

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 AUTHORIZED REPLY TO PETITIONER'S
RESPONSE TO PATENT OWNER'S REQUEST FOR
DISCRETIONARY DENIAL UNDER 35 U.S.C. §314(a)¹**

¹ Reply authorized by EX3101. Emphases and color annotations herein are added, and abbreviations/references are as in Pap.7.

LIST OF EXHIBITS

Exhibit	Description
EX2001	ATOSSA THERAPEUTICS, INC. QUARTERLY REPORT FORM 10-Q (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.intas-pharma.com/financials/
EX2005	Atossa Therapeutics Announces Issuance of Key U.S. Patent Covering Endoxifen (March 08, 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	INTENTIONALLY OMITTED
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)

Exhibit	Description
EX2016	Default Protective Order
EX2017	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , IPR2025-00799, Pap.1 (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?, https://zonalta.in/
EX2021	Atossa Therapeutics Granted Additional Patent Protection for Endoxifen (August 28, 2024)
EX2022	Declaration of Megan Raymond

The Merits Are Weak. Inherency requires that the “‘natural result flowing from’ the *prior art’s explicit disclosure*” is the claimed invention. Pap.7, 27 (“Br.,” “Brief”). Petitioner contends that it need not have “run the *exact method taught by the prior art.*” Pap.10 (“Resp.,” “Response”), 16. But this ignores black letter law: settled Federal Circuit precedent requires that “[t]he inherent result *must inevitably result from the disclosed steps....*” Br.26 (quoting *In re Montgomery*, 677 F.3d 1375, 1380 (Fed. Cir. 2012)). And Petitioner *concedes* Dr. Bihovsky *modified* Liu’s disclosures when performing his experiments—*i.e.*, that his results were *not* based on “the prior art’s *explicit disclosure.*” Br.27. That is fatal to Petitioner’s arguments.

Moreover, even with these modifications, Petitioner’s experts *failed* to show that Liu necessarily discloses the claimed “Form I,” which is not claimed by the other patents Petitioner has challenged in PGR2025-00043 and PGR2023-00043. PO’s Brief notes that Dr. Bihovsky identified at least two sample results as “*XRPD – Not Form I*” and “*Not Form I.*” EX1033, 89, 91. Petitioner does not deny that these samples failed to meet the claim limitations; rather, Petitioner points to a *separate* sample (“15-32-2P”) that it alleges is the claimed Form I. Resp.18. But this sample *also* fails to meet all the limitations of the claims of the ’151 Patent—it is labeled “88% Z,” and all the Challenged Claims require that “*at least 90% by weight of... the (Z)-isomer....*” *Id.* (citing EX1033, 91).

10/24/23	Decidua 15-30-45 (206 mg) in <u>IPrOPc</u> (2.06 ml)
	Wash ΔX. Cool slowly (~1h) to 20° then 15°
Res '651	for 2 days. Vac filter, rinse ppt ~0.1 ml cell
0054	IPrOPc. Dry → 109 mg w/ 97% <u>NOT Form I</u> 15-32-(P
	Rotavap filtrate → 98 mg from 36% <u>Form I</u> -15
10/24/23	Decidua 15-30-3P (98 mg) in ΔX <u>acetone</u> (1.00 ml)
	cool to 20° → 4° (storing) for 1 day. <u>cryst</u>
	Vac filter + dry → 54 mg off white <u>solid</u> 15-32-2P
	<u>88% E-U</u> <u>XRPD = Form I</u>
	Rotavap filtrate → 31 mg v. lt. pink foam -25
	63% <u>Form I</u>

Id. In any case, Petitioner fails to establish inherency.

In addition, Petitioner's inherency argument rests on Dr. Miller's XRPD analysis, which is unsupported by evidence and therefore unreliable. Dr. Miller states that "[t]he experimental test and analysis conditions used for the XRPD testing is attached to this declaration as Appendix B," but his declaration ***does not contain any Appendix B***. EX1034. Absent supporting evidence, Dr. Miller's opinion—that Dr. Bihovsky's modified reproduction of Liu resulted in Form I—amounts to speculation. That is insufficient to carry Petitioner's burden. 37 C.F.R. §42.65(a).

Petitioner's Generic Competition Argument Fails. The Response doesn't dispute that Petitioner's current commercial use of (Z)-endoxifen is for bipolar disorder (in India), not breast cancer in the U.S. Despite its vague suggestions, Petitioner provides no ***evidence*** supporting any suggestion that it is today pursuing or investing in any ongoing clinical breast cancer trials using (Z)-endoxifen. Resp. 7-

8.² Any future impact on hypothetical generic competition is speculative, but the harm from derailing PO's work by undermining the investments needed to continue and complete clinical trials is immediate. *See* Br.7, 10-14; *Amgen Inc. v. Bristol-Myers Squibb Co.*, IPR2025-00601, Pap.9 at 2 (July 24, 2025) (noting “extraordinary... investment, time, and resources dedicated to research, development, trials, and regulatory approval” could give rise to settled expectations). Petitioner also offers no evidence of “threaten[ing of] other parties” (Resp.1), and Petitioner's claim that invalidating the '151 would hasten generic entry is speculation: if PO can't secure investments to complete its trials (including Phase III trials (EX2002)) and secure FDA approval, PO won't have an approved reference drug for generics like Petitioner to rely on; they would instead need to begin their own clinical trials, an uncertain and time-consuming process.

PO's Covenant Is Not Illusory. PO's covenant not to sue moots the only dispute Petitioner put at issue. Petitioner claims the covenant is “illusory” because “the 151 patent does not cover the salt form of (Z)-endoxifen or bipolar disorders.” Resp.9. That cannot be squared with Petitioner's statement that “[a]s described in the 151 patent, Formula (III) *can include the polymorphic salt...*” Pap.2, 25-26.

² The only other breast cancer work Petitioner identifies involves endoxifen *salts*.

See Resp.7-8. But PO's trials use *free base* (Z)-endoxifen. *See e.g.*, EX2002.

While Petitioner claims PO's covenant not to sue (which constrains PO, not Petitioner) does not align with its commercial interests or alleged claim scope, Petitioner failed to provide evidence of any having concrete commercial interest ***not*** covered by the covenant (e.g., investments in ongoing breast cancer trials). Coupled with Petitioner's simultaneous failure to identify any Petitioner-owned patent that could give even arguable cover to ***Petitioner's royalty demand***, this confirms the Petition's purpose is leverage against a small innovator.

Petitioner's Collateral Estoppel Arguments Are Without Merit. Petitioner concedes that it "does not rely significantly on collateral estoppel (and ***certainly does not rely on it for the Form I limitation***)," but asserts that this IPR should go forward because some other issue from the '334 PGR might be raised in some hypothetical future litigation, and that the '334 PGR findings would not be binding on PO in district court. Resp.25. Instituting an IPR (which relies on a different primary reference than the '334 (or '391) PGR) for the purpose of preserving a procedural advantage for Petitioner in a hypothetical case that, given the stipulated covenant not to sue, is remote at best, would, again, be an inefficient use of Board resources and an abuse of the AIA process.

Respectfully submitted,
By: /s/ Megan Raymond

Dated: August 26, 2025

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of Patent Owner's Authorized Reply to Petitioner's Response to Patent Owner's Request for Discretionary Denial Under 35 U.S.C. §314(a) has been served in its entirety on August 26, 2025, by causing the aforementioned document to be electronically mailed to the following attorneys of record for the Petitioner listed below.

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Respectfully submitted,

By: /Sayem Osman/

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