

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALVOTECH USA INC. AND ALVOTECH HF,
Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

PGR2025-00085
Patent 12,168,036

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

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EXHIBITS

- 1001 U.S. Patent No. 12,168,036 (Graham et al.)
- 1002 File History for U.S. Patent No. 12,168,036
- 1003 Declaration of Dr. Donald Joseph D’Amico
- 1004 Declaration of Dr. Robert J. Falconer
- 1005 U.S. Patent No. 7,608,261 (Furfine)
- 1006 U.S. Patent No. 8,921,316 (Dix)
- 1007 U.S. Publication No. 2016/0144025 A1 (Vitti)
- 1008 Center for Drug Evaluation and Research, “Clinical Pharmacology and Biopharmaceutics Review(s)” App. No. 125387Orig1s000 (2011) (“2011 Eylea® Clinical Review”)
- 1009 Product Information EYLEA® aflibercept (rch), (“AU Eylea® Label”)
- 1010 U.S. Publication No. 2015/0071920 A1 (Larson)
- 1011 U.S. Publication No. 2017/0232199 A1 (Fiedler)
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- 1013 PTE Application U.S. Patent No. 7,374,758, (App. No. 11/016,503)
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I. INTRODUCTION

The Director should decline to exercise his discretion to deny institution under 35 U.S.C. §325(d) because the Office committed material error in allowing the claims of the '036 patent. When a petitioner presents evidence of material error, post-grant review constitutes an appropriate use of Office resources. *See, e.g., Anthony Inc. v. Control Tec, LLC*, IPR2025-00559, Paper 12, 2 (Director July 16, 2025) (“Petitioner appears to show a material error by the Office, and it is an appropriate use of Office resources to review the potential error”). Correcting the Examiner’s material errors here—on both obviousness and written description—is an appropriate and necessary use of Office resources.

The '036 patent claims methods of treating angiogenic eye disorders with high-concentration (≥ 100 mg/ml), high-dose (≥ 8 mg) VEGF antagonist formulations having a certain viscosity range suitable for intravitreal injection. Those claims purport to cover EYLEA HD® (8 mg aflibercept product). *See* Discretionary Denial Brief (“Br.”), Paper 6, 3. Patent Owner Regeneron (“PO”) touts EYLEA HD as “groundbreaking,” but PO’s own prior-art patents and publications—such as Vitti (EX1007)—already taught treating angiogenic eye disorders with high-concentration, high-dose aflibercept formulations suitable for intravitreal injection, including protein concentrations ≥ 100 mg/ml and doses up to 10 mg. The Petition relies on the teachings of PO’s own prior art, which appear on the face of the '036

patent, but were overlooked by the Examiner. Notwithstanding the prior art, PO chose to file new applications, just as its earlier patents disclosing high-concentration, high-dose aflibercept formulations were nearing expiration. Pet., 2. This timing underscores the strategic nature of PO's filings and highlights the Examiner's failure to grapple with PO's own prior art.

The Office also materially erred by withdrawing the rejection of the challenged claims for lack of written description. Pet. 81-82. PO persuaded the Examiner that it had solved viscosity problems in high-concentration, high-dose VEGF antagonist formulations. *Id.*, 2-3. But, as explained in the Petition, the challenged claims do not even recite the formulation components that make up the '036 patent's purported solution. *Id.*, 83-86. In fact, the only formulation component mentioned in the '036 patent as impacting viscosity at all is a buffer. EX1001, 38:52-53; Pet. 3.¹ Yet the challenged claims encompass formulations with no buffer at all ("buffer-less" formulations) even though, as explained in the Petition, buffer is always included in the disclosed formulations, all 89 examples include buffers, and, unlike other formulation components, buffer is never characterized as optional. Pet., 83-84. The '036 patent's disclosure does not provide written description support for the very broad scope of the claims.

¹ For example, the '036 patent teaches that the presence or absence of a viscosity reducing agent "showed little difference in viscosity." EX1001, 38:45-47; Pet. 3.

The Office's material errors resulted in the issuance of the obvious and overly broad claims of the '036 patent which, if not corrected, will maintain high treatment costs for patients. This is inconsistent with President Trump's Executive Order 14273 and the administration's efforts to lower drug prices by encouraging the development of biosimilars. Other factors further underscore that discretionary denial is unwarranted here. For example, the '036 patent only issued in December 2024 and has never been involved in litigation or any other proceeding. Also, PO has not claimed any settled expectations in the patent. Trial should be instituted.

