

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMGEN INC.,
Petitioner

v.

BRISTOL-MYERS SQUIBB COMPANY,
Patent Owner

IPR2025-00602
Patent No. 10,174,113

**PATENT OWNER'S REQUEST
FOR DISCRETIONARY DENIAL**

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	BACKGROUND	4
A.	Immunotherapy and BMS's Development of OPDIVO®	4
B.	The '113 Patent.....	7
C.	Amgen	8
D.	Amgen's IPR Petition.....	9
III.	DISCRETIONARY DENIAL IS APPROPRIATE UNDER SECTION 325(d).....	11
A.	Amgen's Arguments are Based on Art that is Substantially the Same as Art Previously Presented and Considered During Prosecution (<i>Advanced Bionics</i> Step 1, <i>Becton, Dickinson</i> Factors (a), (b), (d))	12
1.	Prior Art with the Anti-LAG-3/PD-1 Antibody Combination was Presented to and Considered by the Examiner	13
2.	Prior Art with Anti-PD-1/Anti-CTLA-4 Combinations was Presented to and Considered by the Examiner	19
3.	Amgen's Additional Art Was Presented and Considered by the Examiner	23
B.	Amgen Failed to Show Material Error (<i>Advanced Bionics</i> Step 2, <i>Becton, Dickinson</i> Factors (c), (e), (f))	23
IV.	THE MERITS OF THE PETITION ARE UNLIKELY TO PREVAIL.....	27
V.	AMGEN RELIES ON EXPERT OPINIONS THAT ARE CONCLUSORY AND GO BEYOND THE PRIOR ART	30
VI.	AMGEN'S PATENTABILITY CHALLENGES ARE MORE APPROPRIATELY DEALT WITH THROUGH THE STATUTORILY CREATED BPCIA.....	32
VII.	ADDITIONAL FACTORS ALSO SUPPORT DISCRETIONARY DENIAL.....	34
VIII.	CONCLUSION.....	35

TABLE OF AUTHORITIES

Page(s)

Cases

<i>Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH</i> , IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020).....	<i>passim</i>
<i>Becton, Dickinson & Co. v. B. Braun Melsungen AG</i> , IPR2017-01586, Paper 8 (P.T.A.B. Dec. 15, 2017)	12, 18, 23
<i>Ecto World, LLC v. RAI Strategic Holdings, Inc.</i> , IPR2024-01280, Paper 13 (P.T.A.B. May 19, 2025)	12, 18
<i>Fitesa Simpsonville, Inc. v. Proctor & Gamble Co.</i> , IPR2023-01451, Paper 11 (P.T.A.B. Mar. 20, 2024).....	25
<i>Irhythm Techs., Inc. v. Welch Allyn, Inc.</i> , IPR2025-00363, Paper 10 (P.T.A.B. Jun. 6, 2025)	34
<i>Ivantis, Inc. v. Sight Sci., Inc.</i> , IPR2022-01540, Paper 14 (P.T.A.B. Mar. 22, 2023).....	25
<i>Janssen Biotech, Inc., v. United States</i> , IPR2021-01484, Paper 10 (P.T.A.B. Mar. 2, 2022).....	24
<i>Ocado Grp. PLC v. AutoStore Tech. AS</i> , IPR2021-00412, Paper 9 (P.T.A.B. July 21, 2021).....	26, 27
<i>Xerox Corp. v. Bytemark, Inc.</i> , IPR2022-00624, Paper 12 (P.T.A.B. Feb. 10, 2023).....	30

Statutes

35 U.S.C. § 311(b)	30
35 U.S.C. § 314(a)	3
35 U.S.C. § 325(d)	2, 11, 26
42 U.S.C. § 262(i)	33

IPR2025-00602
U.S. Patent No. 10,174,113

42 U.S.C. § 262(k)	8, 32, 33
42 U.S.C. § 262(l)	8, 9, 32, 33

Regulations and Procedures

37 C.F.R. § 42.65(a).....	30
MPEP (9th ed. Rev. 01.2024) §§ 707.05, 1302.01, 2103	23, 24

EXHIBITS

Exhibit	Description
EX2001	U.S. Patent No. 9,856,320
EX2002	Press Release, Bristol-Myers Squibb, <i>FDA Approves Yervoy™ (ipilimumab) for the Treatment of Patients with Newly Diagnosed or Previously-Treated Unresectable or Metastatic Melanoma, the Deadliest Form of Skin Cancer</i> (Mar. 25, 2011), available at https://news.bms.com/news/details/2011/FDA-Approves-YERVOY-ipilimumab-for-the-Treatment-of-Patients-with-Newly-Diagnosed-or-Previously-Treated-Unresectable-or-Metastatic-Melanoma-the-Deadliest-Form-of-Skin-Cancer/default.aspx
EX2003	Press Release, Bristol-Myers Squibb, <i>Bristol-Myers Squibb Receives Accelerated Approval of Opdivo (nivolumab) from the U.S. Food and Drug Administration</i> (Dec. 22, 2014), available at https://news.bms.com/news/details/2014/Bristol-Myers-Squibb-Receives-Accelerated-Approval-of-Opdivo-nivolumab-from-the-US-Food-and-Drug-Administration/default.aspx
EX2004	YERVOY, FDA Approved label and prescribing information, Rev. 5/2025
EX2005	OPDIVO, FDA Approved label and prescribing information, Rev. 5/2025
EX2006	Amgen Pipeline, available at https://www.amgenpipeline.com/
EX2007	NCT05907122, “A Study to Evaluate Similarity of ABP 206 Compared With OPDIVO® (Nivolumab) in Subjects With Resected Melanoma” (Last Update Posted Nov. 27, 2024), available at https://clinicaltrials.gov/study/NCT05907122?term=NCT05907122&rank=1
EX2008	Press Release, Amgen, <i>Amgen Reports First Quarter 2025 Financial Results</i> (May 1, 2025), available at https://www.amgen.com/newsroom/press-releases/2025/05/amgen-reports-first-quarter-2025-financial-results
EX2009	Press Release, Amgen, <i>Amgen Reports Fourth Quarter and Full Year 2024 Financial Results</i> (Feb. 4, 2025), available at https://www.amgen.com/newsroom/press-releases/2025/02/amgen-reports-fourth-quarter-and-full-year-2024-financial-results
EX2010	U.S. Patent Appl. No. 15/021,102
EX2011	U.S. Patent No. 8,008,449
EX2012	U.S. Patent No. 8,779,105

IPR2025-00602

U.S. Patent No. 10,174,113

Exhibit	Description
EX2013	U.S. Patent No. 9,084,776
EX2014	U.S. Patent No. 9,358,289
EX2015	U.S. Patent No. 9,387,247
EX2016	U.S. Patent No. 9,492,539
EX2017	U.S. Patent No. 9,492,540
EX2018	U.S. Patent No. 10,441,655
EX2019	File History, U.S. Patent Appl. No. 15/021,102, Amendment and Reply Under 37 C.F.R. § 1.111 (Apr. 9, 2018)
EX2020	File History, U.S. Patent Appl. No. 15/021,102, Notice of Allowance and Fee(s) Due (May 23, 2018)
EX2021	Amgen Biosimilars, available at https://www.amgen.com/science/biosimilars

BMS respectfully submits this brief requesting discretionary denial in response to the Petition for inter partes review filed by Amgen Inc. challenging the patentability of claims 1-20 of U.S. Patent No. 10,174,113 (“the ’113 Patent,” EX1001).

