

Filed on behalf of Intas Pharmaceuticals Ltd.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTAS PHARMACEUTICALS LTD.,

Petitioner

v.

ATOSSA THERAPEUTICS, INC.,

Patent Owner

Case PGR2025-00043

Patent No. 12,071,391

**PETITIONER'S RESPONSE TO PATENT OWNER'S REQUEST FOR
DISCRETIONARY DENIAL OF INSTITUTION**

TABLE OF CONTENTS

I. Introduction.....1

II. Discretionary denial is unwarranted5

 A. There are no compelling health interests supporting discretionary denial6

 B. Patent Owner’s incredibly narrow covenant not to sue does not favor discretionary denial.....9

 C. Section 325(d) does not favor discretionary denial11

 D. The merits are exceptionally strong11

 E. The Petition’s use of expert testimony does not favor discretionary denial17

 F. Discretionary denial would eliminate any estoppel effects from the 334 patent, which would not apply in district court.....20

III. Conclusion21

TABLE OF AUTHORITIES

Cases

Biogen Idec, Inc. v. GlaxoSmithKline LLC,
713 F.3d 1090 (Fed. Cir. 2013)17

Eli Lilly & Co. v. Teva Pharms. USA, Inc.,
557 F.3d 1346 (Fed. Cir. 2009)6

Indivior Inc. v. Dr. Reddy's Lab'ys, S.A.,
752 F. App’x 1024 (Fed. Cir. 2018)17

Koninklijke Philips N.V. v. Google LLC,
948 F.3d 1330 (Fed. Cir. 2020)20

OpenSky Industries, LLC v. VLSI Technology LLC,
IPR2021-01064, Paper 102 (Oct. 4, 2022)11

ParkerVision, Inc. v. Qualcomm Inc.,
116 F.4th 1345 (Fed. Cir. 2024)23

Patent Quality Assurance, LLC, et al. v. VLSI Tech. LLC,
IPR2021-01229, Paper 102 (Dec. 22, 2022).....12

SandBox Logistics LLC v. Proppant Express Invs. LLC,
813 F. App’x 548 (Fed. Cir. 2020)16

SimpleAir, Inc. v. Google LLC,
884 F.3d 1160 (Fed. Cir. 2018)17

Ventana Med. Sys., Inc. v. Biogenex Lab’ys, Inc.,
473 F.3d 1173 (Fed. Cir. 2006)16

Xerox Corp. v. Bytemark, Inc.,
IPR2022-00624, Paper 9 (Aug. 24, 2022)19

Statutes

21 U.S.C. § 355(j)(5)(B)(iii)6

35 U.S.C. § 311(a)6

Other Authorities

Memorandum for Interim Processes for PTAB Workload Management.....5

PETITIONER’S EXHIBIT LIST

EX.	DESCRIPTION
1001	USPN 12,071,391 (“391 patent”)
1002	File history of USPN 12,071,391
1003	USPN 9,333,190 (“Ahmad”)
1004	WO2017/70651 (“Liu”)
1005	EXCERPT OF HANDBOOK OF PHARMACEUTICAL SALTS: PROPERTIES, SELECTION, & USE (P. Heinrich Stahl & Camille G. Wermuth eds., 1st ed., 2002) (“Stahl”)
1006	Benameur, H., Capsule Technology, Enteric Capsule Drug Delivery Technology – Achieving Protection Without Coating, 15(5) DRUG DEV. & DELIVERY 34-37 (2015) (“Benameur”)
1007	Melgardt de Villiers, <i>Pharmaceutical Solvents & Solubilizing Agents</i> , in <i>A Practical Guide to Contemporary Pharmacy Practice</i> (3d ed., 2009) (“de Villiers”)
1008	Stegemann, S., Hard gelatin capsules today – and tomorrow, CAPSUGEL LIBRARY (2002) (“Stegemann”)
1009	Excerpts OF HANDBOOK OF PHARMACEUTICAL EXCIPIENTS (Rowe, R., Sheskey, J. & Owen, S., eds., 5th ed., 2006) (The “HPE”)
1010	Cole, E., et al., <i>Enteric coated HPMC capsules designed to achieve intestinal targeting</i> , 231 INTL J. PHARMACEUTICS 83-95 (2002) (“Cole”)
1011	Ahmad, A. et al., <i>Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability and Systemic Bioavailability in Healthy Human Subjects</i> , 88(6) CLIN. PHARMACOLOGY & THERAPEUTICS 814-817 (2010) (“Ahmad 2010”)
1012	Ahmad, A. et al., <i>Endoxifen for breast cancer: Multiple-dose, dose-escalation study characterizing pharmacokinetics and safety in metastatic breast cancer patients</i> , ASCO Meeting Library, presented June 4, 2012 (“Ahmad 2012”)

