

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTAS PHARMACEUTICALS LTD.,
Petitioner

v.

ATOSSA THERAPEUTICS, INC.,
Patent Owner

Case IPR2025-00799
Patent 11,261,151

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

LIST OF EXHIBITS

Exhibit	Description
EX2001	ATOSSA THERAPEUTICS, INC. QUARTERLY REPORT FORM 10-Q for the Quarterly Period Ended March 31, 2025
EX2002	Atossa Therapeutics Proposes Potentially Groundbreaking Study Aimed at Reducing Interval Breast Cancer in High-Risk Women at AACR 2025 (April 29, 2025)
EX2003	Atossa Therapeutics Announces Plans to Pursue Metastatic Breast Cancer Indication for (Z)-Endoxifen and Continued Engagement with FDA on Additional Indications (March 11, 2025)
EX2004	Financials – Intas Pharmaceuticals Ltd., http://www.intaspharma.com/financials/
EX2005	Atossa Therapeutics Announces Issuance of Key U.S. Patent Covering Endoxifen (March 8, 2022)
EX2006	Efficacy and Safety of Endoxifen in Bipolar I Disorder Patients, NCT06608641 (Last Updated March 17, 2025), https://clinicaltrials.gov/study/NCT06608641
EX2007	Declaration of Sayem Osman
EX2008	Atossa Covenant Not to Sue
EX2009	Atossa Therapeutics Announces Full Results from Phase 2 KARISMA-Endoxifen Study Demonstrating Statistically Significant Reductions in Mammographic Breast Density (Dec. 11, 2024)
EX2010	Atossa Therapeutics Announces First Quarter 2025 Financial Results and Provides a Corporate Update (May 13, 2025)
EX2011	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , PGR2023-00043, EX1030
EX2012	Breast Center Year in Review, An Unmet Need in HR-Positive Endocrine-Resistant Breast Cancer, <i>available at</i> https://jons-online.com/special-issues-and-supplements/2021/2021-year-in-review-breast-cancer/an-unmet-need-in-hr-positive-endocrine-resistant-breast-cancer
EX2013	ATOSSA THERAPEUTICS, INC. ANNUAL REPORT FORM 10-K for the Fiscal Year Ended December 31, 2024
EX2014	U.S. Patent No. 11,572,334
EX2015	Intas Requirements for Resolving Disputes with Atossa (FILED UNDER SEAL)
EX2016	Default Protective Order

Exhibit	Description
EX2017	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , PGR2025-00043, Pap.2 (Apr. 3, 2025)
EX2018	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , PGR2023-00043, Pap.1 (Aug. 18, 2023)
EX2019	Rishab Gupta & Swarndeeep Singh, <i>Endoxifen Approval for Bipolar in India, A Premature or a Pragmatic Decision?</i> , 43(1) J. CLINICAL PSYCHOPHARMACOLOGY 3 (2023)
EX2020	Zonalta, Why Zonalta?, available at https://zonalta.in/
EX2021	Atossa Therapeutics Granted Additional Patent Protection for Endoxifen (August 28, 2024)
EX2022	Declaration of Megan Raymond

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I. Introduction

The Petition challenging U.S. Patent No. 11,261,151 (“the ’151 Patent”; EX1001), a foundational patent owned by Atossa Therapeutics (“Atossa” or “Patent Owner”) covering a crystalline polymorph of (Z)-endoxifen, represents precisely the type of inefficient and unduly burdensome proceeding that the USPTO’s current policies seek to prevent. The ’151 Patent and its patent family relate to novel (Z)-endoxifen compositions, and include claims directed to, *e.g.*, the treatment of hormone-dependent and tamoxifen-resistant breast cancer. This patent family is an important asset of Atossa and reflects years of focused research and clinical investment by a small American biopharmaceutical company to develop a stable, purified form of (Z)-endoxifen and to address a critical unmet need in hormone-sensitive breast cancer therapy. As explained below, discretionary denial is appropriate here pursuant to 35 U.S.C. §§ 314(a) and 325(d).

The challenged claims are directed to a crystalline Form I of (Z)-endoxifen, defined by a specific x-ray powder diffraction (XRPD) fingerprint, as well as methods of using this highly pure polymorphic form. These claims are distinct from the claims of the previously adjudicated related patent, U.S. Patent No. 11,572,334 (“the ’334 Patent”), which do not have any Form I or XRPD requirement. EX2014, cl.1. The (Z)-endoxifen claimed in the ’151 Patent provides a direct and reliable therapeutic alternative to tamoxifen, a decades-old standard of care that fails many

patients due to metabolic limitations. As discussed below, Patent Owner is currently pursuing clinical trials on the use of a free base form of the claimed (Z)-endoxifen to treat breast cancer. Petitioner, in contrast, is apparently involved in clinical trials using a salt form of (Z)-endoxifen in India to treat bipolar disorder and appears to be involved in clinical trials in the US using a salt form of (Z)-endoxifen to treat bipolar disorder.

This IPR is not an isolated event. Instead, it is the latest in a series of coordinated attacks by Petitioner against Patent Owner's intellectual property related to (Z)-endoxifen. Patent Owner is demonstrably a small entity, and relies almost entirely on external investment to fund its extensive research and clinical programs. And this Petition comes more than three years after patent issuance and amid ongoing Phase 2 and Phase 3 clinical trials built around the patented compound.

As discussed below, every relevant factor under the USPTO's March 26, 2025 Memorandum on Interim Processes for PTAB Workload Management ("March 26 Guidance") demonstrates that discretionary denial is the proper outcome here.

First, the public health implications are profound: Patent Owner's business is focused on the treatment and prevention of breast cancer. Patent Owner is conducting multiple Phase 2 and 3 clinical trials targeting hormone-dependent and metastatic breast cancers using the claimed (Z)-endoxifen, and institution could disrupt and jeopardize access to these therapies for patients with few alternatives,

particularly as Petitioner's filing is part of a serial attack designed to burden and destabilize a small clinical-stage innovator.

Second, institution here would be a needless waste of Patent Office and party resources. As discussed in more detail below and as reflected by the attached covenant, ***Patent Owner has provided a covenant not to sue Petitioner*** (or its affiliates or commercial partners) in the event Petitioner is able to bring its use of (Z)-endoxifen for treating bipolar disease to market. In light of this covenant, which eliminates any arguably legitimate commercial interest of Petitioner in challenging the '151 Patent, this proceeding would be a waste of resources for the Board and Patent Owner.

Third, Petitioner's delay, including its decision to challenge a ***later-issued*** continuation patent in a PGR in 2023 while holding off and delaying this IPR for several years, is gamesmanship that undermines Patent Owner's settled expectations.