I. INTRODUCTION

BMS and its collaborators revolutionized cancer treatment by developing novel methods of treating by administering antibodies that bind to PD-1 and CTLA-4, two proteins involved in regulating the immune system, and altering the patient’s immune response. These groundbreaking methods of treatment for cancer fall within a field known as “immunotherapy.” The PTO recognized these innovations and granted BMS multiple patents directed to anti-PD-1 and anti-CTLA-4 antibodies, and various methods of treating cancer by administering such antibodies.

The ’113 Patent relates to methods of treating melanoma patients with a specific multi-part regimen that starts with a combination of weight-based doses of anti-PD-1 and anti-CTLA-4 antibodies and continues with flat (non-weight-based) doses of the anti-PD-1 antibody. The innovations protected by the ’113 Patent are the results of BMS’s extensive research and clinical trials programs. The claimed dosing regimen aligns with an approved indication on the label for BMS’s anti-PD-1

antibody OPDIVO® used in combination with its FDA-approved anti-CTLA-4 antibody YERVOY® for the treatment of melanoma.

In its Petition, Amgen argues that the patentability of every claim of the '113 Patent should be reassessed. Consistent with the guidance set forth in the Director's March 26, 2025 Memorandum entitled "Interim Processes for PTAB Workload Management" ("Memorandum"), there are multiple independent reasons why the Director should exercise her discretion to deny institution of Amgen's Petition.

First, the Director should deny institution under 35 U.S.C. § 325(d) because the art and arguments relied upon in every Ground are the same or substantially the same as those considered by the Examiner during prosecution of the '113 Patent. A published patent application, Korman WO 2015/042246 ("Korman") (EX1002, 161-254) was considered and is substantially the same as Amgen's proposed prior art NCT-109. In addition, the Wolchok publication (EX1017) was considered and is substantially the same as Amgen's proposed prior art, NCT-505 and Postow. The Examiner applied Wolchok in making anticipation rejections during prosecution. In sum, Amgen's art is substantially the same as art already considered by the Examiner, and Amgen failed to show that the Examiner made any material error.

Second, Amgen's unpatentability challenges are unlikely to succeed. Amgen's obviousness arguments rely on proposed modifications to existing treatment regimens that are not supported by the prior art. And every one of Amgen's

grounds relies on its mischaracterization of the NCT-109 reference. According to Amgen, “NCT-109 discloses anti-PD-1 monotherapy as a flat dose.” Pet., 17. But NCT-109 **does not** disclose any anti-PD-1 antibody monotherapy.

Third, Amgen improperly relies on expert testimony that is conclusory and goes beyond the scope of the patents and printed prior art that must form the basis for Grounds in *inter partes* review.

Fourth, the Director should exercise her discretion to deny institution of this IPR under 35 U.S.C. § 314(a) because the ’113 Patent will be among the patents addressed between BMS and Amgen in the course of the statutorily provided Biologics and Price Competition Act (“BPCIA”) proceedings that will initiate shortly after Amgen’s filing of an abbreviated Biologics License Application (“aBLA”) for its biosimilar copy of BMS’s OPDIVO®. Amgen has repeatedly signaled to the market that it expects registrational data for its OPDIVO® biosimilar in the second half of this year, and the FDA’s acceptance of Amgen’s data submission will trigger the patent litigation mechanisms of the BPCIA, beginning with the Patent Dance. In the Patent Dance, the parties are required to exchange detailed contentions regarding both infringement and the validity of the ’113 Patent. These exchanges are statutorily mandated by the BPCIA regardless of whether an IPR is instituted and they culminate in the filing of a complaint in district court. Because the parties will likely begin the Patent Dance this year and it only takes 8-9 months

to complete these extensive exchanges and begin litigation, an IPR based on this Petition will guarantee duplicative proceedings and waste PTO resources. And the Patent Dance will involve additional patents not challenged by Amgen in IPRs. Thus, BPCIA proceedings will go forward regardless of institution here. Put simply, there is no scenario in which a favorable outcome for Amgen here will avoid BPCIA litigation.

Finally, additional relevant considerations identified in the Memorandum support discretionary denial, including how long the claims have been in force and the lack of any relevant change in law.

For all of these reasons, the Director should exercise her discretion and deny institution.

II. BACKGROUND

A. Immunotherapy and BMS's Development of OPDIVO®

The human immune system is formed of organs, specialized cells, and substances that protect individuals from infections and disease. T cells are one class of specialized cells that play an important role in the human immune system. One major function of T cells is to destroy pathogens and cancer cells, and to do that the T cells must distinguish between healthy cells and cells that are infected or cancerous. EX2001, 1:33-38; EX1001, 1:45-48. One way in which T cells facilitate

this task is through the activation or deactivation of different receptors on the T cell surface.

One of the receptors that T cells express on their surface is a protein called programmed death-1 receptor (“PD-1”). PD-1 acts as a brake on the immune system by downregulating T cell activity to prevent T cells from killing healthy cells. Cytotoxic T lymphocyte-associated protein 4 (“CTLA-4”) is another inhibitory receptor found on T cells that also acts as a brake on the immune system by downregulating T cell activity. EX1001, 1:53-65.

Immunotherapy is a type of treatment that functions by taking advantage of aspects of a patient’s immune response to fight disease. One form of immunotherapy involves using antibodies to manipulate the immune response. In particular and as relevant here, antibodies that bind to PD-1 (“anti-PD-1 antibodies”) and CTLA-4 (“anti-CTLA-4 antibodies”) can be used to disarm or block the activity of these inhibitory receptors. By blocking the PD-1 and CTLA-4 inhibitory receptors, these antibodies are able to increase or activate an immune response. *Id.* More specifically, by binding to PD-1 and CTLA-4, respectively, these antibodies shut off the brakes on the immune system, freeing the immune cells to recognize, attack and destroy cancer cells. EX2001, 1:57-2:25.

BMS led the industry in developing antibodies that could be used in novel methods of immunotherapy for the treatment of cancer. BMS put its scientific

breakthroughs into practice by developing an anti-CTLA-4 antibody called YERVOY® (ipilimumab) and an anti-PD-1 antibody called OPDIVO® (nivolumab). YERVOY®, approved in March 2011, was the first immune checkpoint inhibitor approved by the FDA for the treatment of cancer. EX2002. Clinical testing of OPDIVO® and YERVOY® confirmed the remarkable promise of checkpoint inhibitors as targets for immunotherapy. OPDIVO®, first approved in Japan in 2014, was the first anti-PD-1 antibody approved anywhere in the world for cancer treatment, and, in December 2014, it was approved in the United States for the treatment of melanoma. EX2003.

