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Paper 13
Entered: March 4, 2018

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-02036
Patent 7,976,838 B2

Before ERICA A. FRANKLIN, SHERIDAN K. SNEDDEN and JACQUELINE T. HARLOW, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Sandoz, Inc. ("Petitioner") filed a Petition (Paper 1; "Pet.") to institute an *inter partes* review of claims 1–14 of US 7,976,838 B2 (Ex. 1001; "the '838 patent"). Genentech, Inc. ("Patent Owner") filed a Patent Owner Preliminary Response. Paper 10 ("Prelim. Resp."). Petitioner filed an authorized Reply to the Patent Owner Preliminary Response.[1] Paper 12.

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a).

Upon consideration of the Petition and Preliminary Response, we determine that the Petition raises the same or substantially the same prior art and arguments previously presented and considered by the Office. Consequently, we exercise our discretion under § 325(d) and *deny* the Petition.

A. Related Proceedings

The parties inform us that two other petitions were filed about the same time as the Petition in the instant proceeding, each concerning the'838 patent: IPR2017-01923 (petitioner Pfizer, Inc.) and IPR2017-02042 (petitioner Sandoz, Inc.). Pet. 3; Paper 6, 2. Previously, claims of the '838 patent were challenged in IPR2015-00417 (petitioner Boehringer Ingelheim

[1] We authorized the Reply only to address factors considered by the Board when evaluating whether to exercise discretion under § 314(a), in view of the recent designation of *General Plastic Industrial Co., Ltd. v. Canon Kabushiki Kaisha*, Case IPR2016-01357, Paper 19 (September 6, 2017) as precedential. Paper 11.

Int'l GmbH). After institution, the case was terminated upon a request by petitioner Boehringer. Case IPR2015-00417, Papers 11, 20. Prior to that termination, another petition challenging claims of the '838 patent was filed in IPR2015-01733 (petitioner Celltrion, Inc.), along with a motion for joinder with IPR2015-00417. Case IPR2015-01733, Papers 2, 3. Subsequently, the petition was dismissed upon a request by Celltrion, Inc. *Id*., Paper 12. Thereafter, Celltrion filed a petition in IPR2016-01667 that was denied on the merits. Case IPR2016-01667, Papers 2, 15.

B. The '838 patent

The '838 patent discloses methods of treating rheumatoid arthritis ("RA") in a human patient who experiences an inadequate response to a TNFα-inhibitor. Ex. 1001, Abstract, 4:3–24. The Specification expressly defines the term "inadequate response to a TNFα-inhibitor" as follows:

> [A]n inadequate response to previous or current treatment with a TNFα-inhibitor because of toxicity and/or inadequate efficacy. The inadequate response can be assessed by a clinician skilled in treating the disease in question.

Id. at 5:25–29. Commercial examples of TNFα-inhibitors include Etanercept (ENBREL®), Infliximab (REMICADE®) and Adalimumab (HUMIRA™). *Id*. at 5:19–24.

The methods of the claimed invention involve administering an antagonist that binds to a B cell surface marker, such as CD20. *Id.* at 4:60–65. The Specification discloses rituximab (RITUXAN®) as such an antagonist, explaining that it is "a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen." *Id*. at 2:32–34.

C. Illustrative Claims

Claims 1, 2, 8, 10 and 11 are the independent claims challenged, and are reproduced below:

> 1. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient an antibody that binds to CD20, wherein the antibody is administered as two intravenous doses of 1000 mg.
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> 2. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient an antibody which binds to CD20 in an amount that is effective to provide an ACR50 response at week 24, ACR70 response at week 24, or no erosive progression at weeks 24 and beyond, wherein the antibody is administered as two intravenous doses of 1000 mg.
>
> 8. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, wherein rituximab is administered as two intravenous doses of 1000 mg.
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> 10. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, and methotrexate, wherein the patient has no erosive progression at weeks 24 and beyond, and wherein rituximab is administered as two intravenous doses of 1000 mg.
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> 11. A method of achieving a clinical response selected from the group consisting of ACR50 response at week 24, ACR70 response at week 24, and no erosive progression at weeks 24 and beyond, in a human rheumatoid arthritis patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, and

> methotrexate, wherein rituximab is administered as two intravenous doses of 1000 mg.