Fourth, discretionary denial is warranted here under 35 U.S.C. § 325(d). All of the art in Petitioner's grounds was already substantively considered and rejected during prosecution. Liu (the only reference in Ground 1, and the primary reference in Ground 2) was explicitly used by the examiner in a rejection and Ahmad (the secondary reference in Ground 2) was cited in an IDS and discussed in the '151 patent's specification. Further, there was no material error by the Examiner.

Fifth, the merits are exceptionally weak. Petitioner relies exclusively on inherency in attempt to show that Liu discloses the claimed Form I and XRPD pattern. But instead of relying on Liu's actual disclosures, Petitioner reimagines, alters, and adds to Liu. Petitioner's own expert, Dr. Bihovsky, initially failed to reproduce the claimed Form I of (Z)-endoxifen based on Liu and then was only able to obtain it after making no fewer than nine distinct deviations from Liu's protocol, undermining any claim of "inherency" and highlighting the weakness of this challenge. This weakness impacts all of the grounds. Petitioner's arguments about "collateral estoppel" are misplaced and do not save the Petition. The prior PGR involved different claims, different art, and did not address, let alone decide, the issues involving Form I, XRPD, or Liu's "inherency" that are presented here.

Sixth, the Petition's excessive reliance on layered expert testimony to fill gaps and also to allege inherency through benchtop testing confirms that the factual issues raised here are ill-suited for an IPR.

For the reasons above, taken individually or based on a holistic assessment, the Board should grant Patent Owner's request for discretionary denial.

II. The '151 Patent: A Lifeline for Breast Cancer Patients

Breast cancer continues to be a formidable public health challenge, remaining as the most common form of cancer in women and second leading cause of cancer death in humans. *See, e.g.*, EX1001, 1:18-20. Hormone-dependent breast cancer

represents the most prevalent subtype. EX2001, 18 (“ER+ breast cancer which comprises approximately...78% of all breast cancers.”). Tamoxifen has been a first-line treatment for hormone-dependent breast cancer, but many patients, due to genetic factors or drug interactions, cannot adequately metabolize tamoxifen into its active metabolite, endoxifen, rendering such treatment ineffective for those individuals. *See* EX1001, 1:61-2:38; 42:43-64. Tamoxifen is also known to have severe side effects. *See id.* at 1:61-2:38. (Z)-endoxifen is the “main active metabolite responsible for the clinical efficacy of tamoxifen” and provides more consistent efficacy, regardless of patient genotype. *See id.*

Obtaining relatively pure and stable forms of (Z)-endoxifen proved a challenge until the ’151 Patent. *See id.* at 27:23-40. The inventors of the ’151 Patent developed a novel synthesis process that avoids the inefficiencies and instabilities of prior methods, yielding a crystalized form of (Z)-endoxifen (at least 90% by weight) with superior stability and commercial-scale feasibility. *See id.*

The ’151 Patent teaches a synthetic pathway and purification process to create this highly pure (Z)-endoxifen. EX1001 at Examples 1, 4-9. The starting isomeric mixture of (E)/(Z)-endoxifen is first subjected to crystallization. *Id.* Because the inventors observed that (E)-endoxifen is much less soluble than (Z)-endoxifen in a variety of solvents, this initial crystallization step results in an enriched (Z)-endoxifen component (*e.g.*, a mother liquor or filtrate). *See id.* at 68:3-11 (“(Z)-

endoxifen was seen to be more soluble than (E)-endoxifen in EtOAc....Serial enrichment of Z-endoxifen by adding filtrates back to the first filtrate (first mother liquor) can also be performed.”). The enriched (Z)-endoxifen component is then subjected to further crystallization to obtain pure (Z)-endoxifen solid in a free base composition. *See id.* at 68:6-8 (“Both solids and filtrates are useful for the preparation of (Z)-endoxifen free base.”). The (Z)-endoxifen free-base solid composition obtained is shown to have increased stability in ambient conditions, with reduced isomeric conversion to the (E)-isomer. *See id.* at 84:20-28 (“Results show that solid Z-endoxifen free base is stable for at least 9 months at 5° C. and 25° C./60% RH.... (Z)-to-(E).

The stable, highly-pure crystalline form of (Z)-endoxifen (“Form I”) claimed in the ’151 Patent aims to address the urgent need for a safer and more effective treatment and has improved bioavailability, bypassing metabolic limitations and providing consistent therapeutic benefit across diverse patient populations. *Id.* at 1:61-2:53, 2:57-11:2, 98:28-100:45. Moreover, unlike existing synthetic methods, the process disclosed in the ’151 Patent to synthesize the claimed Form I with the claimed XPRD pattern achieves high yields, high purity, and improved stability, and is more economical and scalable for commercial production. *Id.* at 23:64-24:1, 27:23-40, 30:8-35, 82:5-19. The claimed Form I with improved stability addresses, *e.g.*, “a need for (Z)-endoxifen free base preparations that are sufficiently stable for

preparation of pharmaceutical compositions that are suitable for administering to subjects, for example, at ambient temperatures as well as at higher temperature and humidity.” *See id.* at 82:5-19. The invention described and claimed in the ‘151 Patent is not merely an incremental improvement; it is a breakthrough innovation for breast cancer therapy.

III. The Parties

Patent Owner Atossa is a small clinical-stage American biopharmaceutical innovator with “small entity” status at the USPTO. *See* EX2001, 16; EX1002, 2, 568. Atossa does not yet have any products on the market and therefore does not yet generate revenue sufficient to cover its operating costs. *See* EX2001, 6-7, 19 (“We are in the research and development phase and are not currently marketing any products. We do not anticipate generating revenue unless and until we develop and launch our pharmaceutical programs.”). For the time being, Atossa depends on investments in the company to fund its research and clinical efforts (*See* EX2001, 7)—as well as its defense of this dispute from Petitioner.

Atossa’s business is focused on developing its claimed (Z)-endoxifen treatment to help patients with or at high risk for breast cancer. *See* EX2001, 7, 16; EX2010 (Atossa’s “focus remains firmly on advancing (Z)-endoxifen as a next-generation therapy for breast cancer patients across the full spectrum of care...”). Patent Owner is actively developing a free base form of (Z)-endoxifen and running

several Phase 2 clinical trials using a free base form of the claimed (Z)-endoxifen. *See* EX2001, 16-18. These trials include the EVANGELINE Trial, investigating it as a neoadjuvant treatment for premenopausal women; the I-SPY Trial, evaluating it in a Phase 2 sub-study for newly diagnosed ER+ invasive breast cancer; the RECAST-DCIS Study, assessing its suitability for neo-adjuvant endocrine therapy in women with Ductal Carcinoma In Situ; and the KARISMA Trial, demonstrating a statistically significant reduction in mammographic density, a major and under-addressed risk factor for breast cancer. *See id.*; EX2009. Additionally, Patent Owner is planning a Phase 3 trial, SMART 2.0, to investigate its potential in reducing interval breast cancer in high-risk women and is prioritizing its development for metastatic breast cancer. EX2002, 1.