Response to Patent Owner's Request for Discretionary Denial

EX.	DESCRIPTION
1013	Fauq, A.H., et al., <i>A convenient synthesis of (Z)-4-hydroxy-N-desmethyltamoxifen (endoxifen)</i> , 20 BIOORGANIC MED. CHEM. LETT. 3036-38 (2010) (“Fauq”)
1014	Milroy, L. et al., <i>A multi-gram-scale stereoselective synthesis of Z-endoxifen</i> , 28 BIOORGANIC MED. CHEM. LETT. 1352-56 (2018) (“Milroy”)
1015	Krahn, F. et al, <i>Effect of type and extent of crystalline order on chemical and physical stability of carbamazepine</i> , 53(1) INT’L J. OF PHARMACEUTICS 25-34 (1989) (“Krahn”)
1016	A FOCUS ON CRYSTALLOGRAPHY (FIZ KARLSRUHE 2005)
1017	Fan, J. et al., <i>Pharmacokinetics</i> , 81 BIOCHEM. PHARMACOLOGY 93-120 (2014) (“Fan”)
1018	Urso, R. et al., <i>A short introduction to pharmacokinetics</i> , 6 EUR. REV. FOR MED. & PHARMACOLOGICAL SCIS., 33-44 (2002) (“Urso”)
1019	<i>Endoxifen</i> , PUB CHEM: COMPOUND SUMMARY (2024)
1020	Ansel, H., et al, PHARMACEUTICAL DOSAGE FORMS AND DRUG DELIVERY SYSTEMS, SEVENTH EDITION (1999) (“Ansel”)
1021	Beasley, D. et al, <i>The Evolution of Stomach Acidity and Its Relevance to the Human Microbiome</i> , 10(7) PLoS ONE 1-12 (2015) (“Beasley”)
1022	WO 2011/107855 (“Gandhi”)
1023	USPN 11,572,334 (“334 patent”)
1024	Supporting information to Milroy, L. et al., <i>A multi-gram-scale stereoselective synthesis of Z-endoxifen</i> , 28 BIOORGANIC MED. CHEM. LETT. 1352-56 (2018)
1025	Ali et al., <i>Endoxifen is a new potent inhibitor of PKC: A potential therapeutic agent for bipolar disorder</i> , 20 BIOORGANIC & MEDICINAL CHEM. LETTERS 2665-67 (2010) (“Ali”)
1026	Supporting information to Fauq, A.H., et al., <i>A convenient synthesis of (Z)-4-hydroxy-N-desmethyltamoxifen (endoxifen)</i> , 20 BIOORGANIC MED. CHEM. LETT. 3036-38 (2010)
1027	Elkins et al., <i>Characterization of the isomeric configuration and</i>

Response to Patent Owner’s Request for Discretionary Denial

EX.	DESCRIPTION
	<i>impurities of (Z)-endoxifen by 2D NMR, high resolution LCMS, and quantitative HPLC analysis</i> , 88 J. PHARMACEUTICAL AND BIOMEDICAL ANALYSIS 174-79 (2014) (“Elkins”)
1028	Reid et al., <i>Pharmacokinetics of endoxifen and tamoxifen in female mice: implications for comparative in vivo activity studies</i> , 74(6) CANCER CHEMOTHERAPY PHARMACOLOGY 1271-78 (2014) (“Reid”)
1029	SHARGEL, LEON & YU, ANDREW, APPLIED BIOPHARMACEUTICS & PHARMACOKINETICS (7th ed. 2016) (“Shargel”)
1030	ALLEN & ANSEL, ANSEL’S PHARMACEUTICAL DOSAGE FORMS & DRUG DELIVERY SYSTEMS (10th ed. 2013) (“Ansel”)
1031	Wieckhusen, D., <i>The Development of API Manufacturing Processes – Targets aand Strategies</i> , 60(9) CHIMIA INT’L J. FOR CHEM. 598-604 (2006) (“Wieckhusen”)
1032	COULSON & RICHARDSON, COULSON & RICHARDSON’S CHEMICAL ENGINEERING (5th ed. 2002) (“Coulson & Richardson”)
1033	Expert Declaration of Jason McConville, Ph.D.
1034	Expert Declaration of Ron Bihovsky, Ph.D.
1035	Chen P. et al, <i>Orally administered endoxifen inhibits tumor growth in melanoma-bearing mice</i> , 23:3 CELLULAR & MOLECULAR BIOLOGY LETTERS (2018)
1036	Goetz MP et al, <i>First-in-Human Phase I Study of the Tamoxifen Metabolite Z-Endoxifen in Women With Endocrine-Refractory Metastatic Breast Cancer</i> , 35(30) J CLIN ONCOLOGY 3391 (2017)
1037	Takebe N et al, <i>Phase I study of Z-endoxifen in patients with advanced gynecologic, desmoid, and hormone receptor-positive solid tumors</i> , 12(4) ONCOTARGET 267-277 (2021)

I. INTRODUCTION

Patent Owner cannot credibly dispute the Petition establishes far more than a reasonable likelihood that Petitioner would prevail with respect to at least one of the challenged claims. Patent Owner cannot dispute that endoxifen was a well-known compound, and multiple references taught synthesizing it, including obtaining highly pure forms of the (Z)-enantiomer. Nor can it dispute that the art taught the use of endoxifen (including the (Z)-isomer) in enteric carriers for the treatment of breast cancer—references reflecting the work of Petitioner Intas Pharmaceuticals and a development partner Jina Pharmaceuticals. Indeed, many of the claims here are identical to or in fact broader than claims found unpatentable in the parent 334 patent by the Board and are unpatentable for the same reasons. That alone weighs strongly against denying institution, as the collateral estoppel effects of the Board's earlier findings would not apply in district court, essentially allowing a discretionary denial to nullify that earlier proceeding.