Claims 3–7 depend from claim 2, either directly or indirectly. Claim 9 depends directly from claim 8. Claims 12–14 depend directly from claim 11.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–14 of the '838 patent as obvious over Edwards 2001[2] in view of DeVita[3] and Curd[4]. Pet. 5.

Petitioner also relies on the Declarations of David Fox, M.D., Ph.D. (Ex. 1007) and William J. Jusko, Ph.D. (Ex. 1008).

II. ANALYSIS

Discretionary Denial under 35 U.S.C. § 325(d)

Patent Owner asserts that we should exercise our discretion to deny the Petition under 35 U.S.C. § 325(d) because Petitioner's asserted ground relies upon the same or substantially the same prior art previously considered by the Office, and Petitioner has not explained why such discretion should not be exercised. Prelim. Resp. 7–18 (citing *Unified Patents, Inc. v. Berman*, IPR2016-01571, Paper 10 at 11–12 (Dec. 14, 2016) (informative). Patent Owner describes in detail how it perceives that the

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[2] Edwards et al., Sustained improvement in rheumatoid arthritis following a protocol designed to deplete B lymphocytes, Rheumatology Vol. 40, No. 3:205–211 (2001) Ex. 1006.

[3] De Vita et al., *Pathogenic Role of B Lymphocytes in Rheumatoid Synovitis: B Cell Selective Blocking Can Induce a Clinical Response in Patients with Refractory Rheumatoid Arthritis*, REUMATISMO, Vol. 53, No. 3 (Suppl. No. 4) (2001) [ENGLISH TRANSLATION]. Ex. 1005.

[4] Patent Application Publication No. WO 00/67796 A1 by John G. Curd et al., published Nov. 16, 2000. Ex. 1016 ("Curd").

Petition relies on "identical (or at minimum substantially the same) prior art and arguments previously presented in both original prosecution and earlier IPRs (IPR2015-00417 by Boehringer; IPR2015-01733 and IPR2016-01667 by Celltrion)." *Id.*

According to Petitioner, "[t]he grounds, evidence, and/or arguments relied upon in th[e] Petition are different than what was relied upon in IPR2016-01667, IPR2015-01733, IPR2015-00417, and IPR2017-01923, and during the prosecution of the '838 patent." Pet. 3. To the extent that any such differences exist, Petitioner has not explained or even alleged that the prior art and the arguments presented in the Petition are not *substantially the same* as those considered and abandoned by the Examiner during prosecution, and as those presented and considered previously by the Board.

Institution of an *inter partes* review is discretionary. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that under § 314(a), "the PTO is permitted, but never compelled, to institute an IPR proceeding"). Specifically, "the Board may authorize the review to proceed" or "deny some or all grounds for unpatentability for some or all of the challenged claims." 37 C.F.R. § 42.108(a), (b). An example of this discretion may be applied with respect to the occurrence of multiple petitions challenging the same patent, as set forth in 35 U.S.C. § 325(d), which states, in relevant part:

> (d) MULTIPLE PROCEEDINGS -- . . . In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

35 U.S.C. § 325(d).

After considering the arguments and evidence, and for the reasons set forth in the following discussion, we agree with Patent Owner that Petitioner's asserted combination of Edwards 2001, De Vita and Curd raises the same or substantially the same prior art and arguments previously presented and considered by the Office. Consequently, we exercise our discretion under § 325(d) and deny the Petition.

In seeking denial of the Petition based upon prior art and arguments previously presented to the Board, Patent Owner focuses on IPR2016-01667. Prelim. Resp. 15–18. In considering whether to exercise our discretion under § 325(d), we focus on IPR2016-01667 also, and refer to it as the "Celltrion proceeding."

The Celltrion proceeding represents the third challenge to claims of the '838 patent. In that proceeding, Celltrion presented three grounds challenging claims of the '838 patent, wherein one ground challenged claims 1–14 as obvious over the combination of Goldenberg, Curd, and De Vita. IPR2016-01667, Paper 2. Regarding that combination, Celltrion asserted that Goldenberg and De Vita each teach treating a patient who experiences an inadequate response to a TNFα-inhibitor with rituximab. IPR2016-01667, Paper 2 at 51. Celltrion asserted also that Goldenberg and Curd each teach combining methotrexate with rituximab therapy. *Id*.