Following these initial approvals, BMS continued investing in research and clinical trials aimed at developing novel dosages and treatment regimens to treat patients with cancer. BMS's groundbreaking work included extensive research related to the administration of anti-PD-1 and anti-CTLA-4 antibodies alone and in combination for the treatment of various cancers, and is reflected in BMS's FDA-approved label for OPDIVO®, which includes indications for non-small cell lung cancer, urothelial carcinoma, renal cell carcinoma, head and neck cancer, malignant pleural mesothelioma, lymphoma, colorectal cancer, hepatocellular carcinomas, esophageal cancer, and gastric cancers. EX2004; EX2005.

B. The '113 Patent

The '113 Patent protects certain uses of OPDIVO[®] for the treatment of melanoma. Specifically, the '113 Patent relates to treating patients with a multi-part regimen. In the first part, patients receive a combination of an anti-PD-1 antibody (like nivolumab) and an anti-CTLA-4 antibody (like YERVOY[®] (ipilimumab)). In that combination, the anti-PD-1 antibody doses are based on the patient's weight. For example, in the regimen in claim 2 of the '113 Patent, the patient is administered:

about 1 mg/kg of an antibody or an antigen-binding portion thereof that binds specifically to a human PD-1 ("an anti-PD-1 antibody") and a dose of an antibody or an antigen-binding portion thereof that binds specifically to a human CTLA-4 ("an anti-CTLA-4 antibody") every three weeks for about 4 doses

EX1001, cl. 2. This is followed by the second part of the regimen, where patients receive the anti-PD-1 antibody at "a flat dose of about 240 mg or about 480 mg."

Id. The flat dose is administered without regard for the patient's body weight—every patient gets the same amount. Every claim of the '113 Patent is directed to (1) weight-based dosing for the anti-PD-1/anti-CTLA-4 combination part of the regimen, and (2) flat dosing for the anti-PD-1 monotherapy part of the regimen. That multi-part regimen is not found in the prior art.

C. Amgen

Amgen is currently developing an OPDIVO[®] biosimilar (i.e., a copy) named ABP 206. EX2006. Amgen is conducting clinical trials designed to show the similarity between ABP 206 and BMS's OPDIVO[®] so that it can rely on data BMS has spent more than a decade generating to obtain FDA approval through an abbreviated pathway. EX2007; *see also* 42 U.S.C. § 262(k). It can do so by taking advantage of the statutory scheme set forth in the BPCIA, which Congress passed as part of the Affordable Care Act in 2010. In that same statute, Congress included protections for companies like BMS that develop innovative biologics and are targeted by biosimilar developers. 42 U.S.C. § 262(l). In particular, the BPCIA includes a step-by-step process for the identification of all patents potentially implicated by the potential biosimilar product and resolution of any disputes regarding those patents. 42 U.S.C. § 262(l)(3)-(6).

If approved, Amgen's biosimilar version of OPDIVO[®] will be sold with a label that copies the information from BMS's OPDIVO[®] label. Although the approval date remains uncertain, Amgen has repeatedly stated that it anticipates a readout from its similarity study in the second half of this year. EX2008, 21; EX2009, 23. As Amgen has foreshadowed in its communications with investors, data from Amgen's clinical trial will undoubtedly be used for the submission of an aBLA relying on OPDIVO[®] as a reference product. The FDA's acceptance of

Amgen's aBLA will statutorily trigger a patent resolution mechanism that begins with a series of detailed exchanges collectively known as the "Patent Dance" and culminates in the filing of a complaint for patent infringement. 42 U.S.C. § 262(l)(2)-(6). With its Petition, Amgen seeks to duplicate that work, wasting both the PTO's and the parties' resources.

D. Amgen's IPR Petition

Amgen filed its Petition on February 28, 2025 along with two other petitions (IPR2025-00601 and IPR2025-00603), both of which challenge patents in other families that are also owned by BMS. All three of the challenged patents claim novel methods of treating cancer with combinations of anti-PD-1 and anti-CTLA-4 antibodies that cover aspects of BMS's label for OPDIVO®. Although the Petitions are substantively unique, relying on different references and different technical experts, the patents challenged in the Amgen Petitions all protect indications on OPDIVO®'s label and fall within the scope of patents that would be subject to the BPCIA Patent Dance and litigation.

For this Petition, Amgen argues that the claims of the '113 Patent would have been obvious over combinations of prior art that are gathered into 4 grounds for unpatentability. To piece together the multiple parts of the claimed regimens, Amgen relies first on disclosures in NCT-505 (in Grounds 1 and 2) and Postow (in Grounds 3 and 4). Amgen points to two-part treatment regimens beginning with

(1) combinations of weight-based doses of anti-PD-1 and anti-CTLA-4 antibodies, followed by (2) monotherapy with weight-based doses of an anti-PD-1 antibody. Importantly, those prior art disclosures use weight-based dosing in both the combination step **and** the monotherapy step.

Amgen argues that a POSA would have modified the second part—the weight-based anti-PD-1 antibody monotherapy—of the NCT-505 and Postow regimens, but only that part. Amgen relies on NCT-109 for its argument that a POSA would implement flat dosing for anti-PD-1 antibody monotherapy. Every Amgen ground relies on the combination of either NCT-505 or Postow (for the weight-based combo) and NCT-109 (for the flat dose).

According to Amgen, “NCT-109 discloses anti-PD-1 monotherapy as a flat dose—including 240 mg nivolumab once every two weeks to treat melanoma tumors.” Pet., 17. But Amgen mischaracterizes the reference. NCT-109 does not disclose any anti-PD-1 antibody monotherapy. Instead, it describes a dose escalation protocol for testing a different antibody that targets a different protein, LAG-3, with or without nivolumab. The **only** use of nivolumab (called BMS-936558 in the study) is with the LAG-3 antibody (called BMS-986016). EX1007, 5 (describing “BMS-986016 + BMS-936558” in Parts B and C). No anti-PD-1 antibody is administered as a monotherapy in NCT-109. Amgen then argues that this combined anti-LAG-3/anti-PD-1 antibody treatment would have somehow led a POSA to

modify the monotherapy part of the of NCT-505 and Postow regimens but leave the combination part of those regimens unchanged. This mischaracterization of NCT-109 underlies all of Amgen's grounds.

For dependent claims 5-9 and 16, Amgen adds another reference, the Cogswell application, to its combinations (in Grounds 2 and 4) to add in limitations directed to, for example, PD-L1 testing and additional therapeutic agents. For each of those claims, Amgen's Grounds depend on the combinations of NCT-109, NCT-505, and/or Postow described above.

BMS will discuss the details of these references in its POPR. As discussed below, references that are substantially the same as each of NCT-505, Postow, and NCT-109 were presented to the Office during prosecution. Cogswell was also considered and is on the face of the '113 Patent.

III. DISCRETIONARY DENIAL IS APPROPRIATE UNDER SECTION 325(d)

The Director should exercise her discretion to deny institution under Section 325(d) because the Petition presents art and arguments that rely on "the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d). The two-part framework for analyzing denial under Section 325(d), set forth in *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (P.T.A.B. Feb. 13, 2020) (precedential), is

satisfied here because (1) the same or substantially the same prior art or argument was presented to the Office, and (2) Amgen has not demonstrated that the Office erred in a manner material to the patentability of the claims of the '113 Patent. Discretionary denial is appropriate.