In fact, the *only* claimed feature Patent Owner argues is novel over the prior art (and distinguishable from the 334 patent) is that “the '391 patent's claims require **the composition itself comprise both an endoxifen and an enteric material**” in contrast to “an endoxifen composition to be ‘encapsulated in an enteric capsule.’” Req. at 1. But that cannot be a distinction because the 391 patent, including the dependent claims, make clear that the claimed “composition” can be a capsule and

Response to Patent Owner's Request for Discretionary Denial

that the capsule as a composition may “comprise” enteric coatings as an enteric material. *E.g.*, Claim 6 (“The composition of claim 1, wherein the composition *is a capsule*”); Claim 8 (“The composition of claim 1, wherein the composition *comprises an enteric coating*”); Ex. 1001, 53:60-67 (“the present disclosure relates to *compositions* comprising (Z)-endoxifen or salts thereof ...**further comprising... an enteric coating agent**”) (all prior emphases added).

That is, the 391 patent is clear that the “composition” may be a capsule and may comprise an enteric coating as the claimed “enteric material” and is not limited to “internal” enteric materials. And Patent Owner acknowledges that such enteric coatings are disclosed in the prior art. Req. at 20 (“Ahmad discloses an endoxifen composition encapsulated in an enteric coating.”). Indeed, the Board so found in holding the 334 claims unpatentable. Because Patent Owner cannot prevail on the merits, it seeks discretionary denial.

Patent Owner first relies on alleged health interests to justify maintenance of its unpatentable claims—arguing the 391 patent is necessary for Patent Owner to bring endoxifen to patients. But Patent Owner does not need the 391 patent to develop endoxifen and attempt to bring it to market—the 391 patent does not vest in Patent Owner the right to make and sell, but only the right to *exclude* others from using or selling endoxifen as claimed in the 391 patent, including those such as Petitioner who had already begun investigating endoxifen well before Patent Owner

Response to Patent Owner's Request for Discretionary Denial

filed its patent applications. Patent Owner has disclosed nothing novel to the public to justify a patent monopoly on endoxifen or its use in treating breast cancer. Indeed, permitting Patent Owner's 391 patent to avoid challenge would undermine public health concerns by preventing others from bringing to market therapies based on the long-known endoxifen molecule (including through an automatic 30-month stay).

Petitioner brings this Petition for the exact reasons Congress envisioned—an early challenge to an improvidently issued patent to resolve patentability long before any actual district court litigation. That there is no current litigation favors *institution*, not denial, as Petitioner cannot bring this challenge in district court, and absent this PGR the 391 patent will continue to threaten other parties from bringing endoxifen breast cancer treatments to market.

Patent Owner then seeks to avoid a patent challenge by offering an erroneous covenant not to sue. Patent Owner's covenant not to sue is not directed to the 391 patent at issue here, but U.S. Patent No. 11,572,334, the grandparent patent already invalid. *See Intas Pharms. Ltd. v. Atossa Therapeutics, Inc.*, PGR2023-00043, Paper 37 (P.T.A.B. January 29, 2025) (“334 FWD”). Even assuming that the covenant was correctly directed to the 391 patent, the covenant not to sue is so narrow it covenants only not to sue Petitioner for the *unclaimed* treatment of bipolar disorder and only for the salt form. But Patent Owner should not be able to dictate for what treatments

Response to Patent Owner's Request for Discretionary Denial

Petitioner (and the public at large) may pursue when the prior art (including that generated by Petitioner) already taught endoxifen for such uses.

Patent Owner then turns to Section 325(d), which Petitioner already addressed in the Petition. Petition at 15-18. As noted there, the Examiner clearly erred in not issuing a single rejection given the teachings of the prior art and the Board has previously rejected Patent Owner's prior identical argument in connection with the grandparent 334 patent. *See Intas Pharms. Ltd. v. Atossa Therapeutics, Inc.*, PGR2023-00043, Paper 11, *33-35 (P.T.A.B. January 31, 2024).

Patent Owner then addresses the merits, but as noted above, Patent Owner acknowledges that the *only* limitation Patent Owner raises as supporting patentability—"the composition itself comprise both an endoxifen and an enteric material"—is taught by Ahmad under the correct construction of the claims.

Finally, there is an additional factor here that weighs *against* discretionary denial. The Board has already addressed the grandparent 334 patent with very similar claims and found all challenged claims unpatentable in an unappealed Final Written Decision. Those earlier findings limit what Patent Owner may argue in this proceeding but would not apply in district court where Patent Owner could proceed on claims and arguments the Board has rejected. The Board should institute review of Patent Owner's 391 patent because like the 334 patent claims, the claims here are similarly unpatentable.