II. THE DIRECTOR SHOULD INSTITUTE TO CORRECT THE OFFICE'S MATERIAL ERRORS AS TO OBVIOUSNESS

The Office employs a two-part framework in evaluating whether to deny institution under §325(d): (1) whether the same or substantially the same prior art or argument previously was presented to the Office; and (2) if the first part is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential). Although the Petition here relies on references submitted to the Office in information disclosures statements ("IDSs") under the first part of the *Advanced Bionics* framework, the Office erred in a manner material to the patentability of the challenged claims under the second part.

Becton Dickinson factors (c), (e), and (f) are relevant to whether an Examiner materially erred under the second part of the *Advanced Bionics* framework. *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13, 5 (Director May 19, 2025) (precedential as to §A) (citing *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph)). The following analysis of those factors here shows that the Examiner materially erred by overlooking that the prior-art references submitted in the IDSs—most notably PO’s own prior-art publications and patents—render the challenged claims obvious. Because the second part of the *Advanced Bionics* two-part framework is satisfied, discretionary denial under §325(d) is not appropriate.

A. *Becton Dickinson* Factor (c) Weighs Against Discretionary Denial

Factor (c) considers “the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection.” Paper 8, 22. None of prior art asserted in the Petition was a basis for rejection during examination. EX1002. In fact, the Examiner did not make *any* prior-art statutory rejections—either for anticipation or for obviousness—during examination. The Examiner issued only one Office Action rejecting the claims under §112(a) for lack of written description, under §112(b) for indefiniteness, and under the doctrine of double-patenting over the ’036 patent’s parent patent U.S. 11,103,552. *Id.*, 2140-2148; *see also* Pet. 8. Thus, this factor weighs against discretionary denial.

B. *Becton Dickinson Factor (e) Weighs Against Discretionary Denial*

Factor (e) considers whether the petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art. *Becton Dickinson*, Paper 8, 22. As explained below, the Examiner materially erred in his evaluation of the prior art. PO's own prior art teaches and claims methods of treating angiogenic eye disorders using high-concentration, high-dose VEGF antagonist formulations suitable for intravitreal injection.

1. *The Examiner materially erred by overlooking that PO's own prior art teaches high-concentration, high-dose VEGF antagonist formulations for intravitreal injection*

To begin, PO filed the application leading to the '036 patent with a preliminary amendment. EX1002, 4792-4795. None of the claims presented in the preliminary amendment recited the volume, protein concentration, or viscosity limitations found in renumbered claim 1 of the '036 patent. *Id.*; Pet. 8. Instead, the broadest independent claim in the preliminary amendment—originally numbered as claim 30—merely recited a dosage of “at least 8 mg” of a VEGF antagonist. *Id.*, 4793. But PO had already disclosed that dosage for a VEGF antagonist formulation in its own prior-art patent Vitti, listed in PO's first IDS. *Id.*, 4090.

As explained in Ground 1 of the Petition, Vitti teaches formulations comprising “0.05 mg to about 10 mg of a VEGF antagonist (e.g., aflibercept).” Pet. 28 (quoting EX1007, ¶139); *id.*, 29 (explaining that Vitti discloses an embodiment

comprising “about 80 mg/ml” VEGF antagonist and that this protein concentration correlates to a dosage of “about 8 mg” in a volume of 100 μ l (citing EX1007, ¶¶94, EX1003, ¶197)). Vitti thus discloses formulations with “at least about 8 mg” of VEGF antagonist, as claimed.

The Examiner plainly overlooked this teaching. Otherwise, the Examiner would have rejected original independent claim 30 for *anticipation* by Vitti. Vitti teaches *each and every limitation* of that claim, including: a method for treating an angiogenic eye disorder in a human (Pet. 27-28; EX1007, ¶¶6, 12, 53); an intravitreal injection into the eye (Pet. 27-28; EX1007, ¶¶7, 12); and a VEGF receptor fusion protein comprising two polypeptides that comprise an Ig domain 2 of VEGFR1, an Ig domain 3 of a VEGFR2, and a multimerizing component (Pet. 31; EX1007, ¶86). Yet despite this clear disclosure, the Examiner failed to make an anticipation rejection—or any statutory prior-art rejection at all.²

And even when PO amended its claims to add the volume limitation (“about 100 microliters or less”), protein-concentration limitation (“at least 100 mg/ml”), and viscosity limitation (“about 5-15 centiPoise (cP) at 20°C”), the Examiner materially erred by failing to reject the claims for obviousness. *See* EX1002, 758

² The Examiner also overlooked that other EYLEA documents—either the “AusPAR” cited during prosecution, or the AU EYLEA Label relied on in the Petition—also teach the 8 mg dosage limitation. Pet. 30, 58-59 (citing EX1009, 35); Br. 10 (citing EX2003, 94-112).