Petitioner Intas is a large foreign manufacturer of generic drugs with billions in annual revenue and significantly greater resources. EX2004, 1. Intas appears to have a relationship with Jina Pharmaceuticals Inc.,¹ which Intas says “may be interested” in the outcome of this IPR (Pet.2), and which is currently involved in

¹ Though Jina is not listed as an RPI in the Petition, Intas and Jina appear to have a relationship related to endoxifen and the treatment of bipolar disorder (*see, e.g.*, EX2019, 1; EX2020) [REDACTED]

[REDACTED]

Phase 3 trials using (Z)-endoxifen (in a salt form) to treat for Bipolar I Disorder (*see* EX2006).

IV. The Board May Take Into Account All Relevant Considerations in Exercising its Discretion to Deny Institution

The Board has discretion to deny institution under 35 U.S.C. §§ 314(a) and 325(d).² Pursuant to the Office’s March 26, 2025 Guidance, the Board may look to “all relevant considerations” in exercising discretionary denial, including: “whether the PTAB or another forum has already adjudicated the validity or patentability of the challenged patent claims;” “the strength of the unpatentability challenge;” “the extent of the petition’s reliance on expert testimony;” “settled expectations of the parties, such as the length of time the claims have been in force;” “compelling economic, public health, or national security interests;” and “any other considerations bearing on the Director's discretion.” *See* March 26 Guidance at 2-3. Each of the considerations addressed below, both taken independently and assessed together, supports discretionary denial.

A. Compelling Public Health Interests Support Discretionary Denial

Public health considerations here favor discretionary denial. Atossa has the potential to substantially improve patient outcomes, as suggested by Patent Owner’s

² Unless stated, statutory and regulatory citations are to 35 U.S.C. or 37 C.F.R., as context indicates, internal citations omitted, and emphases/annotations are added.

ongoing clinical trials using its (Z)-endoxifen. Early results have shown that the (Z)-endoxifen used by Atossa in its clinical trials “more than doubled the median [progression-free survival] compared to tamoxifen” in certain patients. *See* EX2003, 1. Its tolerability is a critical advantage, as it can lead to better patient adherence and an enhanced quality of life, especially for those with incurable metastatic breast cancer. *See id.*

Atossa’s clinical trial programs represent ongoing multi-year, multi-million-dollar investments. *See* EX2013, 8 (listing “Research and development” at \$14.1 million for 2024 and \$17.3 million for 2023). As a small innovative clinical-stage biopharmaceutical company, Patent Owner depends on external investment to fund these programs. *See* EX2001 at 6, 7, 16, 19. Atossa’s IP, including the ’151 Patent and its patent family, helps Patent Owner build and maintain investor confidence, enabling the continued funding of these critical trials. *See id.* at 4, 21, 24, 33-34; EX2013, 8-9. Petitioner’s IPR undermines this confidence at a critical time of the development of (Z)-endoxifen for breast cancer, which could lead to delays, suspension, or even outright termination of ongoing and planned clinical trials, directly impacting patient enrollment and access to investigational therapies, and distracting management. *See id.* at 21 (“If we are unable to raise additional capital when needed on reasonable terms, if at all, we could be forced to curtail or cease our operations. Our future capital uses and requirements will depend on the time and

expenses needed to begin and continue clinical trials for our new drug developments.”), 34 (“Any litigation proceedings relating to our propriety technology... may result in substantial costs and distract our management and other employees”); EX2013, 8-9 (“Intellectual property is important to our business and future income streams will depend, in part, on our ability to obtain and maintain patents”); EX2005 (“the ’151 Patent,’ with its estimated expiration in 2038, strengthens our intellectual property estate and should create long-term stockholder value”); *see also* EX2021 (“this new patent will create long-term stockholder value as it further validates and expands Atossa’s patent protection beyond our previously issued composition of matter patents”); *infra* §IV.(B) (providing covenant not to sue); EX2008.³

Such disruption would not only harm Patent Owner but, more importantly, would directly undermine public health by delaying or preventing access to a promising new therapy for breast cancer—a disease with significant unmet medical

³ This IPR is not an isolated challenge, but instead is the latest in a series of coordinated attacks by Petitioner against Patent Owner’s intellectual property related to (Z)-endoxifen. *See* Pet.2 (acknowledging prior “PGR2023-00043” and noting “at the same time [Petitioner is] filing a petition for Post Grant Review challenging related U.S. Patent No. 12,071,391”).

needs. Individuals suffering from hormone-dependent breast cancer, especially those with metastatic or endocrine-resistant forms, eventually exhaust standard and/or older therapies and depend on newer and novel options to extend survival. Atossa is working to develop those options. The progression of their disease during such delays may render them ineligible for future treatment or diminish the effectiveness of any eventual therapy. The potential for increased progression-free survival using Patent Owner's (Z)-endoxifen also represents a significant quality of life and economic benefit in reducing healthcare costs associated with more aggressive treatments. *See* EX2012, 2; EX2001, 18 (“(Z)-endoxifen for Neoadjuvant Treatment of Breast Cancer. We are also developing (Z)-endoxifen to treat estrogen receptor positive (ER+) / human epidermal growth factor receptor 2 negative (HER2-) breast cancer in the neoadjuvant setting, which is the administration of a therapy before the main treatment, which is usually surgery.”).

And while Intas uses a salt form of (Z)-endoxifen in India to treat bipolar disorder (EX2019, EX2020), and Intas (with Jina) appears to be involved in clinical trials using (Z)-endoxifen only to treat bipolar disorder, Intas has nevertheless chosen to include in its various PTAB challenges claims specifically limited to breast disorders—claims not implicated by their very different work. Pet.35-36 (challenging claim 16, “[a] method of treating a hormone-dependent breast disorder”), 36 (challenging claim 18, “wherein the subject has tamoxifen-refractory

or tamoxifen resistant hormone-dependent breast disorder”); *see* EX2017, 34-37 (challenging claims 42 (“treating a hormone-dependent breast disorder”), claim 43 (“wherein the hormone-dependent breast disorder... is... breast cancer”), claim 44 (“wherein the hormone-dependent breast disorder... is tamoxifen-refractory or tamoxifen resistant”)); EX2018, 33-34 (challenging claim 20 (“treating a hormone-dependent breast disorder”), 34 (challenging claim 21 (“wherein the hormone-dependent breast disorder... is... breast cancer”)), 35 (challenging claim 22 (“wherein the hormone-dependent breast disorder... is tamoxifen-refractory or tamoxifen resistant.”)). Intas’s goal is seemingly to interfere with Atossa’s clinical development of a treatment for breast cancer to the detriment of public health. *See also* §IV(B).