II. DISCRETIONARY DENIAL IS UNWARRANTED

The Director’s interim order provides that “consistent with the discretionary considerations enumerated in existing Board precedent (including *Fintiv*, *General Plastic*, and *Advanced Bionics*) and the Consolidated Trial Practice Guide (Nov. 2019), the parties are permitted to address all relevant considerations....”¹ While Patent Owner argues “every relevant factor...demonstrates that discretionary denial is the proper outcome here,” Patent Owner does not even address the *Fintiv* or *General Plastic* factors, conceding that they do not apply.

Here, no litigation regarding the 391 patent is pending. But Congress created IPRs and PGRs specifically because “[w]hile entities accused of patent infringement have long been able to challenge the validity of the patents asserted against them in court, IPR and PGR allow a party to petition PTAB to hear a challenge to the validity of an already-issued patent in an administrative forum, regardless of whether the petitioner has been sued or threatened with suit for patent infringement.” Zirpoli, C.T. and Hickey, K.J., *The Patent Trial and Appeal Board and Inter Partes Review*, CONGRESSIONAL RESEARCH SERVICE R48016, at *1 (May 28, 2024), available at

¹ Memorandum for Interim Processes for PTAB Workload Management at 2–3, available at <https://www.uspto.gov/sites/default/files/documents/InterimProcesses-PTABWorkloadMgmt-20250326.pdf>.

Response to Patent Owner's Request for Discretionary Denial

<https://www.congress.gov/crs-product/R48016>; see also 35 U.S.C. § 311(a) (any “person who is not the owner of a patent may file with the Office a petition to institute an inter partes review of the patent.”). Treating patents as immune from challenge *until* asserted in litigation would undermine the purpose of IPR/PGR and *Fintiv*.

That is especially untenable in the context of pharmaceutical patents, where the filing of a lawsuit alone entitles the patent owner to an *automatic* 30-month stay against generic competition. See 21 U.S.C. § 355(j)(5)(B)(iii); *Eli Lilly & Co. v. Teva Pharms. USA, Inc.*, 557 F.3d 1346, 1348 (Fed. Cir. 2009) (“If the patentee does file suit, the FDA may not approve the ANDA until expiration of the patent, resolution of the suit, or thirty months after the patentee's receipt of notice, whichever is earlier”). Intas (and the public at large) have an especially weighty interest in the removal of unpatentable pharmaceutical claims *prior* to the filing of any lawsuit, allowing other parties to bring competing drugs to market quicker.

Because Intas has provided strong reasons demonstrating the 391 patent is (like the 334 patent) unpatentable, and there is no basis for discretionary denial, the Board should institute.

A. There are no compelling health interests supporting discretionary denial

Patent Owner suggests that the 391 patent is critical to allowing patients to receive endoxifen for the treatment of breast cancer. But what the 391 patent (like

Response to Patent Owner's Request for Discretionary Denial

all patents) grants is the right to *exclude* others—not the right to practice the alleged invention.² And here, Patent Owner seeks the right to *exclude* others from bringing endoxifen breast cancer treatments to patients, despite the prior art's extensive teachings of how to make highly pure (Z)-endoxifen, and its use for treating breast cancer. *See generally* Pet.; Exs. 1003-1004, 1011-1012, 1014.

Indeed, as expressed below, Patent Owner seeks to preserve the right to *exclude* Petitioner Intas Pharmaceuticals (as well as Jina Pharmaceuticals)³ from pursuing breast cancer treatments *despite* Intas and Jina's *prior art* work on using endoxifen for such treatment. *See, e.g.*, Ex. 1011 (2010 Intas and Jina paper:

² Moreover, Congress provides for regulatory exclusivity encouraging parties to be the first to bring a drug to market. *See, e.g.*, <https://www.fda.gov/files/drugs/published/Exclusivity-and-Generic-Drugs--What-Does-It-Mean-.pdf>. Thus Patent Owner has every incentive to bring its drug to market even without patent protection.

³ As shown in Ahmad 2010 (Ex. 1011), Intas and Jina are separate companies each with an interest in developing endoxifen treatments. Intas is the Petitioner and real party in interest and the sole party funding this PGR, though Jina has its own interest in the outcomes. Regardless, adding Jina as a real party in interest has no effect on this PGR as neither Intas nor Jina are barred from pursuing this PGR.

Response to Patent Owner's Request for Discretionary Denial

“Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability, and Systemic Bioavailability in Healthy Human Subjects”); Ex. 1012 (same authors: “Endoxifen for breast cancer: Multiple-dose, dose-escalation study characterizing pharmacokinetics and safety in metastatic breast cancer patients.”).⁴ Patent Owner seeks the ability to exclude others from practicing the prior art (including by an automatic 30-month stay as described above) and bringing treatments to patients. That harms the public health; it does not favor it.

