

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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HOPEWELL PHARMA VENTURES, INC.,  
Petitioner

v.

ARES TRADING S.A.,  
Patent Owner

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Case IPR2023-00482  
U.S. Patent No. 10,849,919

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

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U.S. Patent and Trademark Office  
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## I. INTRODUCTION

Hopewell submits this Reply to address misrepresentations in the Patent Owner Preliminary Response (Paper No. 6, “POPR”).

### A. Ares misrepresents Alvarez-Gonzalez’s disclosure regarding the clinical efficacy of cladribine for treating PPMS.

Ares’s attorney argument that “a POSA would not have been motivated to treat PPMS as claimed because Alvarez-Gonzalez does not disclose clinical efficacy of cladribine for treating PPMS” (POPR, 14) is baseless and misrepresents Alvarez-Gonzalez. Notwithstanding Ares’s agreement that Alvarez-Gonzalez’s patient “had been diagnosed with PPMS,” Ares alleged that “Alvarez-Gonzalez does not characterize her subsequent treatment with cladribine as [a] ‘successful treatment’ of a progressive form of MS.” POPR, 15; EX1009, 506. Ares asserts Alvarez-Gonzalez “only discloses the use of cladribine” to treat “[r]ebound disease.” POPR, 15 (emphasis added). Ares could not be more wrong. As a threshold matter, Alvarez-Gonzalez itself expressly states that the treatment was “successful,” and on the basis of this success notes that “this case should encourage studies to *more definitely* investigate the effectiveness of immunosuppressive DMT in *pwPMS [PPMS]*.” EX1009, 509 (emphasis added). Alvarez-Gonzalez expressly indicates that cladribine’s “safety, convenience, and unique pharmacokinetics” make it “a promising candidate DMT [disease-modifying treatment] for pwPM[S].” *Id.* Dr. Miller confirms that “a POSA would

have understood from Alvarez-Gonzalez that the PPMS patient's activity was treated with cladribine." EX1002, ¶91. Thus, Ares's characterization of Alvarez-Gonzalez is erroneous. In any event, the challenged claims encompass "[a] method of treating a progressive form of Multiple Sclerosis" (EX1001, 64:45-46), rebound or not, which Alvarez-Gonzalez unambiguously teaches. EX1009, 506; POPR, 15.

Alvarez-Gonzalez's results are also in line with the '919 patent's description of what constitutes a "response to a use according to the invention." EX1001, 33:18. The specification states that "the reduction and/or suppression of MRI T<sub>1</sub> gadolinium-enhanced lesions [GD<sup>+</sup>]" is a "prefer[red]" and "primary efficacy variable" for measuring such a response. EX1001, 33:15-27. This is precisely the result reported in Alvarez-Gonzalez: "[o]n follow-up 3 months after treatment initiation," MRI T<sub>1</sub> GD<sup>+</sup> imaging revealed *no GD<sup>+</sup> lesions*, down from 45 GD<sup>+</sup> lesions observed prior to treatment. EX1009, 507. Ares, thus, misrepresented the relevance of Alvarez-Gonzalez's data that is directly indicative of clinical efficacy.

**B. Ares misrepresents Alvarez-Gonzalez's reason for selecting parenteral cladribine.**

Alvarez-Gonzales did not "prefer" subcutaneous to oral cladribine, contrary to Ares's characterization of Alvarez-Gonzales. POPR, 19. Instead, Alvarez-Gonzalez used a subcutaneous dose of cladribine because of a "lack of any licensed [alternative DMT] options." EX1009, 509. And in doing so, Alvarez-Gonzalez sought to achieve "bio-equivalence with oral" cladribine. *Id.* Moreover,

Alvarez-Gonzalez selected cladribine because it provided “practical and clinical advantages,” and *not* because the parenteral version conferred any advantage that an oral formulation could not. *Id.*

Further, Bodor teaches (EX1026, 2:9-11), and Dr. Miller confirms, that it was well-known that “[o]ral delivery of drugs is often preferred to parenteral delivery for a variety of reasons” (EX1002, ¶¶52-53). Thus, a POSA would have substituted “Alvarez-Gonzalez’s fixed yearly dose of subcutaneous cladribine with oral cladribine,” contrary to Ares’s arguments. Pet, 37.

**C. Ares misrepresents the legal relevance of Alvarez-Gonzalez’s “single patient.”**

Ares’s emphasis on Alvarez-Gonzalez’s “*single patient*” (POPR, 16, 22 (emphasis in the original)) exposes Ares’s fundamental misunderstanding or misrepresentation of the law. A showing of obviousness of a single embodiment within the claim’s scope is sufficient to prove unpatentability. *See Eli Lilly & Co. v. Barr Labs*, 251 F.3d 955, 971 (Fed. Cir. 2001) (“later genus claim limitation is anticipated by, and therefore not patentably distinct from, an earlier species claim”). Thus, Ares’s attempt to misapply the principles underlying a Section 103 obviousness analysis based on Alvarez-Gonzalez’s single patient fails.

**D. Ares misrepresents unambiguous language in the specification affecting construction of “Early Secondary Progressive Multiple Sclerosis” (“ESPMS”).**

In criticizing Hopewell’s construction of the term “ESPMS,” Ares

contradicted the express language in the '919 patent. The specification defines ESPMS as “some form of Multiple Sclerosis that marks some kind of transition state *between* the relapsing remitting forms of MS [RRMS] and the progressive forms of MS....combin[ing] the *very different* aspects and also *very different* mechanisms of both the pure relapsing remitting forms and the progressive forms of MS.” EX1001, 2:63-3:2 (emphasis added). Accordingly, because the specification explicitly states that ESPMS occurs *between* RRMS and SPMS, ESPMS cannot also be “encompassed by SPMS,” as Ares argues. POPR, 7.

**E. Ares misrepresents Montalban’s disclosure of cladribine’s effectiveness in patients with SPMS.**

Ares argued that Montalban “does not motivate a POSA to treat progressive MS” because it is “focused on RRMS.” POPR, 33-34. Ares is wrong. Montalban stated that oral cladribine “demonstrated significant efficacy benefits,” (EX1006, Abstract) in patients, including those with “SPMS with ongoing relapses.” *See also*, EX1002, ¶64. Thus, Montalban does not merely “generally refer[] to ‘SPMS patients with ongoing relapses.’” POPR, 33.

**II. CONCLUSION**

For the reasons stated in the petition, the challenged claims are unpatentable and should be cancelled.

Respectfully submitted,

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**CERTIFICATE OF SERVICE**

The undersigned hereby certifies that the foregoing **PETITIONER'S  
REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE** was served electronically via e-mail on June 9, 2023, on the following counsel of record for Patent Owner:

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