N.J.); *Amgen v. Apotex*, No. 15-62081 (S.D. Fla.); *Amgen v. Apotex*, No. 0:15-cv-61631 (S.D. Fla.).

likely by October, 2026. The Petition’s filing timeline was aligned with the settled expectations of the Parties regarding fair and efficient resolution of patent disputes.

**C. PO is Attempting to Rely on the ’529 Patent to Extend its Market Exclusivity for Opdivo®**

Opdivo® first received FDA approval in December 2014. EX1067. Pursuant to the BPCIA, enacted March 23, 2010, Opdivo® (as a reference product) is entitled to 12.5 years of regulatory (market plus pediatric) exclusivity, irrespective of patent protection, during which other companies are prevented from obtaining FDA approval to market a biosimilar version. EX1068. Opdivo®’s 12-year market exclusivity expires on December 22, 2026, while its pediatric exclusivity expires June 22, 2027. US revenue for Opdivo® in 2024 was \$9.3 billion and “revenues increased 2% in 2024 primarily due to higher average net selling prices.” EX1073, 48-50.

PO has sought additional patents related to Opdivo® and its use. The original composition of matter patent covering Opdivo®, US 8,008,449 (“the ’449 Patent”) (EX1044), received patent term extension and expires on December 22, 2028. EX1070, EX1071. The ’449 Patent family also includes another patent (US 9,358,289; “the ’289 Patent”) with claims directed to methods of administering an anti-PD-1 antibody and an anti-CTLA-4 antibody, for treatment of cancer, which expires in 2026. EX1072. The table below compares claim 5 of the ’289 Patent—part of the original Opdivo® patent family and *claiming priority to 2005 and*

*expiring in 2026* – with claim 1 of the '529 Patent—part of a considerably later-filed patent family *claiming priority to 2016 and expiring in 2037*.

The '289 Patent (Expires in 2026)	The '529 Patent (Expires in 2037)
<p>5. A method of <b>treating cancer</b> in a subject having a tumor that does not express PD-L1 comprising administering to the subject <b>a combination of a dose of an anti-PD-1 monoclonal antibody</b> or an antigen-binding portion thereof and <b>a dose of an anti-CTLA-4 monoclonal antibody</b> or an antigen-binding portion thereof, wherein the combination of the anti-PD-1 antibody or antigen-binding portion thereof and the anti-CTLA-4 antibody or antigen-binding portion thereof treats cancer in the subject.</p> <p>29. The method of claim 5 or 17, wherein the cancer is selected from melanoma, lung cancer, renal cancer, prostate cancer, breast cancer, <b>colorectal cancer</b>, and fibrosarcoma.</p>	<p>1. A method of <b>treating a subject afflicted with a tumor derived from a colorectal cancer</b>, comprising administering to the subject:</p> <p><b>(i) an anti-PD-1 antibody, and</b></p> <p><b>(ii) an anti-CTLA-4 antibody;</b></p> <p>wherein the tumor is a colon cancer or a rectal cancer; and</p> <p>wherein the tumor exhibits a high degree of microsatellite instability (MSI-H).</p>

In view of the upcoming expiry of its composition of matter patent and related patent family members such as the '289 Patent, PO sought and obtained exceedingly weak<sup>3</sup> follow-on patents such as the '529 Patent, which *expires in 2037* and which claims treatment of an indication that had already been disclosed in the prior art (and revoked in Europe, *see* §II.A. *supra*). Indeed, PO has obtained additional granted US patents (and has many more pending patent applications) related to Opdivo®. Almost all of these later filed patents claim known or obvious variations of known uses or indications for Opdivo® and pending applications provide the potential for PO to obtain similarly unpatentable claims. Given this large patent landscape of questionable merit, IPRs provide an important mechanism for a biosimilar developer to reduce the scope and number of erroneously granted patents that it faces in bringing its product to market.

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<sup>3</sup> Notably, the Board recently found similar colorectal cancer immunotherapy method claims unpatentable over a clinical trial protocol with results subsequently reported in the patent being challenged. *Merck Sharp & Dohme LLC v. The Johns Hopkins Univ.*, IPR2024-00240, Paper 90 (PTAB Jun. 9, 2025). Petitioner's Grounds 1 and 2 are analogous, as PO's own description confirms. Br. at 9 ("clinical trial protocol related to the trial ultimately performed and reported in Example 1.").

### **III. THE DIRECTOR SHOULD DECLINE TO EXERCISE HER DISCRETION UNDER SECTION 314(A) TO DENY INSTITUTION<sup>4</sup>**

#### **A. There Is No Parallel Litigation And Any Potential Future Litigation Would Not Be Completed Before A Final Written Decision**

There is no co-pending or parallel litigation concerning the '529 Patent and PO has identified no case in which *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (PTAB March 20, 2020) has been applied to support discretionary denial in the *absence* of parallel litigation. Even were PO's speculation about a future BPCIA litigation credited, however, the facts still do not warrant discretionary denial, in particular because any litigation over Petitioner's Opdivo® biosimilar, which is currently still in development, would not be expected to be completed or even close to completion before issuance of a Final Written Decision in this IPR.