The threat posed by Petitioner’s IPR 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. That potential harm to Patent Owner outweighs any arguable benefit to Petitioner in instituting this petition, particularly in view of Patent Owner’s stipulation discussed below, which leaves Intas and Jina free to pursue the use of (Z)-endoxifen salts for the treatment of bipolar disorders, consistent with their current trial.

The USPTO’s recent guidance on its process for addressing discretionary denial explicitly identifies “compelling economic, public health, or national security

interests” as a factor to be considered. *See* March 26 Guidance at 2. Given the critical unmet needs in breast cancer, the unique advantages of the claimed (Z)-endoxifen for treating breast cancer, Patent Owner’s limited resources, and the advanced stage of Patent Owner’s clinical development, the public health interest in ensuring the uninterrupted progress of this therapy is strong. Allowing institution here would not serve the goals of innovation or fairness; instead, it would enable a large foreign generic to exploit the machinery of the AIA to derail a small American innovator’s efforts to bring a potentially-critical breast cancer treatment to market.

B. This Proceeding Would Waste the Board’s Resources Given Patent Owner’s Stipulation Not to Sue for Infringement

As explained above, Intas’s only commercial interest in (Z)-endoxifen appears to be in treating bipolar disorder using a salt form of (Z)-endoxifen. And Patent Owner attaches herein a covenant not to sue Petitioner Intas, Jina Pharmaceuticals Inc.,⁴ or their respective affiliates, distributors, customers, and users for any infringement of the ’151 Patent based on the manufacture, importation,

⁴ For the avoidance of any related dispute, the covenant also covers Jina Pharmaceuticals Inc., which appears to have partnered with Intas on the clinical trials for treating bipolar disorder using a salt form of (Z)-endoxifen. *See* EX2019, 1; EX2008; EX2020.

distribution, use, sale and/or offering for sale any product that incorporates a salt form of (Z)-endoxifen for the treatment of bipolar disorder or other psychiatric disorders assuming this proceeding is not instituted and Patent Owner is not subjected to the burden of continuing to defend this proceeding. EX2008. Notably, while Intas has no product in development directed to (Z)-endoxifen for treating breast cancer and other hormone-dependent disorders, Intas has nevertheless included in its challenge to Atossa's '151 Patent claims specifically limited to a "method of treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder." *See* Pet.35-37, 56-67 (challenging claims 16-21); cl.16 ("A method of treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in a subject..."). [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]. *See generally OpenSky Indus.*

LLC v. VLSI Tech. LLC, IPR2021-01064, Pap.102, [REDACTED]

[REDACTED] *Patent Quality Assurance, LLC, et al. v. VLSI Tech. LLC*, IPR2021-01229, Pap.102, [REDACTED]

[REDACTED] Even if they are subject to FRE 408, they are admissible here [REDACTED]

See Blackbird Tech LLC v. Health in Motion LLC, 944 F.3d 910, 916 (Fed. Cir. 2019) ([REDACTED])

[REDACTED] The evidence here is not being used “to prove or disprove the validity or amount of a disputed claim or to impeach....” FRE408(a); *see also* FRE408(b) (“The court may admit this evidence for another purpose....”).

The March 26 Guidance confirms the Office’s case-by-case flexibility in considering arguments that may support discretionary denial. *See* March 26 Guidance at 3 (referring to “any other considerations bearing on the Director’s discretion”). In light of this covenant eliminating any arguably legitimate commercial interest of Petitioner in challenging the ’151 Patent, separately or together with the public health considerations, institution should be denied.

C. Patent Owner’s Settled Expectations Deserve Protection Where Petitioner Challenged a Related Patent in 2023 but Delayed in Filing This Challenge

The PTAB has explicitly recognized “settled expectations of the parties, such as the length of time the claims have been in force” as a key factor in determining whether to exercise its discretion to deny institution. *See* March 26 Guidance at 2; *iRhythm Techs., Inc. v. Welch Allyn, Inc.*, IPR2025-00363,-00363,-00374,-00376,-00377,-00378, Pap.10 (June 6, 2025) (denying institution based on patent owner’s settled expectations); *Dabico Airport Sols., Inc. v. AXA Power ApS*, IPR2025-00408, Pap.21, 2-3 (June 18, 2025) (denying institution based on patent owner’s settled expectations). Petitioner’s delay in filing this IPR in view of its *earlier* PGR of a *later-issued* parent patent suggests Intas was not going to challenge the ’151 Patent and supports discretionary denial based on Atossa’s “settled expectations.”

The ’151 Patent issued on March 1, 2022. U.S. Patent 11,572,334, the child of the ’151 Patent, issued February 7, 2023. On August 18, 2023, Petitioner filed

PGR2023-00043 challenging the child '334 Patent, and acknowledging that the '334 was a continuation of the '151 Patent that it would later challenge here. EX2018, 5. The final written decision in that PGR issued on January 29, 2025. But instead of filing this IPR earlier (along with the previous PGR, for example), Petitioner waited until April 3, 2025 to file. And by delaying filing of this IPR,⁶ Petitioner signaled that it would not be challenging the '151 Patent. Even if Petitioner had only learned of the '151 Patent when it learned of its child '334 Patent, it could certainly have challenged the two patents simultaneously.

The Board's discretion should be exercised to protect the "settled expectations" of innovators like Atossa, especially where a petitioner has affirmatively withheld bringing an earlier PGR or IPR, and where there is no legitimate commercial purpose to be served by bringing it later. This is certainly true here, where any purported "dispute" has already been resolved by a covenant not to sue.

⁶ Like PGR2023-00043, Petitioner's IPR cites laboratory experiments related to Liu and carried out by Dr. Bihvosky. *See* EX2011, ¶¶ 36-52.

D. The Board Should Additionally Deny Institution Under 35 U.S.C. §325(d) Because the Office Has Already Rejected the Same Art During Prosecution

Section 325(d) provides that the Board may deny institution if “the same or substantially the same prior art or arguments previously were presented to the Office.” Part 1 of the *Advanced Bionics* test considers three factors, including “(a) the similarities and material differences between the asserted art and the prior art involved during examination,” “(b) the cumulative nature of the asserted art and the prior art evaluated during examination,” and “(d) the extent of the overlap between the arguments made during examination and the manner in which petitioner relies on the prior art.” *Advanced Bionics, LLC v. Med-El Elektromedizinische Gerate GmbH*, IPR2019-01469, Pap.6, 9n.10 (Feb. 13, 2020) (precedential) (“AB”), citing *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Pap.8 (Dec. 15, 2017). And Part 2 of *Advanced Bionics* considers “(c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection,” “(e) whether petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art,” and “(f) the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments.” *Id.*

Here, the two-part *Advanced Bionics* test confirms that institution should be denied. First, the Liu reference (WO 2017/070651; EX1003), which is the linchpin

of Petitioner's entire challenge, was already presented and substantively considered during original prosecution. Second, there was no material error in the Office's treatment of Liu or in its ultimate decision to allow the claims over Liu.