The public health interest favors removing the 391 patent—which is unpatentable as explained in Intas’s petition—not granting Atossa the exclusive right

⁴ Atossa seeks to create the impression that it alone is working on cancer therapies employing endoxifen. Req. at 13 (“The threat posed by Petitioner’s PGR is not just to Patent Owner’s patent rights and clinical development, but to the patients who stand to benefit from a safer, more reliable breast cancer treatment.”) Such an understanding is wrong. Several others, including Intas and Jina Pharmaceuticals, have conducted substantial and independent research and development on endoxifen, including preclinical, clinical, and regulatory work. See Exs. 1011-1012, 1035-1037; *see also e.g.*,

<https://clinicaltrials.gov/study/NCT01273168?term=endoxifen&rank=2>;

<https://clinicaltrials.gov/study/NCT03931928?term=endoxifen&rank=4>.

to pursue breast cancer treatment even over parties who began such research years before.

B. Patent Owner's incredibly narrow covenant not to sue does not favor discretionary denial

Patent Owner's covenant not to sue is illusory. Patent Owner covenants not to sue Intas or Jina for any alleged infringement of U.S. 11,572,334, which has already been held to be unpatentable. *See* 334 FWD.

Even if the covenant accurately identified the 391 patent, it is still illusory. Patent owner covenants not sue for the use of (Z)-endoxifen for bipolar disorder or other psychiatric disorders. But the 391 patent does not mention or cover the use of (Z)-endoxifen for biopolar disorders or other psychiatric disorders. Thus, Patent Owner's "covenant not to sue" is little more than a covenant not to assert its claims over methods that its claims do not cover while reserving the right to sue Petitioner (and others) for any use of the free base and all other uses of the salt.

Patent Owner's arguments hinge on the unproven and unexplained assumption that "Intas's only commercial interest in (Z)-endoxifen appears to be in treating bipolar disorder using a salt form of (Z)-endoxifen." Req. at 14. But that is Petitioner's speculation about Intas's (and others') commercial interest. While Intas (and Jina) are not required to share their highly sensitive "commercial interests," Patent Owner should certainly not be able to dictate what those interests are and avoid PGR by "permitting" Intas and Jina to use a (Z)-endoxifen salt for *only* bipolar

Response to Patent Owner’s Request for Discretionary Denial

disorder and psychiatric disorders—uses that are not claimed by the 391 patent. As discussed above, Intas and Jina have already invested in pursuing breast cancer treatment, demonstrating their commercial interest in such treatments.

Further, Patent Owner misrepresents the prior history between the parties in an attempt to suggest that Intas is merely trying to extract payment from Patent Owner by the filing of these proceedings. Intas (and Jina) did not request any compensation from Patent Owner simply to drop these proceedings. Indeed, as Patent Owner acknowledges, Intas offered terms for settlement only “*when Atossa initially reached out about settlement*” to discuss a cross-license. (Req. at 15.) Intas has an entirely proper purpose in seeking to invalidate the 391 patent—the right to prevent Patent Owner from unfairly excluding Intas (and all others) from practicing what was already taught in the prior art—not to extract money from Patent Owner.⁵ *Contrast OpenSky Industries, LLC v. VLSI Technology LLC*, IPR2021-01064, Paper 102, at *1, *3 (Oct. 4, 2022) (recognizing “OpenSky’s behavior in this proceeding is entirely distinguishable from conventional settlement negotiations that take place

⁵ Patent Owner also argues that Petitioner has not asserted any patents against Patent Owner yet still seeks a royalty. (Req. at 15.) Neither Intas nor Jina have asserted any patents because Patent Owner does not sell a product, and development for FDA approval is protected under 35 U.S.C. §271(e)(1).

Response to Patent Owner's Request for Discretionary Denial

in an adversarial proceeding” where “OpenSky’s only apparent business activity is the filing of two IPR petitions against VLSI” and its “conduct made clear that OpenSky was using the IPR process to extract payment from either Intel or VLSI without meaningfully pursuing unpatentability grounds” which “differs from typical settlement negotiations between adversaries during AIA proceedings, in which parties may offer payment or other consideration in return for settlement of the dispute”); *Patent Quality Assurance, LLC, et al. v. VLSI Tech. LLC*, IPR2021-01229, Paper 102 (Dec. 22, 2022) (same).

C. Section 325(d) does not favor discretionary denial

As Intas explained in its Petition, section 325(d) does not favor discretionary denial here, where it is undisputed that the Examiner did not issue a single art-based rejection of the claims and none of the references in the Petition were discussed by the Examiner or were the basis for rejection. Because these references are highly relevant, the Examiner erred in not substantively considering them.” Indeed, the Board has previously rejected Patent Owner’s prior identical argument in connection with the grandparent 334 patent. *See Intas Pharms. Ltd. v. Atossa Therapeutics, Inc.*, PGR2023-00043, Paper 11, *33-35 (P.T.A.B. January 31, 2024).