#### **B. The *Fintiv* Factors Disfavor Denial**

##### **1. *Fintiv* Factor 1 Disfavors Denial**

There is no current pending litigation between PO and Petitioner. Consideration of a potential stay in litigation is wholly inapplicable, disfavoring denial.

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<sup>4</sup> There is no previous petition concerning the '529 Patent warranting discretionary denial under the *General Plastic* factors.

## 2. *Fintiv* Factor 2 Disfavors Denial

A Final Written Decision will be issued in this case approximately 12 months from Institution. As discussed above, there is no current pending litigation between PO and Petitioner.

PO provides a purely speculative hypothetical timeline to assert that litigation could *commence* in 8-9 months. It is unclear what this speculative timeline is based on, but PO provides no support for its general estimate, which should be disregarded. To the contrary, the (pre-complaint) BPCIA Patent Exchange process itself can take approximately ten months and that process does not begin until after the aBLA has been filed. Moreover, if the Patent Exchange is initiated by the biosimilar applicant and honored by both parties, the filing of a complaint for infringement cannot occur until the Patent Exchange process is completed. And, the time through trial for a biosimilar litigation (based on existing case data) is at least 2.5-3.5 years *after the filing of a complaint*. See *supra* note 2. Thus, even based on PO's speculation about future events, and accounting for each of these phases (time to aBLA filing, Patent Exchange process, complaint filing and litigation) resolution of any BPCIA litigation over the '529 Patent would not occur until 4-5 or more years into the future. This timeline would of course be considerably longer than the issuance of a Final Written Decision in this IPR.

Thus, to credit PO's logic that IPRs should be discretionarily denied because of the *hypothetical possibility* of future BPCIA litigation, is tantamount to ruling that biosimilar developers should never be afforded the opportunity to make use of IPR and PGR proceedings at all. Given the significant uncertainty in even assessing the "proximity of the court's trial date to the Board's projected statutory deadline for a Final Written Decision," *Fintiv* factor 2 disfavors discretionary denial.

### **3. *Fintiv* Factors 3 And 4 Disfavor Denial**

There is no parallel proceeding between PO and Petitioner in a district court. Thus, neither party nor any district court has invested any resources in a way that would support discretionary denial. Factors 3 and 4 disfavor denial.

### **4. *Fintiv* Factor 5 Disfavors Denial**

There is no parallel proceeding between PO and Petitioner in a district court and the '529 Patent has not been the subject of any other district court or Federal Circuit proceedings. Factor 5 disfavors denial.

### **5. *Fintiv* Factor 6 Disfavors Denial**

As discussed above, *Fintiv* Factors 1-5 disfavor discretionary denial. Thus, the Board need not consider Factor 6. *Commscope Tech. LLC v. Dali Wireless, Inc.*, IPR2022-01242, Paper 23 (PTAB Feb. 27, 2023). But, as noted herein, compelling art, prior adjudication, and the public interest all compel institution.

#### **IV. OTHER FACTORS ALSO DISFAVOR DISCRETIONARY DENIAL**

The Memorandum explicitly contemplates consideration of discretionary denial against the backdrop of “Compelling economic, public health, or national security interests” and “Settled expectations of the parties.” Memorandum, 2. All of these interests are at issue in this IPR and overwhelmingly weigh against discretionary denial.

##### **A. Compelling Economic Interest In Accelerating Access To Biosimilars**

##### **1. Biosimilars Play A Critical Role In Advancing Access To Lower Cost Options For Treatment**

Biosimilars and the BPCIA have contributed to a significant expansion of the biologics industry. As summarized by IQVIA in 2023, “The U.S. biologics market has grown 12.5% annually on average over the last five years on an invoice-price basis, faster than non-biologics, and now comprising 46% of spending.” EX1087. However, compared to small-molecule drugs, biologics are more costly to produce, partly due to their complexity. The Biosimilars Forum recently noted that reference biologic drugs “were 46% of U.S. prescription drug spending in 2022 despite only making up 3% of prescriptions. Patient and taxpayer spending on biologics increased from \$100 billion to \$260 billion (adjusted for inflation) over the last decade.” EX1088. Notably, biosimilars have been reported to consistently drive down drug costs, averaging more than 40 percent less than the

reference brand at biosimilar launch, and providing \$12.4 billion in savings in 2023. EX1089, 7-9.