AB Part 1. The prior art in Grounds 1 and 2 of the Petition was previously presented to the PTO during prosecution. *AB*, 8, 9n.10, 10. Indeed, both Liu (the sole reference relied on in Ground 1, and Petitioner's base reference for Ground 2) and Ahmad (the sole secondary reference in Ground 2) were before the Office during prosecution. EX1002, 188 (Ahmad), 190 (Liu). Liu was explicitly considered by the examiner in a rejection. *See* EX1002, 431 (referencing rejection based on WO 2017/070651). Ahmad was cited in an IDS (EX1002, 188) and was explicitly discussed in the '151 Patent's specification (EX1001, 18:4-17 (addressing U.S. Pat. No. 9,333,190)). Thus, the first condition of the AB framework is satisfied for both Grounds 1 (anticipation based on Liu) and 2 (obviousness based on Liu in view of Ahmad).

AB Part 2. Liu was explicitly considered during examination and was used as a basis in rejecting then-pending, later-cancelled claim 62 (a process claim for manufacturing (Z)-endoxifen) as obvious over Liu. EX1002, 423-434. Thus, the Examiner plainly did not overlook Liu or the processes Liu relies on in recrystallizing a (Z)/(E)-endoxifen crystalline mixture into a crystalline solid with a higher ratio of (Z)-endoxifen. *See GoFire, Inc. v. Canopy Growth Corp.*, PGR2020-

00044, Pap.8, 14 (Oct. 9, 2020) (“Petitioner’s contention amounts to a disagreement with the Examiner’s finding that the art does not teach or suggest the ‘comparing’ limitation. Moreover, it is a disagreement based not on teachings of the prior art that the Examiner may have misapprehended or overlooked, but rather on mere attorney argument as to what ‘natural presumption’ the Examiner allegedly should have drawn from the reference. This is not sufficient to demonstrate that the Examiner’s prior evaluation of the art was in error.”).

Petitioner asserts the Office erred because the Examiner was “not being capable of performing XRPD on Liu” (Pet.22), but this is not a basis for claiming material error.⁷ The Examiner was fully aware of Liu’s processes and that a key distinguishing feature of the claimed invention was the specific crystalline Form I and its characteristic XRPD pattern. EX1002, 431-32. Indeed, the claims explicitly define Form I by its XRPD pattern. EX1001, cl.1 (“Form I, characterized by an x-ray powder diffraction pattern”). The Examiner did not “err” in failing to predict or commission new experimental data to uncover supposedly “inherent” properties that

⁷ Petitioner relies solely on a theory of inherency regarding the claimed x-ray powder diffraction powder limitation in both Grounds 1 and 2. *See* Pet.29, 38 (explaining Ground 2, and stating “[a]s discussed above, the claimed XRPD patterns are inherently taught by Liu”).

were not apparent from the prior art’s disclosure. As discussed in Section §IV.E below, Petitioner’s new “evidence” is merely the cherry-picked post-hoc reconstruction by its expert, which involved repeatedly *altering* Liu’s process until he coaxed out the claimed Form I that Liu never disclosed. As a matter of law, this cannot establish inherency—which requires the limitation at issue “necessarily must be present” in the “combination of elements explicitly disclosed by the prior art.” *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1195-97 (Fed. Cir. 2014) (“A party must, therefore, meet a high standard in order to rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis—the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art.”); *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981) (“Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.”); *see infra* §IV.E. Petitioner’s legally insufficient inherency theory improperly ***modifies*** Liu’s own disclosed processes, and therefore could not demonstrate material error by the Examiner in considering what Liu ***actually*** discloses. Indeed, allowing institution here would invite petitioners to perpetually challenge patents by ginning up experimental “data” to “prove” what the Examiner “should have known” from prior art that does not explicitly disclose or suggest something, and would not, in fact, yield that something

when a POSITA follows what the art *does* disclose. *See also infra* §VI.F. Institution here should be denied because both of Petitioner’s asserted grounds rely on Liu to “inherently” disclose the claimed Form I (Pet.29, 38).⁸

The two §325(d) cases Petitioner cites in passing (Pet.23) are readily distinguishable. In *Apple*, the Board found material error because the Examiner had entirely *overlooked* paragraph 23 of the prior art reference, which expressly disclosed the claim limitation at issue. *See Apple Inc. v. Immervision, Inc.*, IPR2023-00471, Pap.10, 27-28 (July 11, 2023). Here, by contrast, Petitioner concedes that Liu does not contain *any* express disclosure of the claimed (Z)-endoxifen (Pet. 29); instead, Petitioner relies entirely on expert-driven post-hoc *modifications* of Liu’s process to try to create, by experiment, a supposedly supporting disclosure today. *Amazon* is likewise inapposite: there, the Board declined to exercise discretion under §325(d) because, although the cited reference was listed in an IDS, it was never substantively considered or used as a basis for rejection. *See Amazon.com, Inc. v.*

⁸ Petitioner relies on Ahmad solely for different disclosures than those for which it argues inherency based on Liu (Pet.39), and different from the claim limitation the Examiner identified in allowing the claim (the “polymorph of Form I”) (EX1002, 537). Petitioner’s use of Ahmad therefore cannot create a material error relevant to Petitioner’s Ground 2 and §325(d).

Vb Assets, LLC, IPR2020-01346, Pap.7, 8-9 (Feb. 4, 2021). In contrast, here, Liu was not merely listed on an IDS but, rather, was substantively applied in rejecting related claims during prosecution of the '151 Patent.

E. The Merits Are Weak

1. Petitioner's Inherency Arguments Are Legally Insufficient

The “the strength of the unpatentability challenge” is a factor explicitly identified in the Office’s March 26 Guidance as a consideration for discretionary denial. *See* March 26 Guidance at 2. Where, as here (and as PO’s forthcoming Preliminary Response will confirm), the asserted grounds rest entirely on a legally-flawed “inherency” theory, the Board should deny institution under §314(a) based on the weakness of the merits alone.

