THE FEDERAL CIRCUIT AFFIRMS THE PATENT TRIAL AND APPEAL BOARD'S INVALIDATION OF ALL CLAIMS OF A GILENYA® PATENT

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IP Litigation Alert

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Torrent Pharmaceuticals ("Torrent"), Apotex Inc., and Mylan Pharmaceuticals filed two *inter partes* review ("IPR") petitions in 2014 seeking review of all claims of U.S. Patent 8,324,283 (the "'283 patent"), which is related to Novartis AG's *Gilenya*® product.[1] On April 12, 2017, the Federal Circuit affirmed the Final Written Decision of the Patent Trial and Appeal Board ("the Board"), which had found all claims unpatentable as obvious.[2]

BACKGROUND

The '283 patent, owned by Novartis AG and Mitsubishi Tanabe Pharma Corp. (collectively, "Novartis"), is listed in the FDA Orange Book as covering *Gilenya*®. *Gilenya*® is a solid oral dosage form of the active ingredient fingolimod, indicated for the treatment of multiple sclerosis. The '283 patent claims solid oral pharmaceutical compositions containing a sphingosine-1 phosphate ("S1P") receptor agonist, *e.g.,* fingolimod, and a sugar alcohol, *e.g.,* mannitol. Torrent filed an IPR petition asserting that the claims of the '283 patent were unpatentable on three grounds:

1. obviousness over the prior art references Chiba, which disclosed fingolimod solid oral dosage formulations,[3] and Aulton, which disclosed mannitol;[4]
2. anticipation over Sakai, which disclosed liquid and lyophilized compositions of fingolimod and mannitol;[5] and
3. obviousness over the combination of Chiba and Sakai.

The Board granted institution on the first ground, the combination of Chiba and Aulton. The Board denied institution on the second and third grounds, which both included Sakai, because "Sakai does not describe a solid composition suitable for oral formulation," and its "stated reasons for using mannitol in liquid pharmaceutical compositions are inapplicable to its potential use in connection with solid pharmaceutical compositions."[6]

When the Board issued its Final Written Decision,[7] however, it held the claims of the '283 patent unpatentable for obviousness over Chiba and Aulton, and it stated that Sakai provided an additional reason to combine fingolimod and mannitol. The Board found that in view of Chiba's teaching of an oral fingolimod composition with excipients and Aulton's teaching that mannitol was a well-known diluent used in wet granulation, "mannitol likely would have been a target of investigation for a person of ordinary skill in the art interested in finding an excipient compatible with fingolimod."[8] The Board also explained that there was "additional evidence of the reason to

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combine fingolimod and mannitol," including Sakai, which "directly instructs that the two ingredients should be combined."[9]

The Board also considered and rejected Novartis's evidence of objective indicia of nonobviousness. Novartis had argued, for example, that the claims were not obvious because the combination of fingolimod and mannitol unexpectedly solved the problem of fingolimod's low dose instability. The Board noted, however, that independent claims 1 and 19 contain no dosage limitation, so the alleged unexpected results evidence was not commensurate with the full scope of the claims. Novartis also argued that its formulation fulfilled a long-felt but unmet need, received industry praise, and enjoyed commercial success. The Board ruled against all of Novartis's arguments.[10]

FEDERAL CIRCUIT DECISION

Novartis appealed to the Federal Circuit, challenging aspects of the Board's Final Written Decision. First, Novartis argued that the Board's reliance on Sakai as additional evidence of reason to combine the teachings of Chiba and Aulton was in violation of the Administrative Procedure Act ("APA"). Novartis contended that when the Board denied institution based on combinations including Sakai, the Board excluded Sakai from the case. Novartis noted that the APA requires that an agency "must provide the patent owner with timely notice of the matters of fact and law asserted, and an opportunity to submit facts and argument."[11] Novartis argued that it was not provided sufficient notice under this standard and did not receive sufficient opportunity to distinguish the Sakai reference.