D. The merits are exceptionally strong

Patent Owner’s sole assertion regarding alleged novelty of the 391 claims over the prior art is that they require “internal enteric content.” Req. at 22. But the claims

Response to Patent Owner's Request for Discretionary Denial

nowhere contain such a limitation requiring “internal enteric content.” To the contrary, the specification and dependent claims make abundantly clear that the enteric material may be an enteric coating.

Though the specification never uses the term “enteric material,” it explains that enteric coatings are a part of the invention:

For time delay or delayed-release pharmaceutical preparations of oral dosage forms, glyceryl monostearate, glyceryl distearate, and acid-insoluble polymers, for example polymethacrylate pH-sensitive polymer-based coatings can be used, (e.g., as coating **material, i.e., enteric coating agents, for enteric coating of capsules, caplets, and tablets**).

Ex. 1001, 39:52-57 (emphasis added).⁶ Indeed, the specification expressly states that the “composition” itself may comprise such “enteric coatings”:

In yet another aspect, the present disclosure relates to *compositions* comprising (Z)-endoxifen or salts thereof prepared according to any of the methods disclosed herein, **further comprising one or more excipient, wherein the excipient is** a binder, a filler, a disintegrating agent, a lubricant, a glidant, a control release agent, **an enteric coating agent**, a film forming agent, a plasticizer, a sweetening agent, a flavoring agent, or a combination thereof.

Ex. 1001, 53:60-67 (emphases added).

⁶ Patent Owner acknowledges that pH-sensitive polymer-based coatings are enteric coatings. Req. at 24: “**compositions** may comprise one or more of **pH-dependent [i.e., enteric] polymers** such as acid insoluble polymers.” (Latter emphasis added.)

Examples of excipients that can be used *in the compositions* formulated for oral administration are provided herein and **can include**, but are not limited to, one or more of bulking agents, binders, fillers, disintegrating agents, lubricants, glidants, control release agents, **enteric coatings**, film-forming agents, plasticizers, colorants, sweeteners, flavoring agents and the like, or any combination thereof.

Ex. 1001, 36:65-37:4 (emphases added). These passages from the 391 patent specification expressly state that the enteric coatings are part of the “composition” regardless of whether they are “internal.” Enteric coatings are not a component separate from the “composition” as Patent Owner argues.

Patent Owner cites to claims 6, 9, and 30 as supposedly evidencing that an enteric coating cannot be a part of the composition or comprise the claimed “enteric material” (Req. at 22-23), but none of those claims supports Patent Owner’s conclusion.

In fact, Claim 6 ***disproves*** Patent Owner’s arguments. Claim 6 recites that the “composition is a capsule” making clear that “composition” does not simply refer to the “internal content.” Such a capsule may include as the enteric material an enteric coating. Indeed, claim 8 (which Patent Owner ignores) specifically claims that the “composition comprises an enteric coating” making clear that the *composition* encapsulated with the coating “comprises” that coating as an enteric material. Patent Owner does not and cannot explain how for dependent claim 8 the composition can “comprise an enteric coating” yet for the broader independent claim 1 from which claim 8 depends, external coatings are not a part of the composition. In short, claim

Response to Patent Owner's Request for Discretionary Denial

1 covers any enteric material—whether external or internal—that comprises part of the composition.

Patent Owner's reliance on Claims 9 and 30 is similarly unavailing. That narrower dependent claims are directed to particular embodiments in which the enteric material may also be interior does not somehow narrow the broader independent claim to such embodiments. For example, claim 9 claims that the "composition is formulated as a suspension." While Claim 30 claims "suspending the endoxifen and the enteric material in a fluid." They provide no guidance to understand the claim term "enteric material" in claim 1 or otherwise limit its scope (especially in light of dependent claim 8 as described above).

The prosecution history similarly demonstrates that claim 1 is not limited to "internal enteric materials." Indeed, the Examiner explicitly recognized that the claims are broader than those of the 334 patent and cover such enteric coatings:

Claims 158-201 are rejected on the ground of nonstatutory double patenting as being unpatentable over (a) claims 1-22 of U.S. Patent No. 11,680,036 or (b) claims 1-22 of U.S. Patent No. 11,572,334, (each cited by Applicant). Although the claims at issue are not identical, they are not patentably distinct from each other because **the present claims provide broadly for an "enteric material", (e.g., at least claim 1),** while the patented claims are directed to **specific types of enteric formulations**, i.e., a suspension or a capsule, thus making the presently claimed subject matter obvious to one of ordinary skill in the art.