A. Amgen's Arguments are Based on Art that is Substantially the Same as Art Previously Presented and Considered During Prosecution (*Advanced Bionics* Step 1, *Becton, Dickinson* Factors (a), (b), (d))

Amgen argues that its asserted references NCT-109, NCT-505, and Postow are new and could not have been considered during prosecution of the '113 Patent. But the art and arguments presented in the Petition were considered by the Examiner and are cumulative of the art evaluated during prosecution. The first step of the *Advanced Bionics* test is met. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8 (“whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office”); *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17-18 (P.T.A.B. Dec. 15, 2017) (precedential as to § III.C.5); *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 3 (P.T.A.B. May 19, 2025).

1. Prior Art with the Anti-LAG-3/PD-1 Antibody Combination was Presented to and Considered by the Examiner

For every ground, Amgen relies on the anti-LAG-3 antibody dose escalation study in NCT-109. Amgen mischaracterizes NCT-109 as disclosing “anti-PD-1 monotherapy as a flat dose—including 240 mg nivolumab once every two weeks to treat melanoma tumors.” Pet., 17. Amgen then goes on to suggest that only the anti-PD-1 antibody is present. (Pet., 19, 24, 28-29, 34-35, 47-48, 52). But Amgen leaves out the fact that the anti-PD-1 antibody is not used as monotherapy in NCT-109; instead, it is always used in combination with the anti-LAG-3 antibody BMS-986016. EX1007, 5 (describing “BMS-986016 + BMS-936558”). NCT-109 simply does not disclose a flat dose of anti-PD-1 antibody monotherapy.

Even so, the exact combination of anti-LAG-3/anti-PD-1 antibody doses in NCT-109 was presented to the Examiner during prosecution when BMS submitted published patent application WO 2015/042246 (“Korman”). See EX1002, 161-254. As described below, BMS submitted Korman in an IDS on May 29, 2018 (*id.* at 80-85) **the exact same day** that it amended the pending claims to include the flat dose step that overcame the prior art. *Id.* at 67-79. Korman was not buried; the IDS contained only 23 references. *Id.* at 80-85. In addition, the anti-LAG-3/PD-1 disclosure was not new to the Examiner—he was, at the same time, examining application 15/021,102 from the same Korman family (EX2010) with the identical

disclosure of the flat dose anti-LAG-3/PD-1 treatment. Amgen's Petition says nothing at all about this Korman disclosure.

Specifically, Korman, entitled "Combination of Anti-LAG-3 Antibodies and Anti-PD-1 Antibodies to Treat Tumors" (EX1002, 161), describes the study design for a Phase 1 dose escalation clinical study of the anti-LAG-3 antibody named BMS-986016 and the anti-PD-1 antibody named BMS-936558 (nivolumab). *Id.* at 195. The study design is shown schematically:

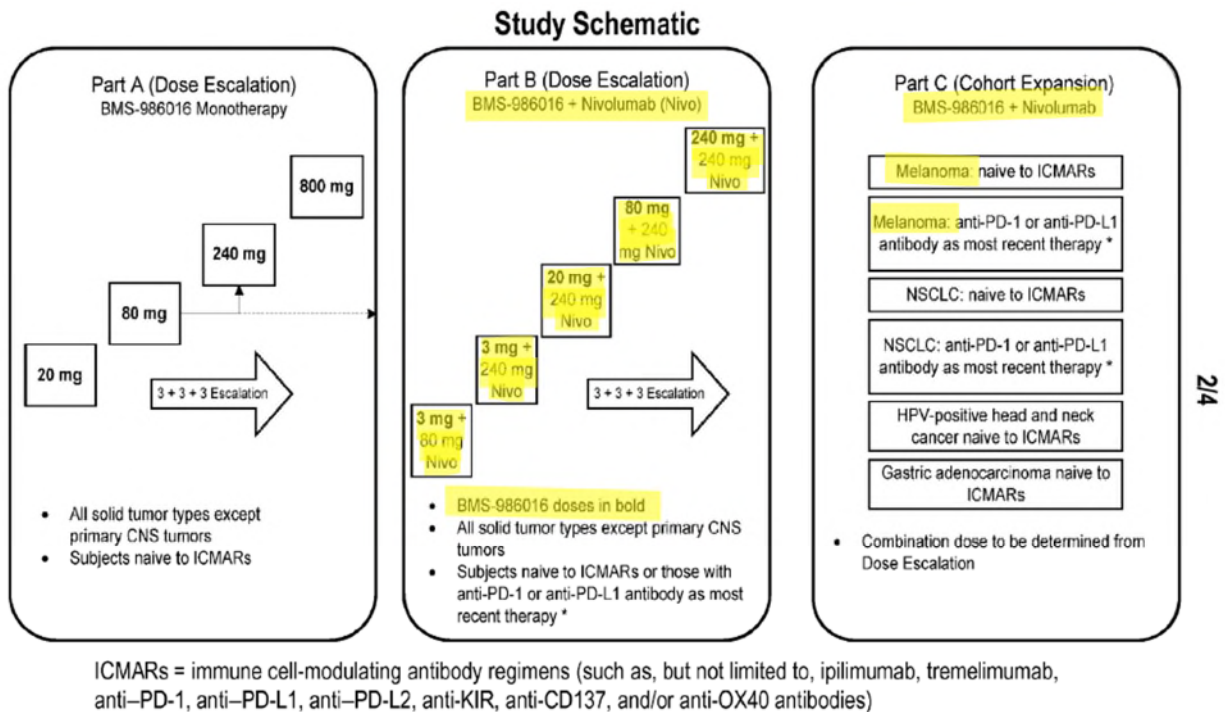
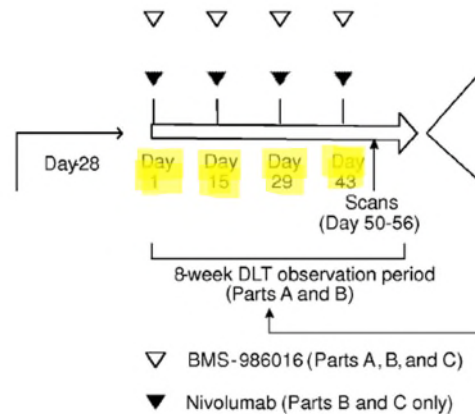