(amendments to claim 30). As to the volume and protein-concentration limitations, the Examiner overlooked that Vitti teaches “a volume of approximately upto [sic] 100 μ L” (Pet. 28; EX1007, ¶127) and a protein concentration of “100 $\pm$ 15.0 mg/mL” of VEGF antagonist (Pet. 31-32; EX1007, ¶87). The Examiner also overlooked, as explained in Ground 2 of the Petition, that PO’s patents to Furfine (EX1005) and Dix (EX1006) both disclose and claim VEGF antagonist formulations satisfying the protein-concentration limitation. Pet. 61 (citing EX1005, 2:4-6, 19:31-34; EX1006, 10:60-11:1, 19:37-42, 20:37-41).

As to the claimed viscosity range, the Examiner overlooked that a viscosity of about 5-15 cP was routine in the art for high-concentration pharmaceutical formulations, as PO itself acknowledges. Br. 11-12. Indeed, the references PO listed on IDSs—Whitaker and Borwankar—along with the reference used in the Petition—Larson—all teach this well-known fact. Larson teaches pharmaceutical formulations with a viscosity of “less than or about 20 cP, or most preferably less than or about 10 cP, when measured at 25° C.” Pet. 32-33 (citing EX1010, ¶¶75, 77). Whitaker discloses “acceptable” (<20 cP) and “preferred” ($\leq$ 10 cP) viscosity ranges for both “high” (50 and 150 mg/mL) and “ultra-high” (175 mg/mL) protein-concentration formulations. EX2005, 3, 6. And Borwankar discloses the same range as Larson. Br. 11-12 (citing EX2004, 1, 3).

PO argued during prosecution that the amended claims were allowable

because “[f]ormulations having high concentrations of VEGF receptor fusion protein, however, must have a viscosity suitable for injection via syringe,” and that it had “successfully developed several formulations that meet these criteria.” EX1002, 764-765; *see also* Br. 4-5. But Vitti itself teaches that its VEGF antagonist formulations are administered intravitreally using a syringe fitted with a 30-gauge needle—the same size syringe injection needle exemplified in the ’036 patent. Pet. 32-33 (citing EX1007, ¶¶18, 115, 127); EX1001, 30:39-43. Vitti also teaches using excipients to “provide a desired consistency, **viscosity**, or stabilizing effect” for its pharmaceutical formulations. Pet. 32 (quoting EX1007, ¶96 (emphasis added)). And Larson teaches that “[a]ny protein can be formulated” and ***expressly identifies aflibercept***—the VEGF antagonist in EYLEA that is also disclosed in Vitti—as an example of a protein that can be formulated to reduce viscosity. Pet. 34 (citing EX1010, ¶¶89, 161, 167). Thus, the Examiner materially erred by failing to recognize that a POSA would have readily known that Vitti’s high-dose, high-concentration VEGF antagonist formulation would have a viscosity within the claimed range because Vitti teaches that its formulations are suitable for intravitreal injection—using the same syringe injection needle disclosed in the ’036 patent. *Id.*, 32 (citing EX1003, ¶208; EX1004, ¶¶119-128).

2. PO’s Brief admits that all elements of the claims were known

In addition to admitting that the claimed viscosity range was replete in the art

for high-concentration protein formulations, PO also admits that all other elements of the challenged claims were known. Br. 7-13. For example, PO admits that Fiedler '126 (disclosed in an IDS) provides the “same or nearly identical disclosures” as the Fiedler (EX1010) used in the Petition, including the volume limitation (“preferable volumes for intravitreal injections to a patient are 30 to 100 μ L”) and the protein-concentration limitation (“VEGF antagonist concentration is between 1 to 100 mg/ml”). *Id.*, 8-9. PO also admits that “AusPAR” (disclosed in an IDS) contains “essentially verbatim passages” as the AU Eylea Label (EX1009) used in the Petition, including the “8 mg” dosage limitation. *Id.*, 9-10.

