

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 PGR2023-00043

Patent No. 11,572,334

**PETITIONER'S REPLY TO PATENT OWNER'S PRELIMINARY
RESPONSE**

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PETITIONER’S EXHIBIT LIST

EX.	DESCRIPTION
1001	USPN 11,572,334 (“334 patent”)
1002	File history of USPN 11,572,334
1003	USPN 9,333,190 (“Ahmad”)
1004	WO2017/70651 (“Liu”)
1005	WO 2012/050263 (“Song”)
1006	Ahmad, A. et al., Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability and Systemic Bioavailability in Healthy Human Subjects, 88(6) CLIN. PHARMACOLOGY & THERAPEUTICS 814-817 (2010) (“Ahmad 2010”)
1007	Ahmad, A. et al., Endoxifen for breast cancer: Multiple-dose, dose-escalation study characterizing pharmacokinetics and safety in metastatic breast cancer patients, ASCO MEETING LIBRARY, presented June 4, 2012 (“Ahmad 2012”)
1008	Cole, E., et al., Enteric coated HPMC capsules designed to achieve intestinal targeting, 231 INTL J. PHARMACEUTICS 83-95 (2002) (“Cole”)
1009	Ku, M., et al., Performance qualification of a new hypromellose capsule: Part I. Comparative evaluation of physical, mechanical, and processability quality attributes of Vcaps Plus®, Quali-V® and gelatin capsules, 386 INTL J. PHARMACEUTICS 30-41 (2010) (“Ku”)
1010	Benameur, H., Capsule Technology, Enteric Capsule Drug Delivery Technology – Achieving Protection Without Coating, 15(5) DRUG DEV. & DELIVERY 34-37 (2015) (“Benameur”)
1011	Stegemann, S., Hard gelatin capsules today – and tomorrow, CAPSUGEL LIBRARY (2002) (“Stegemann”)
1012	Excerpts of HANDBOOK OF PHARMACEUTICAL EXCIPIENTS FIFTH EDITION (Rowe, R., Sheskey, J. & Owen, S., eds., 2006) (The “HPE”)
1013	Office Action dated 2/25/2020 from prosecution of Application No. 16/641,985

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EX.	DESCRIPTION
1014	Prescribing Information for Zonalta
1015	USP 711
1016	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).
1017	Evans, D. et al, <i>Measurement of gastrointestinal pH profiles in normal ambulant human subjects</i> , 29 GUT 1035-41 (1988)
1018	Ahmad, A. et al., <i>Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen</i> , Clin Transl Sci (2016) 9, 252–259 (“Ahmad 2016”)
1019	Milroy, L. et al., <i>A multi-gram-scale stereoselective synthesis of Z-endoxifen</i> , Bioorganic Med. Chem. Lett. 28 (2018) 1352-1356 (“Milroy”)
1020	Expert Declaration of Jason McConville, Ph.D.
1021	Ansel, H., et al, PHARMACEUTICAL DOSAGE FORMS AND DRUG DELIVERY SYSTEMS, SEVENTH EDITION (1999)

I. Discretionary denial under 325(d) is not warranted

Petitioner explained why the prosecution history of the 334 patent does not warrant discretionary denial, as the Examiner erred in not issuing a single rejection, despite Ahmad’s disclosure of each element of the independent claims. Paper 1 at 23-27. In its *Advanced Bionics* step 2 discussion, Patent Owner cannot explain away this error, and merely repeats arguments that go only to Step 1 of *Advanced Bionics*.

For example, Patent Owner relies on *Bicon Pharma Ltd. v. Novartis Pharm. Corp.*, IPR2020-01363, Paper 12 at 9 (PTAB Feb. 16, 2021) (Paper 7 at 22-23) to support a Step 2 analysis. But the cited portion of *Bicon* is an analysis under **Step 1**. *Bicon*, Paper 12 at 9. The Board denied institution only after addressing Step 2 and finding no material error because even considering the art, it would not refute the basis of the Examiner’s patentability determination. *Id.* at 11-18.¹ Here, Ahmad’s teachings show error in the Examiner’s reason for allowance that she “did not discover any reference which anticipates...” Ex. 1002 at 388.

Patent Owner also misstates the prosecution history of the parent 151 patent, saying “The Parent Patent Of The ’334 Patent Overcame Rejections Involving

¹ Patent Owner also cites to *Shire, LLC v. Amneal Pharm, LLC*, 802 F.3d 1301, 1307 (Fed. Cir. 2015), which does not relate to Board proceedings. Paper 7 at 22.

EX1003, EX1004, EX1006, EX1007, and EX1018.” Paper 7 at 9. Not so. While these exhibits were identified to the Examiner (as Petitioner acknowledged was the case for the 334 patent in the Petition), only Ex. 1004 (Liu) was used in a rejection. Patent Owner acknowledges as much in its POPR at page 16. Paper 7 at 16.