Fig. 2A

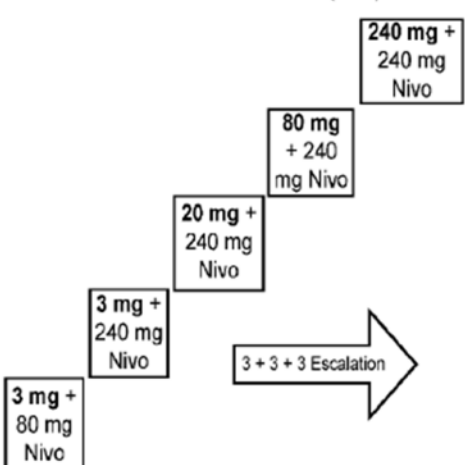
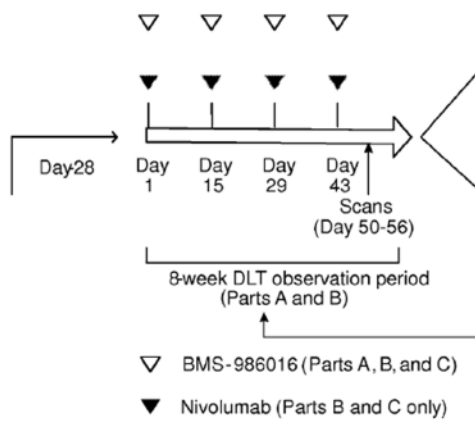
Id. at 248, Fig. 2A. As shown, the anti-PD-1 antibody ("Nivo") is administered in the dose escalation at 80 or 240 mg in combination with the anti-LAG-3 antibody

BMS-986016. *Id.* The study includes patients with melanoma, shown in Part C above. The dosing schedule from this study design is every two weeks:



EX1002, 250, Fig. 3. The Korman claim set also describes the combination treatment “wherein . . . four doses of the anti-LAG-3 antibody are administered at a dose of 3, 20, 80, or 240 mg and four doses of the anti-PD-1 antibody are administered at a dose of 80 or 240 mg.” EX1002, 242, cl. 1.

For each part of NCT-109 (EX1007) that Amgen relies on, the Korman application describes the same substance.

Amgen's reliance on NCT-109	Korman WO 2015/042246
Experimental: Part B-Dose Escalation: BMS-986016 + BMS-936558 BMS-986016 3, 20, 80, and 240 mg solution + BMS-936558 80 and 240 mg solution intravenously, during each 8 week cycle: every 2 weeks (i.e. during weeks 1, 3, 5, 7), up to 96 weeks EX1007, 5.	Part B (Dose Escalation) BMS-986016 + Nivolumab (Nivo)  • BMS-986016 doses in bold • All solid tumor types except primary CNS tumors • Subjects naive to ICMARs or those with anti-PD-1 or anti-PD-L1 antibody as most recent therapy * EX1002, 248.  EX1002, 250.

Amgen’s reliance on NCT-109	Korman WO 2015/042246
Part C Cohort Expansion: Advanced (metastatic and/or unresectable) and incurable melanoma (with or without the last therapy being anti-PD-1 or anti-PD-L1); non-small cell lung cancer (NSCLC) (with or without the last therapy being anti-PD-1 or anti-PD-L1) (melanoma and NSCLC subjects with anti-PD-1 or anti-PDL-1 therapy must have been unresponsive and progressed within 16 weeks of starting therapy); human papilloma virus (HPV) positive head and neck squamous cell carcinomas; or gastric adenocarcinoma EX1007, 6.	Part C (Cohort Expansion) BMS-986016 + Nivolumab Melanoma: naive to ICMARs Melanoma: anti-PD-1 or anti-PD-L1 antibody as most recent therapy * NSCLC: naive to ICMARs NSCLC: anti-PD-1 or anti-PD-L1 antibody as most recent therapy * HPV-positive head and neck cancer naive to ICMARs Gastric adenocarcinoma naive to ICMARs Combination dose to be determined from Dose Escalation EX1002, 248. Subjects with “Melanoma: prior anti-CTLA-4 <u>and</u> anti-PD-1 or anti-PD-L1 antibody therapy” EX1002, 201-02 (Table 3B).

Quite simply, there is no difference between NCT-109 and Korman that is material to Amgen’s arguments.

Korman was presented to the Office. “Previously presented art includes . . . art provided to the Office by an applicant, such as on an Information Disclosure

Statement (IDS), in the prosecution history of the challenged patent.” *Advanced Bionics*, IPR2019-01469, Paper 6 at 7-8; *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17-18; *Ecto World*, IPR2024-01280, Paper 13 at 3. Here, BMS submitted Korman in an IDS on May 29, 2018 (EX1002, 80-85), the same date that the flat dose of anti-PD-1 antibody monotherapy limitation was added to the pending claims. EX1002, 67-79. The Examiner then indicated that he considered Korman along with the 22 other references submitted on the IDS. EX1002, 63; *see Ecto World*, IPR2024-01280, Paper 13 at 3.

Furthermore, during the same period in April and May 2018, the same Examiner, who has years of experience examining BMS’s patent applications about anti-PD-1 antibodies, anti-CTLA-4 antibodies, and immunotherapy methods, *see* EX2011; EX2012; EX2013; EX2014; EX2015; EX2016; EX2017; EX2018, was also examining the corresponding U.S. Korman patent application (15/021,102) (EX2010) disclosing the combined anti-LAG-3/PD-1 antibody treatment. For that Korman application, BMS submitted amended claims April 9, 2018 in response to the Examiner’s rejections, and the notice of allowance was sent May 23, 2018. EX2019 (2018-04-09 amendment); EX2020 (2018-05-23 notice of allowance). The content of Korman was available, and the Examiner was actively engaged with examining the corresponding U.S. Korman application.

There is nothing new in Amgen's argument. The substance of the anti-LAG-3/anti-PD-1 antibody combination therapy trial was provided to the Examiner in the form of the Korman application at the exact time the Examiner needed to consider flat dose limitations. Amgen ignores the reality of prosecution of this patent and does not even mention the Korman reference in its Petition.

2. Prior Art with Anti-PD-1/Anti-CTLA-4 Combinations was Presented to and Considered by the Examiner

Each of Amgen's Grounds is based on a regimen in NCT-505 or Postow where anti-PD-1 antibodies and anti-CTLA-4 antibodies are administered in weight-based doses. But these weight-based doses of anti-PD-1 and anti-CTLA-4 antibodies in combination were also in front of the Examiner, who applied them to make anticipation rejections during prosecution.

Wolchok was relied on by the Examiner during prosecution and describes a treatment regimen for patients with advanced melanoma. EX1017. In this Phase 1 trial, patients received (1) a combination of an anti-PD-1 antibody and an anti-CTLA-4 antibody for four cycles, followed by (2) anti-PD-1 antibody monotherapy. *Id.* at 123. Different cohorts received different specific doses, but all regimens were weight-based. Some patients, for example, were treated with a combination of 1 mg/kg anti-PD-1 antibody (nivolumab) and 3 mg/kg anti-CTLA-4 antibody (ipilimumab) followed by anti-PD-1 antibody monotherapy at 1 mg/kg. *Id.*

Wolchok disclosed clinical outcomes of these weight-based combinations. Specifically, for the 1 mg/kg nivolumab/3 mg/kg ipilimumab combination, 53% of patients had an objective response, all with tumor reduction of 80% or more. *Id.* at 122, 128. These disclosures correspond to Amgen’s proposed prior art NCT-505 and Postow.