Yet PO contends that the challenged claims are non-obvious because the prior art did not “teach[] how to achieve such viscosity with aflibercept.” Br. 11-12. But, again, Vitti makes clear that PO itself had already taught high-concentration, high-dose aflibercept formulations for intravitreal administration—using the very same 30-gauge needle exemplified in the '036 patent. Pet. 32; EX1007, ¶¶18, 115, 127. And Furfine leaves no doubt, expressly confirming that PO’s prior-art 100 mg/ml aflibercept formulations were “suitable for intravitreal injection.” Pet., 16, 62; EX1009, 31; EX1005, 1:17-24, 4:65-67. Against this backdrop, the purported failures of *other* molecules (abicipar, brolucizumab, and ranibizumab) (Br. 2-3) lack relevance. They do nothing to undermine the fact that PO’s *own prior art* establishes that high-concentration, high-dose aflibercept formulations with suitable viscosity

were not only possible, but expressly taught for intravitreal injection.

C. *Becton Dickinson* Factor (f) Weighs Against Discretionary Denial

Ecto World explains that “additional evidence and facts” under *Becton Dickinson* factor (f) may “warrant reconsideration of the prior art or arguments” independently of factors (c) and (e). Paper 13, 6. The additional evidence and facts here weigh against discretionary denial.

Voluminous prior art. As one example, *Ecto World* states that “the Board should consider a petitioner’s argument based on the volume of the references submitted to the Office during examination and any applicant information or assistance regarding the relevance of references.” *Id.*, 6-7. Here, the face of the ’036 patent lists approximately 645 references, which is over 25 times the size of a typical IDS. *Id.*, 7 n.3. PO never pointed out that its own prior-art patents and publications taught all the limitations of the claims. EX1002.

Serial Requests for Continued Examination (“RCEs”) filed after the first Notice of Allowance (“NOA”). The Examiner issued only one Office Action and, following PO’s response, issued an NOA. EX1002, 692-695. PO then filed *seven RCEs*, each time dumping more and more prior-art references on the Examiner.³ All

³ RCEs are dated Oct. 11, 2023 (EX1002, 675), Nov. 22, 2023 (*id.*, 632), Dec. 15, 2023 (*id.*, 597), Apr. 29, 2024 (*id.*, 541), June 7, 2024 (*id.*, 143), July 15, 2024 (*id.*, 97), and Aug. 27, 2024 (*id.*, 42).

told, PO submitted *thirteen IDSs* with its RCEs—many dated within mere days of one another.⁴

And many of those IDSs listed key prior-art references publicly available well before the '036 patent's filing date. As one example, PO disclosed AusPAR to the Office after the Examiner had already issued two NOAs. EX1002, 619. PO failed to disclose this reference earlier even though AusPAR is a regulatory review of the *EYLEA product* that published in 2012, almost a decade before the '036 patent's filing date. EX2003, 1. Further, PO admits that AusPAR—like the AU EYLEA Label relied on in all the Petition's obviousness grounds—teaches that “overdoses with 8 mg were generally well tolerated.” Br. 10 (citing EX2003, 111). PO cannot argue that this 8 mg “overdose” is immaterial, because PO told the FDA that unintentional doses of 8 mg were “well tolerated” and that its “similar safety profile” supported a dose selection of 8 mg for EYLEA HD. EX1066, 19.

As another example, PO did not disclose Borwankar—which PO admits teaches the claimed viscosity range (Br. 12)—until its very last IDS filed on August 27, 2024 (EX1002, 43-45), fewer than four months before the '036 patent issued on

⁴ Post-NOA IDSs are dated Oct. 11, 2023 (EX1002, 667-669), Oct. 16, 2023 (*id.*, 654-656), Nov. 22, 2023 (*id.*, 619-621), Dec. 15, 2023 (*id.*, 594-596), Jan. 16, 2024 (*id.*, 584-586), Apr. 29, 2024 (*id.*, 444-448), May 8, 2024 (*id.*, 185-187), May 10, 2024 (*id.*, 176-179), June 7, 2024 (*id.*, 129-131), June 18, 2024 (*id.*, 120-122), July 15, 2024 (*id.*, 89-91), July 23, 2024 (*id.*, 77-79), Aug. 27, 2024 (*id.*, 43-45).