And while “Patent Owner overcame the rejections over Liu and the parent ’151 patent issued” (*id.*), it did so only because Patent Owner cancelled the rejected claims. Ex. 2005 at 34; Ex. 2006 at 7. The allowed claims contained a limitation reciting a specific polymorph form not recited in the claims of the 334 patent. Ex. 2005 at 27; *see also* Ex. 2006 at 16 (“the key to the instant claims is the polymorph of Form I”); *compare* Ex. 1001 at claims *with* Ex. 2004 at *e.g.* Claim 1. In truth, it wasn’t so much “[overcoming] the rejection based on Liu” as it was agreeing to the rejection and cancelling the objectionable subject matter.

Thus, it was error for the Examiner not to apply Liu (or Ahmad) to the pending 334 claims, which contain no Form I requirement, as had been done in the parent application and to which the Patent Owner acquiesced. *See, e.g., Roofr Inc. v. Pictometry Int’l Corp.*, IPR2023-00435, 2023 WL 5154720 (P.T.A.B. July 21, 2023) (“Although Patent Owner overcame four of the five asserted references during the parent application’s prosecution, it did so by adding a limitation that is not in the challenged claims.”); *Target Corp. v. Proxicom Wireless*, IPR2020-00979, 2020 WL 7094095, at *6 (P.T.A.B. Dec. 4, 2020) (“because the distinguishing feature of the

claims in those cases is not present at least in claim 1 of the '164 patent that is the subject of this proceeding, allowance of the claims on this basis would constitute an error material to the patentability of the claims and we would not exercise discretion to deny institution.”).

Here, Patent Owner does not assert that Ahmad fails to disclose any limitation, but only whether the disclosure is enabled (Paper 7 at 32). As “[i]t is well-established that prior art patents and printed publications ... are presumed enabling” (*Apple Inc. v. Corephotonics, Ltd.*, 861 F. App’x 443, 449 (Fed. Cir. 2021)), it was *necessarily* error for the Examiner to fail to issue a rejection over Ahmad and place the burden on the applicant to demonstrate lack of enablement. Thus, there is no basis for the Board to use its discretion to deny institution.

II. Patent Owner’s enablement arguments are not relevant to the institution decision

Patent Owner does not dispute Petitioner’s showing that Ahmad *discloses* every limitation of Claims 1, 2, 4, 15, and 20-22, but argues only that the disclosure is not enabling. But again, a reference is *presumed* enabling. *See Apple*, *supra*. Thus, by definition “the information presented in the petition...., if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable”—all that is required to institute. 35 U.S.C. § 324(a) (emphasis added). The statutory threshold for PGR does not focus on

weighing rebuttal evidence against the Petition’s evidence—but only on whether the Petition’s evidence, if not rebutted, would show invalidity by a preponderance of the evidence.² Thus, Patent Owner’s attempts to rebut the presumption of enablement (and supporting expert testimony) should be addressed at trial.

Even in the IPR context, which involves weighing Patent Owner’s evidence, the Board has recognized that purported lack of enablement “raise factual disputes that are best resolved upon a full record” and “in view of the presumption of prior art enablement” institution should be granted. *10x Genomics, Inc. v. Bio-Rad Lab’s, Inc.*, No. IPR2020-00089, 2020 WL 2026695, at *15 (P.T.A.B. Apr. 27, 2020); *see also Apple*, 861 F. App’x at 449 (“the Board shifted the burden to Apple to provide evidence before institution (i.e., in its petition) that Konno was enabling as part of its burden to prove anticipation. This was error...because the Board in effect shifted

² That the PGR institution statute focuses on the information in the petition and not rebuttal evidence is further made clear by comparison to the IPR institution statute. 35 U.S.C. § 314(a) (considering “the information presented in the petition filed under section 311 **and any response filed under section 313** shows that there is a reasonable likelihood that the petitioner would prevail.”) (emphasis added).

the burden to Apple to prove enablement before any assertion of nonenablement was raised.”).

Moreover, despite having no burden to do so, Petitioner *did* provide additional evidence of enablement. Paper 1 at 30 (“To the extent it is argued there is not a specific, enabling disclosure of 90% pure (Z)-endoxifen by Ahmad, forming such pure formulations was known in the art as taught by e.g., Liu and Song. *See* §VII.B. *supra*; Ex. 1004 at [0076]; Ex. 1005 at [92]-[94], [97]-[98]; McConville ¶ 59.”). Again this information is sufficient to show it is more likely than not that at least one claim is invalid.³ As Petitioner will make clear at trial, Patent Owner’s arguments regarding Liu relate to limitations not present in the claimed invention (e.g. stability), and thus cannot rebut the presumption of enablement.