The Federal Circuit rejected Novartis's argument.[12] The Circuit harmonized the Board's decision not institute review based on Sakai with the Board's reliance on Sakai (to support the combination of mannitol and fingolimod) by explaining that Sakai "merely reinforced" the combination that was already suggested by Chiba and Aulton.[13] The Federal Circuit also rejected the argument that Novartis was unfairly surprised because Novartis had ample notice and opportunity to be heard on Sakai's relevance throughout the proceeding. Sakai was addressed at length in the initial petition, preliminary response, patent owner response, expert declarations, and at the hearing.[14] Finally, the Circuit rejected Novartis's argument that Sakai was the missing link in the Board's obviousness analysis, and explained that Sakai was only one of several separate grounds to support a motivation to combine. Sakai was not the "linchpin" of the Board's analysis, as Novartis wrongly contended.[15]

The Federal Circuit also rejected Novartis's arguments relating to objective indicia of nonobviousness. It held that Novartis waived its "low dosage" unexpected results argument because its arguments to the Board focused on stability across the full range of doses, and was not limited in the way Novartis asserted on appeal.[16] Regarding commercial success, the Circuit upheld the Board's decision that *Gilenya*® succeeded because it was a solid, oral treatment for multiple sclerosis. The Board had reasoned, and the Federal Circuit agreed, that any solid, oral dosage form would have succeeded in the marketplace, and the purported novelty of *Gilenya*® as claimed in the '283 patent was the combination of mannitol and fingolimod, not the fact that the drug was offered in a solid, oral dosage form. The fact that *Gilenya*® was "the first to receive FDA approval for commercial marketing does not overcome the fact that" such treatments were known in the art.[17]

LOOKING FORWARD

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One of Novartis's strategic mistakes in this case was that its motion to exclude evidence was overly broad and did not focus specifically on Sakai. Novartis's motion challenged over fifty references; and in Novartis's motion, Sakai was "identified by exhibit number only and listed in one long string cite."[18] The Federal Circuit stated, "[t]his superficial treatment amounts to little more than a request that the Board peruse the cited evidence and piece together a coherent argument on Novartis' behalf."[19] Going forward, patent owners will want to focus their motions to exclude on the specific references they believe are unfairly discussed during the IPR and explain with specificity why those references should not be considered.

NOTES:

[1] Petition for *Inter Partes* Review of U.S. Patent 8,324,283 under 35 U.S.C. §§ 311–319 and 37 C.F.R. § 42, *Torrent Pharm. Ltd. v. Novartis AG*, No. IPR2014-784 (P.T.A.B. May 27, 2014), Paper No. 2; *Apotex, Inc. v. Novartis AG, No*. IPR2015-518 (P.T.A.B. Dec. 31, 2014), Paper No. 1.

[2] *Novartis AG v. Torrent Pharm. Ltd*., 853 F.3d 1316 (Fed. Cir. 2017).

[3] Kenji Chiba & Kunitomo Adachi, Compositions And Methods Of Using Compositions With Accelerated Lymphocyte Homing Immunosuppressive Properties, U.S. Patent 6,004,565 (1999).

[4] Michael E. Aulton, Pharmaceutics: The Science Of Dosage Form Design (1988).

[5] Atsushi Sakai & Rumiko Masuda, Drug Composition, U.S. Patent 6,277,888 (2001).

[6] *Novartis*, 853 F.3d at 1322; Institution of *Inter Partes* Review, *Torrent Pharm. Ltd. v. Novartis AG*, No. IPR2014-784 (P.T.A.B. Dec. 1, 2014), Paper No. 11. Apotex and Mylan subsequently filed a separate petition seeking review of all claims based on Chiba and Aulton and requested joinder with Torrent's petition. Petition for *Inter Partes* Review of U.S. Patent 8,324,283 under 35 U.S.C. §§ 311–319 and 37 C.F.R. § 42, *Apotex, Inc. v. Novartis AG*, No. IPR2015-518 (P.T.A.B. Dec. 31, 2014), Paper No. 1. The Board granted review, and consolidated the petitions on February 17, 2015.

[7] *Torrent Pharm. Ltd. v. Novartis AG*, Nos. IPR2014-784, IPR2015-518, 2015 WL 5719630 (P.T.A.B. Sept. 24, 2015).

[8] *Id*. at *8.

[9] *Id*.

[10] *Id*. at **11–14.

[11] *Novartis AG v. Torrent Pharm. Ltd*., 853 F.3d at 1324 (citing 5 U.S.C. §§ 554(b)–(c), 557(c); *Dell Inc. v Acceleron, LLC*, 818 F.3d 1293, 1301 (Fed. Cir. 2016)).

[12] The Federal Circuit reviewed the Board's decision *de novo* for legal conclusions and for substantial evidence for factual determinations. *Id*. at 1323–24.

[13] *Id*. at 1324–25.

[14] *Id*. at 1325–26.

[15] *Id*. at 1326.

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[16] *Id*. at 1330.

[17] *Id*. at 1330–31.

[18] *Id*. at 1326 n.2.

[19] *Id*.

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