Petitioner and all three of its experts concede that Liu *fails* to disclose the claimed Form I with the x-ray powder diffraction pattern. Pet.29 (“***Liu does not disclose*** that the (Z)-endoxifen he creates is the claimed ‘Form I’ or provide an XRPD characterization of the resulting crystalline solids.”); EX1034, ¶ 29 (“***Liu does not disclose*** that the (Z)-endoxifen created is the claimed ‘Form I’ or provide an XRPD characterization of the resulting crystalline solids.”); EX1033, ¶ 33 (“***Liu does not report*** whether its compounds exhibited the XRPD pattern recited in the claims of the 151 Patent (*i.e.*, Form I).”); EX1032, ¶ 65 (“***[N]either Liu nor Ahmad specifically disclose*** that their Z-endoxifen is the claimed ‘Form 1’”).

Instead, Petitioner rests its entire invalidity theory for both Grounds 1 and 2 (Pet.3, 29, 38) on legally inadequate assertions of inherency in attempt to establish disclosure of the Form I (Z)-endoxifen with the claimed XRPD. *See* Pet.29, 34, 35 (cl.1, cl.16 (“(Z)-isomer is Form I, characterized by an x-ray powder diffraction pattern comprising major peaks at 16.8 16.8±0.3°, 17.1±0.3° and 21.8±0.3° two theta”); cl.6 (“wherein greater than 90% by weight of the (Z)-isomer in the composition is crystalline Form I”).⁹ Although Patent Owner may address the deficiencies of Petitioner’s grounds more fully in its Preliminary Response, in short, the Petition’s reliance on inherency is fundamentally undercut by its own expert’s admissions, which show Petitioner’s expert *modified* Liu, *filled in gaps, and made choices among various available implementation options* in Liu’s disclosure to allegedly achieve supposedly “inherent” results that Petitioner argues satisfy the claims. *See e.g.*, EX1033, ¶¶ 51 (“I synthesized compound (5) by a *modification* of the procedure described by Liu”), 52n.3 (“*Liu does not explicitly state to use Celite*

⁹ Indeed, Petitioner does not allege (nor could it) that any teaching from any other reference or knowledge of POSITA that discloses the XRPD pattern missing from Liu. *See* Pet.29, 38. Ground 2 rests on the same inherency theory advanced in Ground 1 and provides no independent evidence or motivation concerning the XRPD limitation.

at this step.”), 52n.4 (“While *Liu does not specifically describe using chromatography...*”), 54n.5 (“*Liu states...argon atmosphere.... Instead of an argon atmosphere, I placed the reaction under a nitrogen atmosphere.*”). The declaration of Petitioner’s expert, Dr. Bihovsky, reveals that *Liu’s process would not give him the result* he desired and relies upon *until he rewrote it in at least nine separate ways* (as numbered below)—and even then, *multiple results failed to yield the claimed Form I*, a fact that Petitioner conspicuously omits despite its direct bearing on inherency. *See id.* Indeed, Petitioner’s deliberate alterations and resulting failures are the *opposite* of inherency, which requires that the missing element be *necessarily, unavoidably, and inevitably* present based on the reference’s explicit disclosure. *See In re Montgomery*, 677 F.3d 1375, 1380 (Fed. Cir. 2012) (“The inherent result *must inevitably result* from the disclosed steps...”); *Millennium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017) (“fact that a certain thing *may* result” is insufficient); *Azurity Pharms., Inc. v. Exelixis Inc.*, IPR2025-00210, Pap.11, 28 (June 4, 2025) (“That is not, however, the standard for inherency. It *must be the necessary result, not a possible expected result.*”); *Celltrion, Inc. v. Chugai Seiyaku Kabushiki Kaisha*, IPR2022-00579, Pap.72, 27 (Aug, 29, 2023) (“A reference may anticipate inherently if a claim limitation that is not expressly disclosed ‘is necessarily present, or inherent, in the single anticipating reference.’”) (citing *Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325,

1337 (Fed. Cir. 2010)); *see also Agilent Techs., Inc. v. Affymetrix, Inc.*, 567 F.3d 1366, 1383 (Fed. Cir. 2009) (holding that the “very essence of inherency is that one of ordinary skill in the art would recognize that a reference unavoidably teaches the property in question”); *see also Arbutus Biopharma Corp. v. Modernatx, Inc.*, 65 F.4th 656, 662 (Fed. Cir. 2023) (“A limitation is inherent if it is the ‘natural result flowing from’ the prior art’s explicit disclosure.”) (citations omitted); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343–44 (Fed. Cir. 2005).

To begin with, Dr. Bihovsky did not follow Liu as written. Instead, (1) he ran the synthesis at a markedly smaller laboratory scale than Liu’s commercial-scale disclosures, making various changes to Liu as a result. EX1033, ¶¶ 48, 52n.4, 59n.6 (“centrifugation is a minor deviation from Liu’s procedure...was simply a more practical approach given the scale of the recrystallization I conducted...”). Contrary to Liu’s explicit disclosures, he then (2) increased the temperature in the first reaction step to 70 °C, even though Liu expressly instructs 45–50 °C; he admitted that the reaction would not proceed as written and was “mostly complete” only after the temperature was elevated and reaction time was extended by five hours. *Id.* at ¶ 51. He also (3) pre-dried zinc bromide at 230 °C to remove moisture, a step Liu does not mention. *Id.* at ¶ 51n.1. Dr. Bihovsky does not show Liu removed the moisture at all, and even if Liu did, he did not establish that every way in which the moisture could have been removed would have yielded the same result. *Pfizer, Inc.*

v. Chugai Pharm. Co, IPR2017-01357, Pap.56, 19-20 (Nov. 28. 2018) (“Petitioner does not argue either that there is only a single method for making Shadle’s elution buffer, which always yields a buffer having 100 mM or less total solute, or that every method for producing Shadle’s buffer results in a buffer with 100 mM or less total solute...The probability or possibility that an ordinarily skilled artisan would have used one of the four methods described by Dr. Przybycien to prepare Shadle’s elution buffer is insufficient to establish inherency”).

Throughout the synthesis, Dr. Bihovsky also experimented with process ***steps not found in Liu***. For example, he (4) used a Celite pad to filter an emulsion, claiming it was a judgment a skilled chemist would make (EX1033, ¶ 52n.3 (“Liu does not explicitly state to use Celite... Celite is a commonly employed filtration medium...”)), and he (5) added a column chromatography purification that Liu does not disclose, justifying it as a “common” small-scale adjustment (*id.* at ¶ 52n.4 (“I decided to employ chromatography”)). He also (6) substituted a nitrogen atmosphere in place of Liu’s argon (*id.* at ¶ 54n.5), and (7) replaced filtration with centrifugation during a key recrystallization step because it was more “practical” (*id.* at ¶ 59n.6). Despite these interventions, the (8) resulting product still differed in E/Z isomer ratio: 33% Z, rather than the 47% Z disclosed in Liu (*id.* at ¶ 60n.7). Finally, because only a “small amount of precipitate” had formed, Dr. Bihovsky (9)

physically scratched the flask and continued stirring for 24 more hours to **force** crystallization (*id.* at ¶ 61).

