UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TWI PHARMACEUTICALS INC.,

Petitioner,

v.

MERCK SERONO SA,

Patent Owner.

IPR2023-00049 (Patent 7,713,947 B2)
IPR2023-00050 (Patent 8,377,903 B2)[1]

Before ULRIKE W. JENKS, ZHENYU YANG and TINA HULSE,
Administrative Patent Judges.

REBUTTAL DECLARATION OF BENJAMIN M. GREENBERG, M.D.

[1] The identical paper is filed in each proceeding identified in the caption.

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1. I have had the opportunity to review the opinion submitted by Dr. Fred Lublin and now submit a rebuttal to his opinions.

I. Summary of My Opinions

2. It remains my opinion that at least claims 36, 38–39, and 41–48 of the '947 patent are invalid because they are either anticipated by or obvious over Bodor WO '101 (Ex. 1007) and/or its US counterpart, Bodor '328 (Ex. 1029) (collectively "Bodor"). It is further my opinion that each of these claims are invalid as obvious over Bodor in view of Rice 2000 (Ex. 1008).

3. It is my opinion that at least claims 17, 19–20, and 22–29 of the '903 patent are invalid because they are either anticipated by or obvious over Bodor. It is further my opinion that these claims are invalid as obvious over Bodor in view of Rice 2000.

4. Dr. Lublin did not disagree with my testimony concerning the standard for obviousness. Specifically, I have been told that a reference may be modified or combined with other references or with the person of ordinary skill in the art's own knowledge if the person would have found the modification or combination obvious.

5. Additionally, Dr. Lublin acknowledged that Bodor incorporates by reference multiple publications including the Selby article (Ex. 1031), the Tortorella article (Ex. 1026), the Rice article (Ex. 1008) and the Romine article (Ex. 1016) (e.g. Lublin deposition, page 78, lines 12-13.) It is my understanding that Bodor thus

discloses everything written in the patent ***and*** all incorporated references. Thus, when addressing the issue of anticipation and obviousness I considered all of the disclosures included in the Bodor patent.

6. Additionally, I understand that prior art must disclose the invention, but does not have to provide proof of safety and efficacy required by drug approval authorities. For example, a disclosure of a treatment for a given indication is enough to render a later patent application anticipated or obvious without reporting phase 3 clinical trial confirmatory evidence.

7. Finally, I understand that a disclosure in prior art does not have to disclose the entire range of a patent's claims. For example, relative to dosing, if Bodor discloses a dose within the range of doses recited in the '947 and '903 patent, then the '947 and '903 patent that claim element would be disclosed by Bodor for purposes of anticipation and obviousness.

II. Bodor Discloses Cladribine as a Treatment for Multiple Sclerosis

8. Bodor discloses the use of "10mg of cladribine . . . in the [disclosed] solid dosage form" for the "treatment of multiple sclerosis." (Bodor WO '101, Ex. 1007 at 25; Bodor '328 col. 13, ℓℓ. 19–25, Ex. 1029 at 10.)

III. POSAs Would Preferentially Apply The Bodor Disclosure to Relapsing Remitting Multiple Sclerosis and Active Secondary Progressive Multiple Sclerosis Patients

9. The most common form of multiple sclerosis was relapsing remitting multiple sclerosis. Dr. Lublin agrees with this (Ex. 2019 ¶ 47). It has been and remains quite common for clinicians, scientists and POSAs to use the term "Multiple Sclerosis" in place of specifying "Relapsing Remitting Multiple Sclerosis" because that phenotype is the overwhelming dominant form. This includes papers authored by Dr. Lublin, who utilizes the term "Multiple Sclerosis" as a synonym or shorthand when referring to relapsing remitting multiple sclerosis (Ex. 2025, Tullman 2002 at 273, 275; Exhibit 2013, Lublin 2005 at III/4).

10. Bodor incorporates by reference Romine 1999 (Ex. 1016). (Ex. 1029 col. 12, ℓℓ. 67–col. 13 ℓ. 2.) This study reported positive clinical and radiographic results from an 18-month placebo-controlled trial of cladribine in relapsing remitting multiple sclerosis.

11. The applicability of Bodor to relapsing remitting multiple sclerosis and active secondary multiple sclerosis patient populations is important in light of MRI data from Rice 2000 (Ex. 1008). While Dr. Lublin reports having "skepticism of cladribine's utility for treating MS…" (Exhibit 2019 ¶ 199), this is not a full portrayal of his published statements, the conclusions of the study authors, or the views a POSA would have. Importantly, while Dr. Lublin asserts that Rice 2000 (Ex.

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