NCT-505	Postow	Wolchok
Regimen Part 1: “Nivolumab 1 mg/kg” was “combined with Ipilimumab 3 mg/kg ... every 3 weeks for 4 doses” EX1014, 4.	Regimen Part 1: “ipilimumab (3 mg per kilogram of body weight) combined with either nivolumab (1 mg per kilogram) or placebo every 3 weeks for four doses” EX1005, 2006.	Regimen Part 1: “escalating doses of intravenous nivolumab and ipilimumab administered concurrently every 3 weeks for four doses” including cohort 2 receiving “1 mg of nivolumab per kilogram of body weight and 3 mg of ipilimumab per kilogram” EX1017, 123.
Regimen Part 2: nivolumab administered “3 mg/kg solution intravenously every 2 weeks” EX1014, 4.	Regimen Part 2: “nivolumab (3 mg per kilogram) or placebo every 2 weeks” EX1005, 2006.	Regimen Part 2: “nivolumab alone every 3 weeks for four doses” with cohort 2 receiving 1 mg/kg and other cohorts receiving 0.3 mg/kg, 3 mg/kg, 10 mg/kg. EX1017, 123.
	Clinical Outcomes:	Clinical Outcomes:

NCT-505	Postow	Wolchok
	“complete response was observed in 16 patients (22%) in the combination group” EX1005, 2009. “median change in investigator-assessed tumor volume was a 68.1% decrease in the combination group” EX1005, 2009. “the median progression-free survival was not reached with the combination therapy” EX1005, 2006.	“A total of 16 patients had tumor reduction of 80% or more at 12 weeks, including 5 with a complete response” EX1017, 128. “Among patients who received the maximum doses associated with an acceptable level of adverse events (cohort 2, with nivolumab at a dose of 1 mg per kilogram and ipilimumab at a dose of 3 mg per kilogram), objective responses occurred in 9 of 17 patients (53% . . .), including 3 with a complete response. All 9 patients who had a response had tumor reduction of 80% or more at their first scheduled assessment during treatment” EX1017, 128. “In the concurrent-regimen cohorts, across all dose levels, confirmed objective responses according to modified WHO criteria were

NCT-505	Postow	Wolchok
		observed in 21 of 52 patients (40% . . .) who had a response that could be evaluated” EX1017, 128.

The Examiner certainly understood this disclosure because he applied Wolchok to make anticipation rejections for pending claims with only weight-based dosing. EX1002, 433. BMS amended the second part of the claimed regimen from weight-based to flat dosing of anti-PD-1 antibody, distinguishing Wolchok. EX1002, 68.

Amgen now relies on the weight-based regimens of anti-PD-1 and anti-CTLA-4 antibodies and following up with PD-1 antibody monotherapy in NCT-505 and Postow. Amgen also points to clinical outcomes for these treatments in Postow. But as described above, the contents of NCT-505 and Postow are coextensive with Wolchok, which was distinguished during prosecution.

Faced with the Examiner’s detailed consideration of weight-based dosing in Wolchok, Amgen makes the half-hearted argument that the disclosures of NCT-505 and Postow are materially different because they disclose changing the weight-based dose at the monotherapy step to 3 mg/kg, rather than Wolchok’s 1 mg/kg. Pet., 66.

But that difference is immaterial to the patentability of the challenged claims. The claims do not recite anti-PD-1 antibody monotherapy with any specific weight-based dosing—the monotherapy portion of the claimed regimens uses *flat dosing* administered irrespective of weight. The difference between 1 mg/kg and 3 mg/kg is beside the point because not one of NCT-505, Postow, and Wolchok discloses a flat dose for anti-PD-1 antibody monotherapy.

3. Amgen’s Additional Art Was Presented and Considered by the Examiner

Amgen’s other alleged prior art was also before the Office. As Amgen concedes, the Cogswell application (EX1015) was cited by the Examiner and is on the face of the ’113 Patent. Pet., 16; EX1001.

B. Amgen Failed to Show Material Error (*Advanced Bionics* Step 2, *Becton, Dickinson* Factors (c), (e), (f))

Turning to the second part of the *Advanced Bionics* test, Amgen failed to show that the Examiner made any material error.

Amgen argues the Examiner erred by not issuing an obviousness rejection. Pet., 65-67. That speculative argument contravenes fundamental principles of patent examination. See MPEP (9th ed. Rev. 01.2024) § 707.05 (“The examiner must consider all the prior art references (*alone and in combination*) cited in the application or reexamination, including those cited by the applicant in a properly submitted Information Disclosure Statement.”); *id.* at § 2103 (“Under the principles

of compact prosecution, ***each claim should be reviewed for compliance with every statutory requirement for patentability*** in the initial review of the application, even if one or more claims are found to be deficient with respect to some statutory requirement. Thus, ***examiners should state all reasons and bases for rejecting claims in the first Office action.***”); *id.* at § 1302.01 (“When an application is apparently ready for allowance, it should be ***reviewed by the examiner to make certain that the whole application meets all formal and substantive (i.e., statutory) requirements*** and that the language of the claims is enabled by, and finds adequate descriptive support in, the application disclosure as originally filed.”) (emphases added); *see also Janssen Biotech, Inc., v. United States*, IPR2021-01484, Paper 10 at 29-30 (P.T.A.B. Mar. 2, 2022) (denying institution under Section 325(d) where the examiner, who was clearly familiar with the art, only issued an anticipation rejection and not an obviousness one).

The Examiner here rejected pending claims in the application as anticipated by the combination dosing regimens in Wolchok, which are substantially the same as those in the NCT-505 and Postow art that Amgen now relies on. Amending the claims to add the flat dose of anti-PD-1 antibody in the second portion of the regimen overcame the rejection. The Examiner did not misunderstand the flat dosing claim elements. To the contrary, after the amendment, the Examiner specifically focused on whether the ’113 Patent specification provided support for the use of a flat dose

of PD-1 antibodies in the monotherapy part of the regimen. EX1002, 57-59. The '113 patent specification does support that regimen, and when the applicant pointed to that support, the Examiner allowed the claims. EX1002 19-20, 37-41. As described above, the substance of the other art that Amgen now relies on, including the anti-LAG-3/PD-1 antibody combination study, was presented to the Examiner. The Examiner did not err, at a minimum, because none of that art describes monotherapy with a flat dose of an anti-PD-1 antibody.

Amgen cannot satisfy its burden to show material error by pointing out that the Examiner did not rely on Korman, which discloses anti-LAG-3/PD-1 antibody weight-based dosing, as the basis for a rejection. *See, e.g., Ivantis, Inc. v. Sight Sci., Inc.*, IPR2022-01540, Paper 14 at 14 (P.T.A.B. Mar. 22, 2023) (“To the extent Petitioner equates the examiner’s silence in discussing relevant prior art to a material error, we are not persuaded.”); *Fitesa Simpsonville, Inc. v. Proctor & Gamble Co.*, IPR2023-01451, Paper 11 at 21 (P.T.A.B. Mar. 20, 2024) (“Petitioner must demonstrate that the Examiner erred in the evaluation of the prior art, for example, by showing that the Examiner misapprehended or overlooked specific teachings in the relevant prior art”). Additionally, as described above, the Examiner has deep subject matter expertise and has examined many patent applications related to anti-PD-1 antibodies, including the Korman patent application. Korman is cumulative of the art Amgen relies on and, more importantly, there is no description of anti-PD-1

monotherapy flat dosing in Korman. That the Examiner did not cite Korman in a rejection does not establish material error—it evidences that the Examiner concluded that the disclosure of an anti-LAG-3/anti-PD-1 combination did not teach or suggest the claimed dosing regimen.