The Board rejected a similar inherency argument in *SNF S.A. v. Chevron U.S.A., Inc.*, where the alleged inherent property (a specific filter ratio) was only achieved after petitioner’s expert added a “dewatering” step not described in the reference. IPR2022-01534, Pap.46, 25-27 (Apr. 18, 2024). The Board emphasized that inherency “may not be established by probabilities or possibilities,” and “the mere fact that a certain thing **may** result from a given set of circumstances is not sufficient.” *Id.* at 23–24 (quoting *Cont’l Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)); see *Crown Operations Int’l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1377 (Fed. Cir. 2002).

The same reasoning applies here. Petitioner’s expert modified Liu’s process not once, as in *SNF*, but in at least nine ways, ***and still repeatedly failed to yield the claimed Form I***. The purported “inherency” here is merely the result of Petitioner selectively reporting the one success while omitting the multiple failures. As in *SNF*, Petitioner’s numerous modifications and failures affirmatively negate its claim that Form I naturally flows from Liu’s teachings.

Further, Dr. Bihovsky tries to wave away his changes to Liu as “minor,” and asserts that certain changes would have “no effect” on the final crystal form, but these self-serving assertions (although critical to his inherency argument) are merely

conclusory and lack citation to and support by evidence. EX1033, ¶¶ 47, 52n.4, 54n.5 (“A POSA would understand that nitrogen could be used in place of argon to achieve an inert atmosphere”), 59n.6 “POSA would understand this has no effect on the final crystal form”); *see cxLoyalty, Inc. v. Maritz Holdings Inc.*, 986 F.3d 1367, 1378 (Fed. Cir. 2021) (“We do not accord weight to conclusory expert testimony.”); 37 C.F.R. §42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002) (quoting *In Re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (“Inherent anticipation requires that the missing descriptive material is ‘necessarily present,’ not merely probably or possibly present, in the prior art.”)); *Atrium Med. Corp. v. Bard Peripheral Vascular, Inc.*, IPR2021-01197, Pap.11, 16n.5 (Jan. 10, 2022) (denying institution, noting that Petitioner’s evidence, including expert testimony, of an inherent disclosure was weak when the expert provided a conclusion “without citation to supporting evidence.”). Further, when Dr. Behivsky added steps not in Liu, he never showed that *any and all* ways to perform that step would have still resulted in the claimed XRPD pattern. *See Pfizer*, Pap.56, 19-20. Indeed, he did not provide support showing each change, whether in temperature, atmosphere, purification, isolation method, physical handling, or the very act of triggering crystallization, did not affect the crystallization pathway and outcome. As in *Pfizer*, Petitioner offers only a menu

of concocted process variations, proving that the claimed XRPD patterns are, at best, only one possible outcome among many—**not** the inevitable result of following Liu. *See id.* (“The probability or possibility that an ordinarily skilled artisan would have used one of the four methods described by Dr. Przybycien to prepare Shadle’s elution buffer is insufficient to establish inherency.”).

And, even after all of these modifications, multiple samples produced by Dr. Bihovsky still ***failed to produce the claimed Form I***. Dr. Bihovsky’s lab notebook entries explicitly state this: sample “15-30-1P” is annotated with the clear conclusion: “***XRPD – Not Form I***,” and sample “15-32-1P” is likewise marked “***Not Form I***.” EX1033, ¶¶ 89, 91. Dr. Miller, who performed the XRPD testing for all of Dr. Bihovsky’s synthesized samples (*see* EX1032, ¶¶ 9-10), would also have known that these particular samples failed to yield Form I. Yet neither Petitioner nor any of its three experts makes any attempt to explain ***or even acknowledge*** these failed results, which are conspicuously omitted from the declarations’ main text and buried only in an appendix. *See* EX1033, 89, 91. This underscores not only that Liu’s methods did not yield the claimed Form I (and are therefore not inherent), but also that Petitioner’s inherency theory depends entirely on selectively reporting only favorable outcomes while masking the very evidence that affirmatively ***disproves*** inherency. *See Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047-48 (Fed. Cir. 1995) (finding no inherency when claimed compound was not produced every time

by following the reference's teachings even though expert performed prior art example 13 times and obtained claimed material). The Board should not permit such deceptive and manufactured disclosures to serve as the basis for institution.

In sum, the many modifications and failed attempts quietly undertaken by Petitioner demonstrate that its synthesis of the claimed Form I was far from a straightforward execution of Liu's teachings; instead, it was a trial-and-error process affirmatively departing from Liu and marked by hindsight-driven adjustments and selective reporting of only the favorable outcomes. Indeed, if the outcome had truly been inherent, Petitioner would have had no need to resort to these extensive laboratory interventions and alterations, and it would not have experienced multiple failed attempts to yield the claimed subject matter.

This fundamental weakness in Petitioner's challenge highlights its reliance on expert testimony as a substitute for actual disclosure in Liu and strongly weighs in favor of discretionary denial. *Azurity Pharms.*, Pap.11, 29 (denying institution based on the merits, finding that "on the current record Petitioner has not shown that the combination of [the asserted art] would inherently result in [the claimed limitation] and Petitioner has not shown that it has a reasonable likelihood that it would prevail on the obviousness ground."). Here, Petitioner's invalidity theory for both Grounds 1 and 2 rests entirely on the assertion that Liu inherently discloses the claimed Form I, yet that argument is plainly untenable on its face. Indeed, it is

affirmatively disproven by Petitioner’s own expert, who had to significantly reengineer Liu’s process, making at least nine modifications and still encountering failed results, to coax out one unrepeated instance of the claimed Form I. That alone confirms that Liu does not necessarily and inevitably yield Form I, as required for inherency. *See SNF S.A.*, IPR2022-01534, Pap.46, 27. Moreover, the Petition glosses over these failures and modifications, presenting the Board with a selective and misleading portrayal of the experimental record. The Board should not expend its resources on a Petition whose central premise is so legally and factually flawed, or reward a Petitioner for attempting to paper over these failures. Patent Owner’s request for discretionary denial should be granted.