Petitioner has been a pioneer in the science of biotechnology—using living cells to make “large molecule” medicines, also called “biologics,” such as proteins and antibodies. Petitioner helped invent the processes and tools that built the global biotech industry—turning it into what is today the leading source of new therapies for patients—and currently has over two dozen products on the market that treat diseases as wide ranging as anemia, rheumatoid arthritis and post-menopausal osteoporosis and life-threatening illnesses like cardiovascular disease and cancer.

In view of its extensive manufacturing and clinical development capabilities for biologics, Petitioner has chosen to also apply this expertise to reach additional patients by bringing biosimilar products to the market. While innovators ought to be rewarded for making new and important biologic discoveries and deserve patent protection for those discoveries, once valid patent protection expires, the introduction of biosimilars is important for patients. Biosimilars have the potential to lower healthcare costs and bring savings to both patients and the healthcare system. Biosimilars increase competition in the marketplace, generally cost less to develop compared to originator biologics.

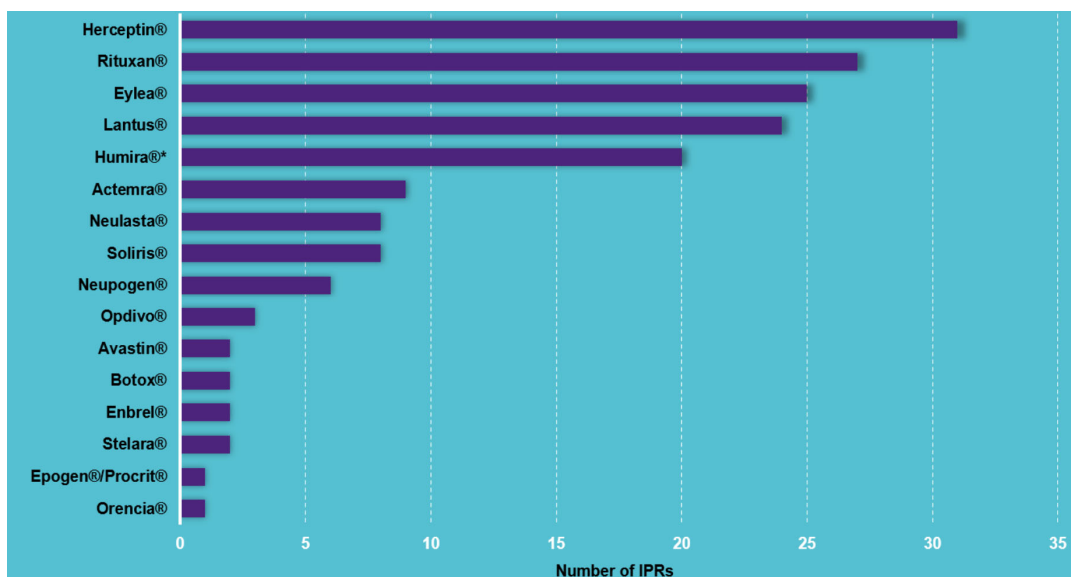
The '529 Patent represents an example of a mistakenly granted patent claiming an otherwise unpatentable method of treatment, standing in the way of

fair competition by companies otherwise seeking to market biosimilars of Opdivo®. Since Opdivo® is already patented for a full statutory period, that exclusivity should not be extended by an additional patent that recites little more than applying a known combination to a known indication.

## **2. IPRs Play An Important Role In Advancing Biosimilars To Market.**

A first biosimilar developer for a biologic generally faces significant patent uncertainty. This is especially relevant for the development of anti-PD-1 biosimilars given the large number of indications for which these antibodies have been approved and the large numbers of patents related to these indications. Even for biosimilar developers who later participate in the Patent Exchange, IPRs can increase efficiency in biosimilar development by reducing the issues (particularly those stemming from patent office error) necessary to litigate.

IPRs have been effectively used by biosimilar developers to clear a path to market entry. Overall, approximately 165 biosimilar-related IPRs have been filed, challenging 77 patents covering 16 CDER-listed Reference Products (EX1083), as reflected in the graph shown below. EX1084.



Out of the number of patents that have been subject to biosimilar-related IPRs and litigation, approximately 23% were subject to only IPRs, meaning that disputes over those patents were resolved without the need for time-consuming and costly litigation, to the benefit of the American public. EX1085.

As noted in a White Paper published by The Biosimilars Council “IPRs lend high value to biosimilar companies by providing a more accurate picture of the patent landscape in a *timely and less-expensive manner than typical biosimilar litigation*. This value is compounded by the ability of the biosimilar manufacturer to file IPRs earlier in the development process so that there is certainty in how to proceed . . . Successful IPR challenges are *more efficient than the patent challenge* procedures in court—getting biosimilar drugs into patients’ hands faster.” EX1086, 8 (emphasis added). In view of the current Administration’s

priority to promote and accelerate biosimilar development and commercialization, IPRs such as those requested in the Petition should be evaluated on their merits.