Ex. 1002, page 284 of 408. And rather than overcoming that rejection or arguing that the present claims are in fact distinct from the 334 enteric coating claims, the

Response to Patent Owner's Request for Discretionary Denial

applicant filed a terminal disclaimer. *Id.* at page 302. By not disputing the Examiner's understanding, the applicant informed the public of this construction. See *Ventana Med. Sys., Inc. v. Biogenex Lab'ys, Inc.*, 473 F.3d 1173, 1182–83 (Fed. Cir. 2006) (agreeing “that the prosecution history of the '861 patent supports a broad construction of ‘dispensing’” where the Examiner’s “statement shows that the patent examiner did not consider the ‘dispensing’ claim term to be limited to the ‘direct dispensing’ embodiment disclosed in the specification.”); *SandBox Logistics LLC v. Proppant Express Invs. LLC*, 813 F. App'x 548, 554–55 (Fed. Cir. 2020) (“SandBox’s failure to challenge the Examiner’s understanding amounts to a disclaimer.”); *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1096 (Fed. Cir. 2013) (“If an applicant chooses, she can challenge an examiner’s characterization in order to avoid any chance for disclaimer, but the applicants in this case did not directly challenge the examiner’s characterization.”).

Indeed, the prosecution history confirms not only that the present claims cover enteric coatings, but that they are not patentably distinct from the 334 claims. A “terminal disclaimer is a strong clue that a patent examiner and, by concession, the applicant, thought the claims in the continuation lacked a patentable distinction over the parent.” *SimpleAir, Inc. v. Google LLC*, 884 F.3d 1160, 1168 (Fed. Cir. 2018). “Although a terminal disclaimer does not conclusively show that a child patent involves the same cause of action as its parent, the terminal disclaimer is still very

Response to Patent Owner's Request for Discretionary Denial

relevant to that inquiry.” *Id.*; see also *Indivior Inc. v. Dr. Reddy's Lab 'ys, S.A.*, 752 F. App'x 1024, 1035 (Fed. Cir. 2018) (“While not dispositive, the filing of a terminal disclaimer here is a ‘strong clue’ that the claims of the ’305 patent are patentably indistinct from those of the ’514 patent”). If the applicants thought their claims were distinct from the 334 patent claims by excluding enteric coatings, they should have so advised the Patent Office and the public at large.

Thus, when the claim term “enteric materials” is properly understood to include enteric coatings, there can be no dispute that the prior art discloses highly pure (Z)-endoxifen with such enteric materials. The Board already so found in the 334 PGR and Patent Owner concedes as much: “Ahmad discloses an endoxifen composition encapsulated in an enteric coating” (Req. at 20), thus conceding anticipation of many of the claims of the 391 patent. Further, collateral estoppel applies in full force against many of the claims of the 391 patent and factual findings resolved against Patent Owner in PGR2023-00043 as discussed below and in the Petition. *See* 334 FWD.⁷

⁷ Patent Owner further criticizes Petition Ground 8 based on 35 US.C. § 112 enablement and written description. Whether a patent meets the enablement and written description requirements is entirely based on the patent disclosure.

E. The Petition's use of expert testimony does not favor discretionary denial

The Petition relies on expert testimony to explain the prior art and how it teaches each and every limitation of the claims of the 391 patent and to establish that Ahmad is enabled justifying reliance on Ahmad as an anticipating reference (this issue of Ahmad enablement was fully considered in PGR2023-00043). That is hardly the type of “gap-filling” that favors discretionary denial. *Contrast Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9, at *16 (Aug. 24, 2022) (precedential) (“Petitioner’s only support for the assertion that ‘[a] POSITA would find it obvious that blocking the account of the purchaser from further use of the system would including storing a data value indicating the fraudulent activity in a data record associated with the user account’ is Dr. Jones’ Declaration. Pet. 28. Again, however, Dr. Jones offers only a *verbatim* restatement of the assertion being supported, without any supporting evidence or technical reasoning.”).

Notably, Patent Owner does not even argue that Ground 1 relies on expert testimony to fill gaps. *See* Req. at 30 (jumping straight to Ground 2). And Patent

Petitioner explained in the Petition that the 391 patent on its face does not provide enabling or written description support for the claims identified. That is all that is required.

Response to Patent Owner's Request for Discretionary Denial

Owner is demonstrably incorrect in arguing that the Petition does not rely on Ahmad for each limitation in Ground 2. The Petition explicitly states “although Ahmad discloses every element of claims 1-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44 of the 391 patent, each of the elements of these claims were also separately known and obvious in view of the knowledge of a POSA” and “arriving at the invention claimed in the 391 patent from Ahmad would have involved simply utilizing known, conventional, and predictable processes, and a POSA would have had a reasonable expectation of success in doing so.” Pet. at 38-39. And contrary to Patent Owner’s arguments, Petitioner did not rely “on extensive conclusory assertions from its experts” but rather as Patent Owner admits on “certain *other* references” to “represent the ‘view of the knowledge of a POSA.’” Req. at 30.

While Patent Owner suggests (without authority) that this is improper, it is exactly what Federal Circuit precedent calls for. *See, e.g., Koninklijke Philips N.V. v. Google LLC*, 948 F.3d 1330, 1338 (Fed. Cir. 2020) (“[H]ere the Board relied on expert evidence, ***which was corroborated by Hua***, in concluding that pipelining was not only in the prior art, but also within the general knowledge of a skilled artisan.... In sum, we conclude that the Board did not violate § 311(b) or the inter partes review statute in determining that the claims would have been obvious over SMIL 1.0 in light of the general knowledge of a skilled artisan.”) (emphasis added). In other words, Ground 2 simply demonstrated that *to the extent Petitioner argued any*

Response to Patent Owner's Request for Discretionary Denial

limitation was absent from Ahmad (which they are not), the limitations were also taught in other prior art references and were well-known to a POSA.