2. Collateral Estoppel Does Not Apply and Does Not Fix the Gap Caused by the Petition’s Failed Inherency Arguments

Petitioner’s cursory attempt to invoke “collateral estoppel,” without identifying a single specific issue that is “identical” to that decided in PGR2023-00043 (*see, e.g., EX2018*, 24–25), is legally deficient and fundamentally inapplicable, and cannot save the failing merits of this Petition. *See VirnetX Inc. v. Apple, Inc.*, 909 F.3d 1375, 1377 (Fed. Cir. 2018) (requiring “a prior action present[ing] an identical issue” and that “the prior action actually [was] litigated” for collateral estoppel to apply). The anticipation and obviousness grounds asserted in PGR2023-00043 were based on *a different reference (Ahmad)*, and the claims of the challenged ’334 Patent *did not recite any Form I or XRPD limitations at issue*

here. See, e.g., EX2014, cl.1. Thus, the issues of Form I, XRPD, and Liu’s alleged inherency were neither raised nor adjudicated, let alone “essential” to the ’334 PGR judgment. Petitioner’s attempt to invoke “collateral estoppel” fails under the very authority it cites. See *Google LLC v. Hammond Develop. Int’l, Inc.*, 54 F.4th 1377, 1381 (Fed. Cir. 2022) (holding that for collateral estoppel to apply, a party must show, *inter alia*, “resolution of the issue was essential to a final judgment in the first action”). The Board’s conclusions in ’334 PGR for different prior art (Ahmad) and different claim limitations (lacking Form I or XRPD requirements) simply cannot supply the missing disclosures in Liu or excuse the deficient inherency showing presented here.

F. Petitioner’s Excessive Reliance on Expert Testimony Highlights Factual Disputes Unsuitable for IPR

The “extent of the petition’s reliance on expert testimony” is another consideration that supports discretionary denial. See March 26 Guidance at 2. As the Board has recognized, “[w]hile the Board may consider expert testimony, as a matter of efficiency, extensive reliance on expert testimony and/or reasonable disputes between experts on dispositive issues may suggest that the questions are better resolved in an Article III court.” PTAB, FAQs for Interim Processes for PTAB Workload Management, <https://www.uspto.gov/patents/ptab/faqs/interim-processes-workload-management> (“FAQs for Interim Processes”). That concern is presented here. As explained above, the Petition’s inherency theory is not only

legally flawed but also procedurally unwieldy, hinging entirely on speculative and fact-intensive laboratory benchtop reconstruction experiments as a purported substitute for the actual teachings of any prior art reference. *See, e.g.*, EX1033, ¶¶ 44-73; EX1034, ¶¶ 23-25. And in performing those benchtop experiments, Petitioner’s expert added steps that were not disclosed in Liu’s method (in addition to altering steps that were). This use of the expert to fill in gaps supports discretionary denial. *See iRhythm Techs.*, Pap.10, 2 (considering whether “Petitioner is using its expert to fill gaps in the prior art” in assessing discretionary denial). Further, while one effective way to prove the *lack* of inherency could be for Patent Owner’s expert to perform experiments of his own, such experiments here would be costly, impractical, and inefficient here—especially in the absence of any litigation or actual commercial dispute (*see* §IV.B, *supra*), and given the time constraints of the timeline for IPR proceedings. The Board and Patent Owner should not be forced towards a fact-heavy expert-driven laboratory reconstruction exercise built around previously considered art as part of an AIA trial.

Discretionary denial is further supported by the conclusory and repetitive nature of Petitioner’s expert’s declarations. For example, Dr. McConville’s “opinions” are largely verbatim or near-verbatim assertions merely parroted from the Petition without any independent analysis or supporting evidence. *Compare* EX1032, ¶¶ 67-103 with Pet.37-67. Such conclusory testimony that merely echoes

the Petition should be accorded little to no weight. *See cxLoyalty*, 986 F.3d at 1378; *see also* 37 C.F.R. §42.65(a). Petitioner’s “failure to provide focused expert testimony” further supports discretionary denial. FAQs for Interim Processes; *see generally Xerox Corp. v. ByteMark, Inc.*, IPR2022-00624, Pap.12, 4 (Feb. 10, 2023) (Director affirming Board’s denial decision because “Petitioner’s only evidence in support of its assertions was the declaration of its expert, which was unsupported by evidence or reasoning” and “merely repeats, verbatim, the conclusory assertion for which it is offered to support”); *TikTok Inc. v NTECH Properties Inc.*, IPR2024-01339, Pap.9, 16 (Feb. 25, 2025) (denying institution and noting Petitioner’s expert testimony “repeats, almost verbatim, the language in the Petition without any further explanation or supporting reasoning or evidence”).

Accordingly, the Petition’s overreliance on expert testimony, particularly to manufacture inherency from the same reference the Office has already reviewed and rejected, further supports discretionary denial.

V. Conclusion

For the foregoing reasons, the Board should exercise its discretion to deny institution here. The public health implications of disrupting Patent Owner’s clinical development of a promising new therapy for breast cancer are significant, particularly where Patent Owner has no products on the market and relies on its patent rights to sustain investor confidence and continue funding critical Phase 2 and

3 trials. The Petition presents no meaningful dispute to resolve, as Patent Owner has stipulated not to sue Petitioner and its related entities for any use of (Z)-endoxifen in the treatment of bipolar disorder—the only use at issue in clinical trials that Petitioner may have been involved in—rendering this proceeding an inefficient and unnecessary expenditure of Board and party resources. Petitioner’s strategic delay in bringing this IPR, following its earlier PGR challenge to a related continuation patent, further undermines the settled expectations of Patent Owner and reflects a pattern of gamesmanship designed to harass rather than resolve any real controversy. The Petition also fails under §325(d), as it merely repackages prior art already substantively considered and rejected during prosecution without showing any material error by the Examiner. Critically, the inherency theory on which the Petition depends is not only legally flawed, but affirmatively disproven by Petitioner’s own expert, whose multiple failed attempts and extensive modifications of Liu’s teachings underscore that the claimed Form I is not an inevitable result. That the Petition relies so heavily on expert-driven reconstructions, conclusory testimony, and selective reporting of outcomes only reinforces that the factual disputes it raises are ill-suited to resolution in an IPR. The USPTO’s guidance invites the Board to consider precisely these circumstances, and here, every relevant factor compels discretionary denial.

Respectfully submitted,

Dated: July 7, 2025

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CERTIFICATE OF WORD COUNT

The undersigned certifies that the foregoing Patent Owner’s Brief In Support Of Discretionary Denial Under 35 U.S.C. §314(a) complies with the type-volume limitation in 37 C.F.R. §42.24(c)(1) and the “Interim Processes for PTAB Workload Management” (Mar. 26, 2025). According to the word-processing system’s word count, the brief contains 8,568 words, excluding the parts of the brief exempted by 37 C.F.R. §42.24(a)(1).

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of Patent Owner's Brief In Support Of Discretionary Denial Under 35 U.S.C. §314(a) and the accompanying exhibits have been served in their entirety on July 7, 2025, by causing the aforementioned documents to be electronically mailed to the following attorneys of record for the Petitioner listed below.

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Dated: July 7, 2025

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