**B. The Petition Was Timely Filed In Accordance With The Settled Expectations Of The Parties**

When the '529 Patent issued in 2022, Petitioner had not even begun its clinical trials on its biosimilar product, and due to the pediatric exclusivity afforded to Opdivo®, Petitioner's product cannot be approved by the FDA until June 2027. Even now, Petitioner is still preparing its aBLA and does not face an infringement lawsuit over the '529 Patent. In view of this sequence of events, Petitioner's filing of the instant petition in early 2025 was not untimely.

In addition, PO has argued in prior litigation that where a competitor initiated an IPR too early (*i.e.*, prior to having an approved product threatened by the challenged claims), it did not have standing to appeal an adverse decision. *Momenta Pharms, Inc. v. Bristol-Myers Squibb Co.*, 915 F.3d 764, 766 (Fed. Cir. 2019). PO's argument that Petitioner filed the instant IPR too late is directly contradictory to its prior arguments that IPRs filed prior to product approval were too early.

Moreover, the 2023 revocation of the European equivalent to the '529 Patent (EP3464373B1 (EX1074)) demonstrated the merits of a challenge to the corresponding U.S. Patent. Petitioner has balanced an extensive series of

competing risks and incentives in bringing a challenge to the '529 Patent and did so in a timely manner and without delay.

**C. A Core Function of IPRs is to Address Errors<sup>5</sup> Made by the Patent Office During Prosecution to Avoid the Time and Cost of Litigation**

The '529 Patent is a clear example of a patent that would not have granted but for an error during examination. It is therefore a highly appropriate patent to challenge via IPR. The Examiner *did not make any prior art rejections* during prosecution of the '529 Patent despite the claims being broadly directed to a combination of drugs known in the art to treat an indication also known in the art. This is in striking contrast to the six Notices of Opposition challenging the corresponding European patent, which included a combined 71 references (EX1078) —including the two primary references relied on in this proceeding— and which resulted in revocation of the corresponding European patent. EX1075. As discussed above, in Europe, PO effectively conceded the unpatentability of its claims through its admission of disapproval of the granted text of such claims and requested revocation of the patent. Yet the equivalent patent remains valid in the U.S. Since Opdivo® is already patented for a full statutory period, that exclusivity

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<sup>5</sup> PO did not argue that the Board should exercise its discretion under 35 USC §325(d), so Petitioner does not address that question here.

should not be extended by an additional patent that recites little more than applying a known combination to a known indication.

The revocation of counterpart claims in Europe following the filing of six Notices of Opposition against such claims based on art similar to that advanced in the Petition is powerful evidence of the Petition's strong merits. Discretionary denial should be rejected while the merits are considered.

## **V. THE APPLICATION OF THE INTERIM MEMO IS UNCONSTITUTIONAL**

The Director's Memorandum was issued on March 26, 2025 and has been applied retroactively by PO here to petitions filed on February 28, 2025 that followed a previous administration memo. If the Memorandum and application of its newly introduced factors relating to discretionary denial are used to deny Petitioner's statutory right to pursue *inter partes* review, then the Memorandum and its application have exceeded the Director's powers and ignored notice-and-comment rulemaking processes. Such a denial would violate at least Petitioner's 5th Amendment's Due Process Clause by retroactively applying the new factors of the March Memo in contravention of statutory authority.

Petitioner reserves all rights to pursue constitutional challenges to any improper retroactive application of the Memorandum to this IPR filing.

## **VI. CONCLUSION**

For at least the foregoing reasons, Petitioner respectfully requests that the Director decline to exercise her discretion in denying institution and instead refer consideration to the merits panel for further review.

Respectfully submitted,

Date: July 10, 2025

/Scott A. McKeown/

Scott A. McKeown, Reg. No. 42,866  
WOLF, GREENFIELD & SACKS, P.C

**CERTIFICATE OF WORD COUNT**

Pursuant to 37 C.F.R. § 42.24, the undersigned certifies that the foregoing  
**PETITIONER'S OPPOSITION TO PATENT OWNER'S  
DISCRETIONARY DENIAL BRIEF** contains 4,860 words excluding; a table of  
contents, a table of authorities, a certificate of service or word count, or appendix  
of exhibits or claim listing. Petitioner has relied on the word count feature of the  
word processing system used to create this paper in making this certification.

Date: July 10, 2025

/MacAulay Rush/  
MacAulay Rush  
Paralegal  
WOLF, GREENFIELD & SACKS, P.C.

**CERTIFICATE OF SERVICE UNDER 37 C.F.R. § 42.6 (e)(4)**

I certify that on July 10, 2025, a copy of the foregoing document, including any exhibits filed therewith, is being served via electronic mail, as previously consented to by Patent Owner, upon the following:

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Date: July 10, 2025

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