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Paper 8
Entered: March 28, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TWI PHARMACEUTICALS, INC.,
Petitioner,

v.

MERCK SERONO SA,
Patent Owner.

IPR2023-00050
Patent 8,377,903 B2

Before ERICA A. FRANKLIN, ULRIKE W. JENKS, and TINA E. HULSE, *Administrative Patent Judges.*

FRANKLIN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

TWi Pharmaceuticals, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 17, 19, 20, and 22–29 of U.S. Patent No. 8,377,903 B2 (Ex. 1002, "the '903 patent"). Paper 1 ("Petition" or "Pet."). Merck Serono SA ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314 (2018). Upon considering the parties' arguments and evidence, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition. Accordingly, we do not institute an *inter partes* review of the challenged claims.

A. Real Parties-in-Interest

Petitioner identifies itself as a real parties-in-interest. Pet. xiii. Patent Owner identifies Merck Serono SA, Merck KGaA, and Ares Trading SA as real parties-in-interest, stating that "Merck Serono SA and Ares Trading SA are wholly owned subsidiaries of Merck KGaA." Paper 4, 1.

B. Related Matters

The parties explain that the '903 patent has been asserted in *Merck KGaA, Merck Serono SA, and Ares Trading SA v. Accord Healthcare, Inc.*, 1-22-cv-00974-GBW (D. Del.). Pet. xiii; Paper 4, 1. Petitioner notes that it is not a party to that district court proceeding. Pet. xiii. Patent Owner also identifies *Merck KGaA, Merck Serono SA, and Ares Trading SA v. Hopewell Pharma Ventures, Inc.*, No. 1:22-cv-1365-GBW (D. Del.) as a related matter. Paper 4, 1.

The parties also identify as a related matter the petition filed in IPR2022-00049, which challenges claims of U.S. Patent No. 7,713,947 B2. Pet. xiii; Paper 4, 1.

C. The '903 Patent

The '903 patent "relates to the use of multiple doses of Cladribine for the treatment of multiple sclerosis, especially relapsing-remitting multiple sclerosis or early secondary progressive multiple sclerosis." Ex. 1001, 1:17–20. The Specification explains,

> Four courses of the disease are individualized: relapsing-remitting (RR), secondary progressive (SP), primary progressive (PP) and progressive relapsing (PR) multiple sclerosis.
>
> More than 80% of patients with MS will initially display a RR course with clinical exacerbation of neurological symptoms, followed by a recovery that may or may not be complete.
>
> During RRMS, accumulation of disability results from incomplete recovery from relapses. Approximately, half of the patients with RRMS switch to a progressive course, called SPMS, 10 years after the diseased onset.

Id. at 1:48–58 (citation omitted).

The '903 patent explains that there have been studies regarding the intravenous or subcutaneous administration of cladribine to treat multiple sclerosis ("MS"). *Id.* at 2:28–49. Those studies provided evidence that cladribine had positive effects in patients with MS but some adverse effects, "such as increased incidence of infections related to compromised immune function or myelosuppression, were observed with the highest doses." *Id.* at 2:50–63. Another study directed to the oral administration of cladribine observed the same side effects but to a lesser degree than subjects administered with cladribine intravenously. *Id.* at 3:3–16. However, the '903 patent states that "the therapeutic efficacy of the oral regimen above

versus the i.v. infusion therapy was questioned" and there was a group of subjects that did not respond to the treatment. *Id.* at 3:17–21.

According to the '903 patent:

> it would be desirable to have a method for treating multiple sclerosis comprising the oral administration of Cladribine that would permit the same or improved effect on MS lesions while decreasing the occurrence and/or severity adverse events. In addition, as MS is a chronic disease, it would be desirable to decrease the occurrence and/or severity adverse events in such a way that re-treatments are possible. A sustained benefit of Cladribine treatment between the treatment periods is also desirable.

Id. at 3:22–30. In view of this, the '903 patent describes the "use of Cladribine for the preparation of a pharmaceutical formulation for the treatment of multiple sclerosis, wherein the preparation is to be the orally administered." *Id.* at 3:34–37. The '903 patent states that each of the induction and the maintenance periods may last up to about four months. *Id.* at 4:58–59, 5:11–12.

D. Illustrative Claim

Petitioner challenges claims 17, 19, 20, and 22–29 of the '903 patent. Claim 17, set forth below, is the only the independent claim challenged and is illustrative of the claimed subject matter.

> 17. A method of treating relapsing-remitting multiple sclerosis or early secondary progressive multiple sclerosis comprising the oral administration of a formulation comprising cladribine to an individual having relapsing-remitting multiple sclerosis or early secondary progressive multiple sclerosis following the sequential steps below:
>
> (i) an induction period lasting from about 2 months to about 4 months wherein said formulation is orally administered and wherein the total dose of cladribine reached at the end of the induction period is from about 1.7 mg/kg to about 3.5 mg/kg;

> (ii) a cladribine-free period lasting from about 8 months to about 10 months, wherein no cladribine is administered;
>
> (iii) a maintenance period lasting from about 2 months to about 4 months, wherein said formulation is orally administered and wherein the total dose of cladribine reached at the end of the maintenance period is about 1.7 mg/kg; and
>
> (iv) a cladribine-free period wherein no cladribine is administered.

Ex. 1001, 18:7–26. Dependent claims 19, 20, and 22–29 recite additional limitations to the method of claim 17. Dependent claims 19 and 22–24 recite time periods for the induction period, cladribine-free period, and maintenance period. Dependent claims 20, 25, and 26 recite doses. Dependent claim 27 recites that the formulation is administered 1–7 days per month during the induction period. Dependent claim 28 recites that certain steps of claim 17 are repeated. Dependent claim 29 requires the formulation of claim 17 to be administered in combination with interferon-beta.

E. Asserted Grounds of Unpatentability

Petitioner asserts that claims 17, 19, 20, and 22–29 are unpatentable on the following three grounds:

Claims Challenged	32 U.S.C. §[1]	Reference(s)
17, 19, 20, 22–29	102(e)	Bodor[2]
17, 19, 20, 22–29	103(a)	Bodor, knowledge of a POSITA[3]

[1] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '947 patent issued has an effective filing date before that date, the pre-AIA version of § 103 applies.
[2] US 7,888,328 B2, issued Feb. 15, 2011 (Ex. 1029, "Bodor").
[3] "POSITA" refers to "person of ordinary skill in the art." The parties and this Decision similarly refer to a "PHOSITA," i.e., "person having ordinary skill in the art."

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