Amgen makes no argument that the Examiner made any material error particular to Cogswell, the other reference included in its combinations. And while the Director’s March 26 Memorandum provides for separate briefing and consideration of discretionary denial issues, the Memorandum should not open the door for Amgen to present arguments regarding Section 325(d) that were not included in the Petition. The Petition was filed prior to the Memorandum’s issuance, BMS’s arguments regarding Section 325(d)—which focus almost entirely on the content in the prosecution history—were foreseeable, and Amgen should have addressed all foreseeable Section 325(d) issues in its Petition.

Because Amgen (1) misrepresented the scope of the art and arguments considered by the Examiner under part 1 of *Advanced Bionics*, and (2) failed to identify a material error or new information that would lead to a different conclusion on the patentability for any challenged claim, the Director should exercise her discretion and deny institution pursuant to Section 325(d). *See Ocado Grp. PLC v. AutoStore Tech. AS*, IPR2021-00412, Paper 9 at 38 (P.T.A.B. July 21, 2021) (“[N]either Petitioner nor [its expert] present any argument or persuasive evidence

that there was any material error by the Office. This is a required element of Petitioner's burden to overcome our exercise of discretionary denial under Section 325(d).").

IV. THE MERITS OF THE PETITION ARE UNLIKELY TO PREVAIL

As outlined in the Memorandum, the strength of the merits of the Petition is relevant when considering whether to deny institution. Here, Amgen's obviousness arguments rely on proposed modifications to existing treatment regimens that are not supported by the prior art—a POSA would have had no motivation to combine the art in the manner Amgen suggests. And by focusing solely on modifying the monotherapy part of the claimed regimens, Amgen fails to consider the claims as a whole, which also **require** weight-based dosing of PD-1 antibodies for combination therapy.

Each of Amgen's arguments requires a finding that a POSA would have been motivated to modify a two-part regimen that starts with a weight-based anti-PD-1/CTLA-4 antibody combination therapy that is followed by a weight-based anti-PD-1 antibody monotherapy. That entirely weight-based regimen in NCT-505 and Postow is Amgen's starting point for every asserted Ground. For Amgen's arguments to succeed, that regimen must be gerrymandered in a particular way to reach a bifurcated regimen: the anti-PD-1 monotherapy changes to a flat dose, but the anti-PD-1/CTLA-4 combination therapy remains weight-based. But Amgen

points to nothing in the prior art that would motivate a POSA to make such a modification. Put simply, Amgen points to no reference or reasoning in the art that suggests a POSA would have administered a dosing regimen to a patient in which the patient first receives combination therapy of anti-PD-1 and anti-CTLA-4 antibodies that is dosed in a weight-based manner and then receives anti-PD-1 antibody monotherapy administered in a flat dose. Further, as discussed below (§ V), Amgen's reliance on conclusory declaration testimony from its expert is an additional factor in favor of discretionary denial.

Amgen's proposed modification suffers from two problems. First, Amgen provides no prior art support for using a Phase 1 dose escalation study of a different therapeutic agent, an anti-LAG-3 antibody, which is what NCT-109 describes, as a basis to change existing anti-PD-1 treatment regimens. EX1007. Amgen incorrectly describes NCT-109 as disclosing "monotherapy" with a flat dose of anti-PD-1 antibody (Pet., 17), leaving out the anti-LAG-3 antibody (Pet., 19, 24, 28-29, 34-35, 47-48, 52). But the dosing plan for the anti-LAG-3/anti-PD-1 antibody combination is for the purpose of gaining information about the combination, it does not teach anything about what would happen if you used the PD-1 antibody alone. EX1007, 4 (describing the purpose of the study "[t]o assess the safety and tolerability, characterize the dose-limiting toxicities, and identify the maximum tolerated dose of BMS-986016 [LAG-3 antibody] alone and in combination with Nivolumab")).

Neither NCT-109 nor the Korman application (which the Examiner considered, but Amgen now ignores) describes flat doses for anti-PD-1 monotherapy. Amgen's Petition never explains why the anti-LAG-3/PD-1 antibody combination dosing would be helpful for determining an anti-PD-1 monotherapy dose, particularly where that monotherapy dose is part of a regimen in which the anti-PD-1 antibody is first administered in combination with a totally different antibody (anti-CTLA-4 antibody) and that combination dose is administered according to a patient's weight. In fact, reading the Petition, it would be easy to miss that the anti-LAG-3 antibody was part of NCT-109 at all.

Second, Amgen's Petition fails to provide any explanation why one would be motivated to modify the weight-based dosages of anti-PD-1 antibody to include a flat dose only for the second part of the regimen, as the claims require. According to Amgen, a POSA would have allegedly used the combination dose from the anti-LAG-3 trial to change the anti-PD-1 monotherapy dose but **would not** have also changed the anti-PD-1/CTLA-4 combination dose. Amgen points to no prior art that suggests such a protocol, with an anti-PD-1 antibody administered sometimes at a weight-based dose and sometimes at a flat dose. In fact, such a protocol is contrary to Amgen's argument that a flat dose was somehow already known to be superior to a weight-based dose for anti-PD-1 antibodies. Pet., 3, 21-23. Likewise, Amgen's Petition never explains why weight-based dosing would have still been implemented

in the anti-PD-1/CTLA-4 antibody combination part of the claimed regimen. Amgen's only motivation to combine the different dosing regimens is because that is what is claimed in the '113 Patent. But working backwards from the claims is improper hindsight.

Additional weaknesses in Amgen's arguments will be set forth in detail in BMS's POPR. The merits here are weak, so discretionary denial is called for.

V. AMGEN RELIES ON EXPERT OPINIONS THAT ARE CONCLUSORY AND GO BEYOND THE PRIOR ART

The extent of Amgen's reliance on expert testimony is another factor that supports discretionary denial pursuant to the Memorandum. Amgen's expert goes beyond the alleged prior art—the patents and printed publications that must form the basis of its arguments in *inter partes* review. 35 U.S.C. § 311(b). His conclusory and unsupported expert testimony is “entitled to little weight.” 37 C.F.R. § 42.65(a); *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 12 at 5 (Director Review: Feb. 10, 2023) (precedential) (“the cited declaration testimony is conclusory and unsupported, adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight”). Amgen's reliance on this expert testimony is improper, and discretionary denial is appropriate.

As described above, Amgen provides no prior art support for how the combination of flat doses of anti-LAG-3 and anti-PD-1 antibodies could show

anything about how anti-PD-1 antibody monotherapy would be used. Amgen's expert Dr. Hanks offers his own conclusory theory that:

POSAs would have understood that a 240 mg nivolumab dose would have been appropriate for a monotherapy as well because nivolumab and BMS-986016 have different mechanisms of action, binding to different targets, and thus a suitable dose of nivolumab in the combination therapy disclosed by NCT-109 would also have been considered a suitable dose for administering nivolumab alone.