December 17, 2024 (EX1002, code [45]).

Sole Office Action containing clear errors. The double-patenting rejection set forth in the sole Office Action also exemplifies the Examiner’s cursory examination of the ’036 patent. There, the Examiner rejected then-pending claims 30-32, 35, and 39-52 on the ground of non-statutory double patenting for being unpatentable over claims 1-36 of U.S. Patent No. 11,103,552, the ’036 patent’s parent patent. EX1002, 2147. But that rejection is replete with errors, including references to “dosing schedules” not found in the claims and to “claims 1-26 of the ’338 patent,” the latter of which must represent a cut-and-paste error from a different application or office action. In response, PO did not point out these errors, but “thank[ed] the Examiner for acknowledging that” a timely-filed terminal disclaimer would overcome the rejection. EX1002, 765.

Each RCE met with the same standard language. After each RCE, the Examiner issued a NOA stating that the IDSs had been considered but that “none of the information contained therein raises new issues of patentability.” EX1002, 18, 62, 106, 150, 549-50, 608, 639.⁵ All told, the Examiner repeated this statement *verbatim seven times*, despite clear evidence that AusPAR and Borwankar raised

⁵ NOAs are dated Sept. 1, 2023 (EX1002, 688), Nov. 8, 2023 (*id.*, 633), Dec. 6, 2023 (*id.*, 602), Jan. 31, 2024 (*id.*, 543), May 28, 2024 (*id.*, 144), July 1, 2024 (*id.*, 102), Aug. 14, 2024 (*id.*, 58), and Sept. 11, 2024 (*id.*, 12).

new issues of patentability at a minimum. *Supra* §II.B.1.

Taken together, the sheer volume of prior-art references, the absence of any statutory prior-art rejections, and the Examiner’s reliance on repeated rote language demonstrate a fundamental failure of adequate review. *Becton Dickinson* factor (f) weighs against discretionary denial.

D. The Director Should Reject PO’s Arguments About Material Error as to Obviousness

To begin, PO’s argument that the Director should deny institution because “Alvotech has not sufficiently identified any error, much less material error” (Br. 14) misapprehends the Office’s published process for discretionary denial. Guidance from the Office provides that arguments and evidence of material error should be provided in a petitioner’s opposition to a patent owner’s request for discretionary denial. Specifically, the Interim Director Discretionary Process webpage states that “[a] petitioner should raise any discretionary issues in its *opposition* to a patent owner’s discretionary denial brief, including issues relating to 35 U.S.C. § 325(d), parallel proceedings, parallel petitions, serial petitions, and any other matter bearing on the Director’s discretion to institute.” §III.A (available at <https://www.uspto.gov/patents/ptab/interim-director-discretionary-process>). The webpage also states that “[t]he petition should *not* address discretionary issues.” *Id.* Petitioner has shown material error here in accordance with the Office’s instructions

to address §325(d) issues in its opposition.

PO relies on *TankLogix, LLC v. SitePro, Inc.*, IPR2025-00761, Paper 10 at 2 (Director Sept. 3, 2025) to support its argument (Br. 14), but that case is inapt. In *TankLogix*, the Director exercised discretion to deny institution because the petitioner's **opposition brief** failed to show material error. *Id.* Indeed, when addressing examiner error under §325(d), the petitioner argued in its opposition that the “sentiment” of examiner error was “implicit throughout” its petition because it had “detail[ed] how the references disclose every element of every claim.” Paper 7, 19. Thus, *TankLogix* does not stand for the PO's proposition that a petitioner must address §325(d) in the petition or else face discretionary denial.

Next, PO's argument that that material error exists only where “no reasonable examiner could have found the claims unpatentable” misapprehends *Ecto World*. Br. 6-7. In *Ecto World*, the Director explained that “**if** the Examiner **applied** the asserted prior art or substantially the same prior art during examination, **then** a petitioner must demonstrate that, for example, the previously presented art teaches the limitations of the challenged claims, and that no reasonable examiner could have found otherwise.” *Id.* at 6 (emphases added). Here, however, the Examiner **never applied any** prior art for a statutory rejection during examination, and thus, the “no reasonable examiner” standard does not apply. But even if that standard did apply, the outcome would be the same. No reasonable examiner could conclude that the

prior art fails to disclose every limitation of the challenged claims. *Supra*, §II.B. Even PO concedes as much. *Id.*, §II.B.2.

