

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HOPEWELL PHARMA VENTURES, INC.,
Petitioner,

v.

ARES TRADING SA,
Patent Owner.

Case IPR2023-00482
Patent 10,849,919

PATENT OWNER'S PRELIMINARY SUR-REPLY

To manufacture good cause for leave to file a reply, Petitioner told this Board that Patent Owner (“PO”) had made “multiple misrepresentations” in PO’s Preliminary Response (Paper No. 6, “POPR”). But there were none: Petitioner simply disagrees with PO’s arguments and uses the Reply to distort those arguments, all so it could place another pleading before the Board. Petitioner’s Reply (Paper No. 7, “Reply”) fails both to show any misrepresentations by PO and to cure the Petition’s deficiencies.

First, PO did not “misrepresent[]” Alvarez-Gonzalez’s disclosure regarding clinical efficacy of cladribine. Petitioner asserts that PO’s argument “misrepresents” Alvarez-Gonzalez’s “successful” treatment of PPMS. Reply, 1. But unlike the Petition, both the POPR and Alvarez-Gonzalez acknowledged this patient was “a case of **rebound** disease after fingolimod cessation in a pwPMS [*i.e.*, “person with progressive MS”], who was successfully treated with Cladribine,” *i.e.*, “a pwPMS who developed **rebound** disease after fingolimod cessation and partially recovered following Cladribine administration.” Ex. 1009, 506, 509; POPR, 15 (hereinafter, all emphasis is added unless otherwise noted). This is the context for Alvarez-Gonzalez’s reported “success,” but the Petition does not mention “rebound” disease. Likewise, Petitioner relies on Dr. Miller to “confirm[] that ‘a POSA would have understood from Alvarez-Gonzalez that the PPMS patient’s **activity** was treated with cladribine,’” (Reply, 1-2 (quoting Ex.

1002 ¶91)), but ignores that the “activity” was *rebound disease* activity caused by fingolimod cessation. As Alvarez-Gonzalez explains, rebound disease is “defined as a degree of disease *activity* significantly exceeding pre-DMT activity,” which can happen “[i]rrespective of the disease course.” Ex. 1009, 506, 507.

While Petitioner claims that Alvarez-Gonzalez’s results are “in line with the ’919 patent’s description of what constitutes a ‘response to a use according to the invention’” (Reply, 2 (quoting Ex. 1001, 33:18)), the ’919 patent’s disclosure of MRI-based measurements as a “primary efficacy variable” relates to “[t]he efficacy of cladribine in the treatment of progressive forms of MS,” not to the treatment of rebound disease caused by fingolimod cessation. Ex. 1001, 6:12-22.

Second, PO did not “misrepresent[]” Alvarez-Gonzalez’s reason for selecting parenteral cladribine. Petitioner contends that “Alvarez-Gonzales did not ‘prefer’ subcutaneous to oral cladribine.” Reply, 2. But as PO explained, Alvarez-Gonzalez identified and specifically considered the oral, weight-based dosing used in the CLARITY study and still chose subcutaneous cladribine using flat dosing. POPR, 19; Ex. 1009, 509 (“Our dosing scheme for Cladribine took into account comments by the European Medicines Agency in their withdrawal assessment of Cladribine *tablets* in 2010/11 regarding the risk of severe lymphopenia. Based on 100% bioavailability of Cladribine s.c. (versus 42% or the oral prodrug) ... Cladribine 10 mg *s.c.* was given[.]” (citation omitted)). Further,

Petitioner states that “Alvarez-Gonzalez selected cladribine because it provided ‘practical and clinical advantages’” (Reply, 3 (quoting Ex. 1009, 509)), but selectively removes the reference to “parenteral” cladribine found in the original quote from Alvarez-Gonzalez: “***parenteral*** cladribine may have some practical and clinical advantages over currently licensed DMT[.]” Ex. 1009, 509.

Third, PO did not “misrepresent[]” the legal relevance of Alvarez-Gonzalez’s “single patient.” Petitioner asserts that PO misrepresents the relevance of a single embodiment in the prior art based solely on PO’s “emphasis on Alvarez-Gonzalez’s ‘***single patient***’[.]” Reply, 3 (quoting POPR, 16, 22) (emphasis in original). But PO never argued that a single embodiment is legally irrelevant, and merely pointed out the ***fact*** of Alvarez-Gonzalez’s limited study population, *i.e.*, ***one*** patient with rebound disease. *See* Ex. 1009, 506 (“We report ***a case*** of rebound disease[.]”). A POSA would have understood the limitations of the results of such a case study.

Fourth, PO did not “misrepresent[]” language in the ’919 patent specification regarding “early Secondary Progressive Multiple Sclerosis.”

Petitioner asserts PO’s proposed construction of the claim term “early SPMS” “contradict[s] the express language in the ’919 patent” (Reply, 3-4), even though PO quoted the same language regarding “some kind of transition state between the relapsing remitting forms of MS and the progressive forms of MS” for support.

POPR, 8-9. Further, Petitioner ignores “the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence,” which “show what a [POSA] would have understood disputed claim language to mean.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc) (internal citations and quotations omitted). As PO has explained, PO’s construction of “early SPMS” is supported by the ’919 patent claims (expressly excluding early SPMS), the specification, and the prosecution history (where the Examiner “advised that SPMS encompasses ‘early’ SPMS”), as well as the state of the art as reflected in Petitioner’s exhibits. POPR, 6-13.

Fifth, PO did not “misrepresent[]” Montalban’s disclosure. Contrary to Petitioner’s characterization, PO explained that Montalban “refers to RRMS and SPMS patients with ‘ongoing relapses,’” while its “‘**Conclusions**’ are focused on RRMS.” POPR, 32, 33 (quoting Ex. 1006, 1). In quoting the POPR, Petitioner selectively removes the word “Conclusions” from PO’s statement, (Reply, 4), and ignores that Montalban’s “Conclusions” in fact state that “[t]hese results support the demonstrated efficacy of cladribine tablets in RRMS shown in CLARITY.” Ex. 1006, 1.

Petitioner’s mere disagreement with PO’s arguments falls far short of establishing any “misrepresentation.” For at least the reasons stated in the POPR, PO respectfully requests that the Board deny institution.

Respectfully submitted,

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By: /Emily R. Whelan/
Emily R. Whelan (Reg. No. 50,391)
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Tel. (617) 526-6567
Email: Emily.Whelelan@wilmerhale.com
Counsel for Patent Owner

CERTIFICATE OF SERVICE

I hereby certify that on June 16, 2023, I caused a true and correct copy of
Patent Owner's Preliminary Sur-Reply to be served via e-mail, as consented to
by Petitioner, on the following attorneys of record:

eellison-PTAB@sternekessler.com
opartington-PTAB@sternekessler.com
cvira-PTAB@sternekessler.com
jcrozendaal-PTAB@sternekessler.com
PTAB@sternekessler.com

By: /Cindy Kan/

Cindy Kan (Reg. No. 76,385)
Wilmer Cutler Pickering Hale and Dorr LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
Tel: 212-295-6470
Email: cindy.kan@wilmerhale.com