Celltrion did not allege that Goldenberg, Curd, or De Vita teaches the claimed dosage of rituximab, i.e., two intravenous doses of 1000 mg. *Id*. at 52. Rather, according to Celltrion, a person of ordinary skill in the art "would have been motivated to optimize the dose of rituximab used to treat RA." *Id*. at 53. In support of that contention, Celltrion asserted that the total dosage administered in the claimed methods, i.e., 2000 mg, falls squarely

between the successful total dose of 1500 mg disclosed in Goldenberg and the successful total dose of 2550 mg disclosed in De Vita. *Id*.

Insofar as Goldenberg administers its dose in a total of five intravenous administrations, while De Vita administers a total of four intravenous administrations, Celltrion asserted that a person of skill would have been motivated to administer rituximab in as few doses as possible to increase patient compliance and convenience. *Id*. at 53. Celltrion asserted also that Curd would have motivated the skilled artisan to optimize the selection of an appropriate dose and schedule. *Id*.

In the instant Petition, Petitioner also relies on De Vita for its teaching to treat RA patients who have not responded adequately to a TNFα-inhibitor with rituximab. Pet. 31–32. Edwards 2001 does not discuss patients who have not adequately responded to a TNFα-inhibitor. Nevertheless, Petitioner relies upon Edwards 2001 also for this claim element. *Id*. at 31. Petitioner also relies on Curd, in the same manner as Celltrion, i.e., as teaching that methotrexate may be combined with rituximab therapy. *Id*. at 52.

Also similar to Celltrion, Petitioner does not allege that any reference in the combination teaches the claimed dosage of rituximab, i.e., two intravenous doses of 1000 mg. *Id*. at 32–33. Rather, Petitioner refers to Edwards 2001's disclosure of four i.v. infusions... on days 2, 8, 15, and 22, of 300, 600, 600 and 600 mg respectively, De Vita's disclosure of 4 intravenous infusions weekly of 375 mg/m^2, and Curd's disclosure of a dose range of about 20 mg/m^2 to about 1000 mg/m^2, asserting that De Vita's dose is interchangeable with the dosage recited in the claims, Edwards 2001's dose is equivalent to De Vita's dose, and Curd's dose range includes a dose that is equivalent to one of the required doses, and such amount may be

administered in one or more initial doses followed by one or more subsequent doses. *Id*. at 33. As did Celltrion, Petitioner asserts that a skilled artisan would have been motivated to decrease the number of infusions disclosed in the cited art to two doses of 1000 mg to improve patient compliance and that doing so would have involved no more than routine optimization. *Id*. at 33–41.

Thus, based upon our comparison of Celltrion's challenge over Goldenberg, De Vita and Curd with Petitioner's challenge over Edwards 2001, De Vita and Curd, it is readily apparent that Petitioner's cited references are the same or, with respect to Edwards 2001,[5] substantially the same as those presented in the earlier Celltrion proceeding. Moreover, our comparison of the challenges reveals that the arguments presented in the Petition are the same or substantially the same as those raised by Celltrion, i.e., absent a teaching in the prior art to treat a patient who experiences an inadequate response to a TNFα-inhibitor with rituximab administered as two intravenous doses of 1000 mg, a person of skill in the art would allegedly be motivated to modify known dosing regimens precisely to the recited dose and schedule to improve patient compliance, and doing so would have amounted to routine optimization. Because we have already considered substantially the same prior art and substantially the same arguments in the Celltrion proceeding, we decline to do so again.

[5] We note also, as Patent Owner asserts, during prosecution of the '838 patent, the Examiner withdrew an obviousness rejection over a combination including Edwards 2001 and allowed the challenged claims after Applicant demonstrated that Edwards 2001 neither discloses any patients who have experienced an inadequate response to a TNFα-inhibitor, nor administering two doses of 1000 mg. Prelim. Resp. 11; Ex. 1042 at 428–29, 985.

III. CONCLUSION

For the foregoing reasons, we exercise our discretion under § 325(d) and deny the Petition.

ORDER

Accordingly, it is hereby:

ORDERED that Petitioner's request for an *inter partes* review of claims 1–14 of the '838 patent is *denied*.

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