In sum, the Examiner materially erred in allowing the claims over the asserted prior art under *Becton Dickinson* factors (c), (e), and (f). Thus, the second part of the *Advanced Bionics* framework is satisfied and discretionary denial under §325(d) is not appropriate here.

III. THE DIRECTOR SHOULD INSTITUTE TO CORRECT THE OFFICE’S MATERIAL ERRORS AS TO WRITTEN DESCRIPTION

The second part of the *Advanced Bionics* framework is also satisfied as to written description. As explained in the Petition, although the Examiner initially made a written-description rejection, the Examiner materially erred by withdrawing it during examination. Pet. 75-86.

As discussed, the Examiner rejected the claims under §112(a) for lack of written description. The Examiner correctly observed that the claims “recite[] a high concentration of a VEGF receptor fusion protein without any recitation of the elements of the composition that permit such a high concentration of the protein.” EX1002, 2145. The Examiner stated that “while the specification provides adequate written description for stable, high concentration formulations of a VEGF receptor fusion protein along with 5% sucrose, polysorbate, a histidine-based buffer, and L-arginine, it does not provide adequate written description for the breadth of the

formulation encompassed by the claims.” *Id.* In response, PO amended the claims to recite the volume, protein-concentration, and viscosity limitations. *Id.*, 758. PO argued that it had successfully developed several formulations “including a variety of excipients” having an acceptable viscosity between 5 and 15 cP at 20°C and thus disclosed a “representative number of species”, but did not amend the claims to recite any specific excipient, much less a complete set of excipients that are necessary to produce the claimed high-concentration, high-dose VEGF antagonist formulation with the claimed viscosity. *Id.*, 764-765.

The Examiner materially erred because the ’036 patent does not show that the inventors possessed the ***full scope*** of the claims (e.g., no upper limit on concentration or dose). Pet. 75-76 (citing *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1337 (Fed. Cir. 2021)). Take buffer, for example. The Examiner correctly pointed out that only those high-concentration formulations containing a buffer were adequately described. EX1002, 2145; Pet. 81-82. Indeed, every formulation disclosed in the specification contains a buffer and the specification never describes buffer as optional—as it does for other excipients. Pet. 78-79, 83-84.

But the challenged claims are not limited to formulations having a buffer, and, in fact, encompass buffer-less formulations. Pet. 83-84. No reasonable examiner could have found that these claims satisfy written description because such a decision cannot be squared with the Federal Circuit’s caselaw. Pet. 85-86. As

explained in the Petition, the specification describes only formulations with a buffer that achieve the claimed viscosity levels, and the Federal Circuit has invalidated unduly broad claims under closely similar facts. *Id.* (citing *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336 (Fed. Cir. 2005); *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479-80 (Fed. Cir. 1998)).

PO argues that its claims are not defective because there is no “need to list every component of the compositions that may be used in the claimed methods.” Br. 18. But even accepting this statement as true, the specification must show that the inventors ***actually invented*** what is claimed, treating with every high-concentration, high-dose formulation, including a buffer-less high-concentration, high-dose VEGF antagonist formulation. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1342 (Fed. Cir. 2010) (*en banc*) (stating that the purpose of the written-description requirement is to prevent a patent owner from later asserting that it invented that which it did not). And that the ’036 patent does not do. Pet. 75-76, 83-86.

PO has a history of overreaching beyond what it actually invented. In litigation over low-dose (2 mg) EYLEA, PO sued Amgen for infringement over Amgen’s buffer-less 2 mg aflibercept formulation. The Federal Circuit affirmed the district court’s rejection of PO’s bid for a preliminary injunction against Amgen’s buffer-less formulation, stating that nothing in PO’s patent suggested that PO’s claims covered a self-buffering (i.e., buffer-less) VEGF antagonist formulation.