EX1003, ¶ 89. Dr. Hanks cites to no evidence or prior art support. Further, his oversimplistic view is inconsistent with the fact that NCT-109 and Korman included *separate* testing of the anti-LAG-3 antibody alone as one arm of the study and, in combination with the anti-PD-1 antibody, as an independent arm of the study. EX1007, 4. The clinical result of the combined doses needed to be tested, despite the anti-LAG-3 antibody having a different clinical target. *Id.* at 4-5.

Second, on the critical issue of why the anti-LAG-3/PD-1 antibody test design would be used to modify a monotherapy dose but not a combination dose for the anti-PD-1/CTLA-4 combination, Amgen again relies not on printed prior art, but on conclusory expert testimony. Dr. Hanks simply says:

POSAs would have also recognized the practical benefits (such as greater convenience and streamlined protocols) of administering both

ipilimumab and nivolumab according to a single dosage scheme, as opposed to administering ipilimumab via a weight-based dose and nivolumab via a flat dose.

EX1003, ¶ 86. Dr. Hanks cites to nothing in support of these conclusory statements, and they run contrary to Amgen's proposed argument that flat dosing was somehow known to be the preferred substitute for weight-based dosing of anti-PD-1 antibodies, including because of "greater convenience." *See id.*; Pet., 21-23.

Amgen's positions lack support from the prior art. That goes beyond the proper use of expert testimony in *inter partes* review. Discretionary denial is appropriate.

VI. AMGEN'S PATENTABILITY CHALLENGES ARE MORE APPROPRIATELY DEALT WITH THROUGH THE STATUTORILY CREATED BPCIA

Consistent with the considerations provided in the Memorandum, the Petition should also be denied because Amgen's challenges to the '113 Patent will be addressed by the BPCIA Patent Dance, which Congress specifically enacted as a means for resolving patent disputes that stem from the development and approval of biosimilar drugs. *See* 42 U.S.C. § 262(l). The BPCIA provides an abbreviated approval pathway for biosimilar drugs, including the OPDIVO® biosimilar that **Amgen is currently developing**. 42 U.S.C. § 262(k). This pathway allows Amgen to submit an application, its aBLA, for approval of its antibody as a biosimilar

version of OPDIVO[®]. In its aBLA, Amgen must show the FDA, among other things, that its product is highly similar to OPDIVO[®] and that there are no clinically meaningful differences between the two products in terms of safety, purity, and potency. 42 U.S.C. §§ 262(i)(2), 262(k)(2)(A)(i). If Amgen can make the requisite showings, the FDA will approve Amgen's product for marketing in the United States. 42 U.S.C. § 262(k)(7)(A).

The BPCIA also provides a structured framework for resolving patent litigation arising from the approval of the biosimilar drug, i.e., the Patent Dance. 42 U.S.C. § 262(l). The Patent Dance requires parties to exchange detailed validity and infringement contentions in an effort to narrow and focus the scope of any eventual patent litigation on only those patents and claims that are truly in dispute. 42 U.S.C. § 262(l)(3)-(6). The Patent Dance culminates with the filing of a district court complaint. In effect, Congress designed the Patent Dance to be a focusing exercise that eliminates unnecessary and superfluous litigation over claims and patents not contested between the involved parties.

Based on Amgen's public statements regarding the development of its OPDIVO[®] biosimilar, the parties are likely to not only begin, but also complete the entirety of the Patent Dance and commence litigation prior to the issuance of a final written decision here. EX2008, 21; EX2009, 23. Thus, institution in this proceeding will provide no efficiencies and serve only to duplicate the parties' efforts—contrary

to Congress's intent in enacting both the BPCIA and the Leahy-Smith America Invents Act. Because the BPCIA was specifically created by Congress to provide an efficient mechanism for parties to narrow their patent disputes prior to engaging an adjudicative body, Amgen's patentability challenges are more appropriately dealt with through the Patent Dance in the first instance and then litigation.

VII. ADDITIONAL FACTORS ALSO SUPPORT DISCRETIONARY DENIAL

The Memorandum enumerates several other considerations the PTO considers relevant to discretionary denial. Several of these considerations weigh in favor of discretionary denial here. First, Amgen cites no change in law or precedent impacting patentability. Rather, the Petition relies on long-standing obviousness precedent. And, as explained above, Congress provided the parties with a distinct pathway intentionally designed to both facilitate the approval of Amgen's biosimilar for OPDIVO® and to provide a mechanism for parties to narrow and resolve their patent disputes. The '113 Patent issued six years ago on January 8, 2019. EX1001. Had Amgen wanted to avoid addressing the '113 Patent through the BPCIA, it could have filed its IPR much sooner—it began Phase III clinical trials of its OPDIVO® biosimilar on July 26, 2023. EX2007; *see also Irhythm Techs., Inc. v. Welch Allyn, Inc.*, IPR2025-00363, Paper 10 at 3 (P.T.A.B. Jun. 6, 2025) (exercising discretion to deny institution based on settled expectations of the parties). Amgen sells multiple

biosimilar products and is a sophisticated litigant that is very familiar with the BPCIA process. EX2021. But Amgen chose to wait and now BPCIA patent proceedings are inevitable. There is no need to duplicate efforts and waste PTO resources through an IPR when the parties will be forced to address the infringement and validity of the '113 Patent independently regardless of institution here.

VIII. CONCLUSION

For at least the reasons discussed here, the Director should exercise her discretion to deny institution of Amgen's request for IPR of the '113 Patent.

Respectfully submitted,

Date: June 10, 2025

By: /Steven D. Maslowski/
Steven D. Maslowski
USPTO Registration No. 46,905
Lead Counsel for Patent Owner

CERTIFICATE OF COMPLIANCE PURSUANT TO 37 C.F.R. § 42.24

This paper complies with the type-volume limitation of 37 C.F.R. § 42.24.

The paper contains 6,931 words, excluding the parts of the paper exempted by § 42.24(a).

This paper also complies with the typeface requirements of 37 C.F.R. § 42.6(a)(ii) and the type style requirements of § 42.6(a)(iii)&(iv).

Respectfully submitted,

Date: June 10, 2025

By: /Steven D. Maslowski/
Steven D. Maslowski
USPTO Registration No. 46,905

Counsel for Patent Owner
Bristol-Myers Squibb Company

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL and EXHIBITS 2001 - 2021 were served on counsel of record on June 10, 2025, by filing these documents through the Patent Trial and Appeal Case Tracking System (P-TACTS), as well as delivering copies via electronic mail to the counsel of record for the Amgen at the following addresses:

WOLF, GREENFIELD & SACKS, P.C.

Scott A. McKeown (SMcKeown-PTAB@wolfgreenfield.com)

Oona M. Johnstone (OJohnstone-PTAB@WolfGreenfield.com)

Chelsea A. Loughran (Chelsea.Loughran@WolfGreenfield.com)

Charles T. Steenburg (Charles.Steenburg@WolfGreenfield.com)

Respectfully submitted,

Date: June 10, 2025

By: /Steven D. Maslowski/

Steven D. Maslowski

USPTO Registration No. 46,905

Counsel for Patent Owner

Bristol-Myers Squibb Company