Trials@uspto.gov
571.272.7822

Paper No. 13
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

KOIOS PHARMACEUTICALS LLC,
Petitioner,

v.

MEDAC GESELLSCHAFT FÜR KLINISCHE SPEZIALPRÄPARATE MBH,
Patent Owner.

Case IPR2016-01370
Patent 8,664,231 B2

Before JACQUELINE WRIGHT BONILLA, TONI R. SCHEINER, and ERICA A. FRANKLIN, *Administrative Patent Judges*.

BONILLA, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

On July 20, 2016, Koios Pharmaceuticals LLC ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–22 of U.S. Patent No. 8,664,231 B2 ("the '231 patent") (Ex. 1001). Paper 1 ("Pet."). medac Gesellschaft für klinische Spezialpräparate mbH ("Patent Owner") filed a Preliminary Response to the Petition. Paper 11 ("Prelim. Resp.").

Under 35 U.S.C. § 314(a), an *inter partes* review may not be instituted unless it is determined that there is "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Based on the information presented in the Petition and Preliminary Response, we are persuaded that there is a reasonable likelihood Petitioner would prevail with respect to the claims challenged in the Petition. Accordingly, we institute an *inter partes* review of claims 1–22 of the '231 patent.

A. Related Proceedings

Petitioner and Patent Owner identify a district court action involving the '231 patent, titled *medac Pharma, Inc. v. Antares Pharma, Inc.*, No. 1:14-cv-01498-JBS-KMW (D.N.J.). Pet. 2; Paper 4, 2. The parties also identify two prior proceedings at the Board, IPR2014-01091 ("the -1091 IPR") and IPR2016-00649 ("the -649 IPR"), as well as Decisions on Institution in each of those cases, addressing challenges of the same patent and claims at issue here. Pet. 2–3; Paper 12, 3; *Frontier Therapeutics, LLC v. medac Gesellschaft für klinische Spezialpräparate mbH*, Case IPR2016-00649 (PTAB Sept. 1, 2016) (Paper 10); *Antares Pharma, Inc. v. medac Gesellschaft für klinische Spezialpräparate mbH*, Case IPR2014-01091 (PTAB Jan. 6, 2015) (Paper 7). The district court litigation settled in April

2015. Paper 4, 2. The -1091 IPR and -649 IPR proceedings were terminated in view of settlements in April 2015 and December 2016, respectively. Pet. 3; Paper 12, 3.

Patent Owner also identifies U.S. Patent Application Serial No. 14/635,542, filed March 2, 2015, which is currently pending at the Office. Paper 4, 2.

B. The '231 Patent

The '231 patent relates to a method for treating inflammatory autoimmune diseases, such as rheumatoid arthritis, juvenile rheumatoid arthritis, or psoriasis, by subcutaneously administering a concentrated methotrexate solution comprising more than 30 mg/ml of methotrexate. Ex. 1001, Abstract, 3:59–67, 8:43–47. Methotrexate is a cytostatic agent that has been known since the early 1950s in the field of oncology, particularly for treating breast cancer and leukemia in children. *Id*. at 1:14–17, 1:24–27. Methotrexate also was used early on to treat psoriasis, and first observed in the late 1950s as a treatment for individual rheumatoid arthritis cases. *Id*. at 1:28–32.

According to the '231 patent, "[o]ver the years, methotrexate has become the gold standard in the treatment of rheumatoid arthritis." *Id*. at 2:34–36. As a basic therapeutic for rheumatoid arthritis, methotrexate is administered orally or parenterally, once a week over a long period of time, sometimes throughout the patient's lifetime. *Id*. at 2:37–41. Methotrexate is dosed significantly lower in the treatment of rheumatoid arthritis than in the treatment of tumors, sometimes up to 1,000 times lower. Thus, antirheumatic therapy is referred to as "low-dosage methotrexate therapy." *Id*. at 1:56–60. In this capacity, methotrexate is administered only once per

week, in dosages ranging from 5.0 to 30.0 mg per week in Germany, and up to 40.0 mg per week in other European countries. *Id.* at 1:60–65.

The '231 patent discloses a ready-made syringe and carpule containing a methotrexate solution, as well as a pen-injector comprising the ready-made syringe and/or carpule. *Id.* at 1:5–13. The '231 patent states that ready-made syringes containing methotrexate for the treatment of rheumatoid arthritis are known from the prior art, where the active substance is present at a concentration of up to 25 mg/ml in a pharmaceutically acceptable solvent. *Id.* at 2:26–31. The '231 patent, however, further states that

> subcutaneous administration in particular has its difficulties . . . due to the problem of having to inject the required relatively large amount of active substance solution (e.g. up to 3 ml in the case of a certain dosage) under the skin every week, which was especially difficult to convey to children.

Id. at 2:44–51. In other words, the '231 patent recognizes that although the prior art ready-made syringes have had a positive impact on patient compliance (i.e., the degree of treatment acceptance on the part of the patient), injecting large amounts of liquid under the skin leads to a reduced patient compliance. *Id.* at 4:14–16, 4:65–5:13.

According to the '231 patent, a need therefore exists for a methotrexate solution that can be administered to patients, including children, as easily and pain-free as possible, and in turn provide a high degree of patient compliance. *Id.* at 2:53–58. The '231 patent seeks to address this need by providing methotrexate formulations in higher concentrations than those known in the prior art, which in turn allows for a smaller liquid volume for injection. *Id.* at 3:16–27, 5:5–23. The '231 patent

states that the smaller volumes of liquid are easier to convey to patients, in particular children, and can be expected to have a further positive impact on patient compliance. *Id.* at 5:5–23.

C. Illustrative Claim

Claim 1 of the '231 patent, the only independent claim, is illustrative and is reproduced below:

> 1. A method for the treatment of inflammatory autoimmune diseases in a patient in need thereof, comprising subcutaneously administering to said patient a medicament comprising methotrexate in a pharmaceutically acceptable solvent at a concentration of more than 30 mg/ml.

Id. at 8:43–47. Dependent claims 2–22 recite additional limitations regarding methotrexate concentrations and dosages, solvent, inflammatory autoimmune diseases, self-administration, and the medicament being contained in an injection device for one or more applications, such as a pen injector, and in a storage container, such as a carpule.

D. Proposed Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–22 of the '231 patent on the following grounds:

Reference(s)	**Statutory Basis**	**Claims Challenged**
Grint (Ex. 1003)[1]	§ 102(b)	1, 2, 4–6, 11–13, 17, and 22

[1] Grint et al., U.S. Patent No. 6,544,504 B1 (issued Apr. 8, 2003) ("Grint") (Ex. 1003).

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