Patent Owner next argues that Petitioner's use of testing for a *single dependent claim* (claim 16) favors discretionary denial because it would allegedly be a burden for Petitioner to conduct similar testing to respond. Req. at 31. But Patent Owner is essentially arguing that a party should be able to obtain claims covering inherent properties (which Examiners have no ability to assess) and then render them immune from challenge. Such a policy is not provided for in the AIA, which created a cost-effective system to challenge patents. If Patent Owner does not wish to defend claim 16, then it should disclaim it, not offer narrow covenants not to sue as discussed above.

Finally, Dr. McConville's opinions are not "largely verbatim or near-verbatim assertions merely parroted from the Petition without any independent analysis or supporting evidence." Req. at 32 (citing Ex. 1032 ¶¶ 53-145). To the contrary, they are replete with citations to the record supporting Dr. McConville's testimony (including testimony directed to how Ahmad's enteric coating is an "enteric material"—the sole limitation Patent Owner addresses in its motion). *E.g.*, Ex. 1033 ¶ 29 (citing specific columns and lines of Ahmad), ¶ 54 (same).

Patent Owner's criticism of Dr. McConville's testimony is especially faulty given that the 334 panel *repeatedly* credited Dr. McConville's testimony on similar

Response to Patent Owner's Request for Discretionary Denial

formulation/pharmacokinetic issues as being well-supported by the same references. *E.g.*, 334 FWD at *35 (“We credit Dr. McConville’s testimony that applying enteric coatings would have been routine (Ex. 1020 ¶ 71; Ex. 1031 ¶ 5), which is consistent with Ahmad’s disclosure that the enteric coating ‘can be done as methods known in the art.’ Ex. 1003, 18:27-29...We credit the formulation expertise of Dr. McConville...we agree with Dr. McConville...”), 38 (“we credit the testimony of Dr. McConville, who explains that a POSA would understand Benamuer’s teachings [of intrinsically enteric capsules] with a model drug would be application to (Z)-endoxifen....”), 42 (“we credit the testimony of Dr. McConville, who notes that the HPE generally lists known incompatibilities...We are persuaded by Dr. McConville’s testimony....”), 46 (“we credit the well-supported testimony of Dr. McConville that it would have been routine for a POSA to run experiments like those described in Ahmad 2010 and 2012”). Dr. McConville’s testimony here is supported by the record, and not a basis for discretionary denial.

F. Discretionary denial would eliminate any estoppel effects from the 334 patent, which would not apply in district court

As explained in the Petition, numerous claims of the 391 patent are nearly identical to claims found unpatentable in the parent 334 or contain limitations already addressed in the 334 IPR. *See, e.g.*, Pet. at 14-15, 19-20, 26, 34, 36, 37, 39, 47-48, 49-50, 53, 55, 61, 64-65, 67, 70-72.

Response to Patent Owner's Request for Discretionary Denial

The findings of the Board, while subject to collateral estoppel effect in this and future Board proceedings, are (under current Federal Circuit precedent) *not* binding on Patent Owner in district court. *See, e.g., ParkerVision, Inc. v. Qualcomm Inc.*, 116 F.4th 1345, 1361–62 (Fed. Cir. 2024) (“Although we have not previously addressed the question of whether a finding underlying an unpatentability decision in an IPR proceeding collaterally estops a patentee from making validity arguments regarding separate, related claims in district court litigation, we now hold that it does not.”).

Discretionary denial here would effectively nullify the effects of the 334 IPR and require Petitioner (or any other party sued on the 391 patent) to argue invalidity from scratch despite the Board’s findings on nearly identical claims and limitations. This strongly weighs *against* discretionary denial and favors the Board continuing to reevaluate the patentability of Patent Owner’s patent claims in light of the arguments presented and certainly does not weigh in favor of denying further review of related patents that contain many overlapping limitations.

III. CONCLUSION

Petitioner has established a reasonable likelihood of prevailing as to each of claims 1-44 of the 391 patent, and therefore respectfully requests that the Board institute post grant review of those claims.

Response to Patent Owner's Request for Discretionary Denial

Respectfully submitted,

McANDREWS, HELD & MALLOY, LTD.

Dated: August 7, 2025

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CERTIFICATE OF WORD COUNT

I certify under 37 CFR § 42.24 that this **RESPONSE TO PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL** contains 6,086 words, as determined by Microsoft Word.

Dated: August 7, 2025

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CERTIFICATE OF SERVICE

Under 37 C.F.R. §§ 42.6(e)(4) and 42.105, the undersigned certifies on this date, a true and correct copy of **PETITIONER'S RESPONSE TO PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL OF INSTITUTION** and **EXHIBITS 1035-1037** were served by electronic mail to:

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