Regeneron Pharms., Inc. v. Mylan Pharms. Inc., 130 F.4th 1372, 1380 (Fed. Cir. 2025). Just as with its low-dose EYLEA formulation, PO has not invented a bufferless, high-concentration, high-dose (8 mg) aflibercept formulation for intravitreal injection.⁶ And, as a matter of sound policy, the Director should not defer to flawed written-description decisions on a patent so new that it remains eligible for PGR, especially before that patent is invariably asserted in litigation. This is precisely the type of case Congress envisioned when it created PGRs—to ensure that patents of immense commercial consequence are subjected to rigorous scrutiny before they distort competition. *SAS Inst., Inc. v. Iancu*, 584 U.S. 357, 360 (2018).

IV. THE REMAINING CONSIDERATIONS WEIGH AGAINST DISCRETIONARY DENIAL

A. Petitions for PGR Are Favored

Petitions for PGR, like this one, “are favored because they must be filed no later than nine months from the grant of the patent (35 U.S.C. § 321(c)), are close in time to examination, and occur before expectations in the patent rights are strongly settled.” *LifeVac, LLC v. DCSTAR Inc.*, IPR2025-00454, Paper 11, 2 (Director July 11, 2025). This consideration weighs against discretionary denial.

B. PO Has Not Alleged Settled Expectations and None Exist

⁶ In contrast to the challenged claims, the claims of U.S. 11,103,552—the ’036 patent’s parent—are limited to VEGF antagonist formulations containing a histidine-based buffer and methods of using those buffered formulations to treat angiogenic eye disorders. *See* EX1067, 61:29-64:39.

The Office considers the “[s]ettled expectations of the parties, such as the length of time the claims have been in force” as another factor in determining whether to exercise discretion to deny institution. March 26, 2025 Memo, 2. The ’036 patent issued in 2024. EX1001, code [45]. Accordingly, PO “has not developed settled expectations settled expectations that favor discretionary denial.” *Intas Pharms. Ltd. v. Attossa Therapeutics, Inc.*, PGR2025-00043, Paper 12, 2-3 (Director Aug. 29, 2025). Moreover, “[e]arly challenges to patents favor robust, predictable patent rights and weigh against discretionary denial.” *Id.* This consideration weighs against discretionary denial.

C. No Proceeding Involving the ’036 Patent Weighs Against Discretionary Denial

No other forum has or is adjudicating any claims of the ’036 patent. Thus, “there is no concern of inconsistent outcomes or significant duplication of errors resulting from two proceedings operating in parallel.” *See, e.g., Intas*, Paper 12, 2-3. This consideration weighs against discretionary denial.

D. Institution Would Further the Administration’s Goal of Lowering Drug Prices by Increasing Competition

The Director should also decline to exercise discretion to deny institution to further the economic, public health, and national interests set forth in President Trump’s Executive Order 14273 (“EO”), titled “Lowering Drug Prices by Once Again Putting Americans First,” issued April 15, 2025. EX1068. The President

states in the EO that “[i]t is the policy of the United States that Federal health care programs, intellectual property protections, and safety regulations are optimized to provide access to prescription drugs at lower costs to American patients and taxpayers.” *Id.*, §2; *see also* EX1069 (describing President Trump’s efforts to lower drug prices for American patients). The EO supports lowering drug prices by encouraging competitors to enter the U.S. market with lower-cost biosimilar alternatives to biologics. EX1068, §1.

Petitioner Alvotech is attempting to do just that. Alvotech and Teva Pharmaceuticals recently announced the launch of a 2 mg EYLEA biosimilar product (“AVT06”) in 2026. EX1070. Alvotech and Teva are also collaborating on the development and manufacture of a proposed 8 mg EYLEA HD biosimilar product (“AVT29”). EX1071. Biosimilars significantly lower health care costs, and the introduction of EYLEA biosimilars into the market will help reduce the financial burden of treating angiogenic eye diseases and make treatment more accessible to patients. EX1072. Thus, the EO weighs against the Director exercising discretion to deny institution here, particularly in view of the overly broad and obvious claims of the ’036 patent.

V. CONCLUSION

The Director should grant institution to remedy the Office’s material errors in allowing overly broad and obvious claims of the ’036 patent.

Respectfully submitted,

Dated December 26, 2025

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CERTIFICATE OF SERVICE

Pursuant to 37 CFR § 42.6(e)(4), the undersigned certifies that on December 26, 2025, a complete and entire copy of this this Petitioner's Opposition to Patent Owner's Discretionary Denial Brief and added supporting exhibits were provided via email to the Patent Owner via electronic mail on Patent Owner's lead and backup counsel listed below at the following email address:

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