³ Contrary to Patent Owner’s arguments, additional references may be used “to show that the claimed subject matter, as disclosed in [the anticipatory reference], was in the public’s possession.” *In re Donohue*, 766 F.2d 531, 534 (Fed. Cir. 1985); *see also Bristol-Myers Squibb Co. v. Ben Venue Lab ’ys, Inc.*, 246 F.3d 1368, 1379 (Fed. Cir. 2001) (“Enablement of an anticipatory reference may be demonstrated by a later reference.”)

III. Patent Owner’s challenges to the public availability of supporting references is not a valid basis for denying institution

Finally, Patent Owner suggests that institution should be denied because Petitioner “failed to establish any cited non-patent publication qualifies as prior art.” Paper 7 at 24. But Patent Owner does not challenge that the primary reference (Ahmad, Ex. 1003) is a patent that constitutes a printed publication (as well as Liu, Ex. 1004 and Song, Ex. 2005). As Ground I and II rely only on these patents, Patent Owner’s arguments cannot refute the requirement for institution—that the Petition shows it is more likely than not that at least one claim is invalid. 35 U.S.C. § 324(a).

Moreover, all of the non-patent art relied on in additional grounds addressing dependent claims bears strong indicia demonstrating it is more likely than not that the reference is a prior art printed publication. Patent Owner relies on *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 2 (PTAB Dec. 20, 2019) (precedential). But Hulu notes the Board often finds it sufficient when “the evidence relied on in a petition provides strong indicia that an asserted reference was publicly accessible.” *Id.* at 17.

Exhibits 1006, 1008, 1010, 1016-1018 are all journal articles, with clear indications of when they were published and in what journal. *See, e.g., Provepharm Inc. v. Wista Lab’ys Ltd.*, IPR2018-00323, 2018 WL 3326805, at *7 (P.T.A.B. July 6, 2018); *Hologic, Inc. v. Enzo Life Scis., Inc.*, IPR2016-00822, 2017 WL 1016761,

at *2-3 (P.T.A.B. Mar. 13, 2017) (“the references are either journal articles or excerpts from a book, and thus appear to have been publicly disseminated”). Similarly, Exhibit 1015 is an excerpt of the USP (United States Pharmacopeia) which is clearly dated as “Official December 1, 2011.” Ex. 1015.

Ex. 1007 is a printout of the Abstract presented at the 2012 ASCO (“American Society of Clinical Oncology”) Annual Meeting from the online Journal of Clinical Oncology presented by that same society, that states “Published online May 20, 2012” on its face, again bearing indicia it was publicly available. Ex. 1007. While Patent Owner argues that this webpage has not yet been authenticated “a party is not entitled to an evidentiary ruling prior to institution...our regulations create a post-institution procedure for challenging evidence and ruling on those challenges.” *Hologic, Inc. v. Enzo Life Scis., Inc.*, 2017 WL 1016761, at *2; 37 C.F.R. § 42.123(a). Patent Owner provides no authority for denying institution because a secondary reference has not yet been authenticated prior to the opportunity to respond to any evidentiary objection—especially when Patent Owner has given no reason to question the authenticity of the document.

Patent Owner’s suggestion that Exs. 1006-1008 and 1015 may not have been publicly accessible is especially specious as Patent Owner argues these references were already considered by the Examiner and listed on the face of the patent—which

itself is “highly persuasive evidence of public accessibility.” *Valve Corp. v. Ironburg
Inventions Ltd.*, 8 F.4th 1364, 1374 (Fed. Cir. 2021).

Finally, as the Petition explains (Paper 1 at 20), Exhibit 1011 is a PDF retrieved from the website of Capsugel (a well-known manufacturer of capsules identified in the 027 specification, Ex. 1001 at e.g., 40:21-23) and states “2nd Edition 2002” on the front. Ex. 1011 at 1. To the extent support is needed, Petitioner will provide it through the procedures provided for by the Board. *See Hulu* at 14-15. In any event, Exhibit 1011, is only relied on as a secondary reference in a single ground and does not warrant denying institution.⁴

IV. Conclusion

For these reasons and those laid out in the Petition, Petitioner respectfully requests that the Board institute post grant review of those claims.

⁴ Patent Owner also focuses on Exhibits 1014 and 1019. But these are background references to show the state of the art, which need not qualify as statutory prior art. *See, e.g., Yeda Rsch. v. Mylan Pharms. Inc.*, 906 F.3d 1031, 1041 (Fed. Cir. 2018).

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Respectfully submitted,

McANDREWS, HELD & MALLOY, LTD.

Dated: December 26, 2023

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CERTIFICATE OF WORD COUNT

I certify under 37 CFR § 42.24 that this **PETITIONER'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE** contains fewer than 1,820 words, as determined by Microsoft Word.

Dated: December 26, 2023

By: /Alejandro Menchaca/
Alejandro Menchaca *for Petitioner*
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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 the PETITIONER'S REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE was served via email:

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