NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

WARNER CHILCOTT COMPANY, LLC AND HOFFMANN-LA ROCHE INC.,
Plaintiffs-Appellants,

v.

TEVA PHARMACEUTICALS USA, INC., APOTEX CORP., APOTEX INC., MYLAN PHARMACEUTICALS INC. AND SUN PHARMA GLOBAL FZE,
Defendants-Appellees.

2014-1439, -1441, -1444, -1445, -1446

Appeals from the United States District Court for the District of Delaware in Nos. 1:08-cv-00627-LPS, 1:09-cv-00061-LPS, 1:09-cv-00143-LPS, 1:10-cv-00285-LPS, 1:10-cv-01085-LPS, 1:10-cv-01111-LPS, 1:11-cv-00081-LPS, and 1:11-cv-00236-LPS, Judge Leonard P. Stark.

Decided: November 18, 2014

MARK C. FLEMING, Wilmer Cutler Pickering Hale and Dorr LLP, of Boston, Massachusetts, argued for plaintiffs-appellants. With him on the brief for Warner Chilcott Company, LLC, were VINITA FERRERA, SYDENHAM B.

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PHILIP D. SEGREST, JR., Husch Blackwell LLP, of Chicago, Illinois, argued for defendants-appellees. With him on the brief for Apotex Inc., et al., were STEVEN E. FELDMAN, JAMES P. WHITE, DANIEL R. CHERRY, SHERRY L. ROLLO and SAMUEL A. BROWN. On the brief for Teva Pharmaceuticals USA, Inc. were JAMES GALBRAITH, MARIA LUISA PALMESE, A. ANTONY PFEFFER and PETER L. GIUNTA, Kenyon & Kenyon LLP, of New York, New York. On the brief for Mylan Pharmaceuticals Inc. were EDGAR H. HAUG, RICHARD E. PARKE and RICHARD F. KURZ, Frommer Lawrence & Haug LLP, of New York, New York. On the brief for Sun Pharma Global, FZE, was ERIC C. COHEN, Katten Muchin Rosenman LLP, of Chicago, Illinois.

Before LOURIE, REYNA, and TARANTO, *Circuit Judges*.

LOURIE, *Circuit Judge*.

In these consolidated appeals, Warner Chilcott Company, LLC ("Warner") and Hoffmann-La Roche Inc. ("Roche") (collectively, the "Plaintiffs") appeal from the decision of the United States District Court for the District of Delaware granting summary judgment that claims 6, 8, 9, and 13–15 of U.S. Patent 7,192,938 (the "'938 patent") and claims 9 and 10 of U.S. Patent 7,718,634 (the "'634 patent") (collectively, "the asserted claims") were invalid for obviousness. *See Warner Chilcott Co. v. Teva Pharm. USA, Inc.*, __ F. Supp. 2d __, No. 08-cv-00627, 2014 WL 1285656 (D. Del. Mar. 28, 2014) ("*Opinion*").

Because the district court did not err in granting summary judgment of invalidity, we *affirm*.

BACKGROUND

Osteoporosis is a chronic bone disorder characterized by reduced bone density and quality that can lead to increased susceptibility to fractures. Roche owns the '938 and '634 patents, both of which have a priority date of May 10, 2002 and are directed to methods of treating osteoporosis by orally administering a single, monthly dose of 150 mg of risedronate.

Risedronate is a salt of risedronic acid and belongs to a class of pharmaceutical compounds known as bisphosphonates. Bisphosphonates "bind strongly to bone mineral" and are "potent inhibitors of bone resorption." '634 patent col. 1 ll. 46–53. As of May 2002, the U.S. Food and Drug Administration ("FDA") had approved several oral regimens of bisphosphonates for the treatment of osteoporosis, including risedronate dosed daily at 5 mg, which was marketed under the Actonel® brand name, and alendronate dosed daily at 5 mg or weekly at 35 mg, which was marketed under the Fosamax® brand name. Daily oral dosing of bisphosphonates caused irritation to mucous membranes and significant adverse esophageal and gastrointestinal side effects, which resulted in noncompliance of patients on the daily regimens. *Id.* at col. 1 ll. 62–66. Those problems were somewhat alleviated by weekly dosing of bisphosphonates. The patents at issue provide that a monthly dose of 150 mg of a bisphosphonate, among other infrequent dosing regimens, is effective at treating osteoporosis. *Id.* at col. 2 ll. 43–59.

Claim 9 of the '634 patent is representative of the claims on appeal and reads as follows:

> 9. A method for treating or inhibiting postmenopausal osteoporosis in a postmenopausal woman in need of treatment or inhibition of

> postmenopausal osteoporosis by administration of *a pharmaceutically acceptable salt of risedronic acid*, comprising:
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> (a) commencing the administration of the pharmaceutically acceptable salt of risedronic acid by orally administering to the postmenopausal woman, on a single day, a first dose in the form of a tablet, wherein the tablet comprises an amount of the pharmaceutically acceptable salt of risedronic acid that is equivalent to about *150 mg* of risedronic acid; and
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> (b) continuing the administration by orally administering, *once monthly on a single day*, a tablet comprising an amount of the pharmaceutically acceptable salt of risedronic acid that is equivalent to about *150 mg* of risedronic acid.

Id. col. 8 ll. 19–36 (emphases added).

The claims at issue cover the monthly administration of Actonel® (risedronate sodium) 150 mg tablets, which were approved by the FDA in April 2008 for treating postmenopausal osteoporosis in the United States and marketed by Warner, a licensee of Roche. From August 2008 through February 2011, generic pharmaceutical manufacturers Teva Pharmaceuticals USA, Inc., Apotex Corp., Apotex Inc., Mylan Pharmaceuticals Inc., and Sun Pharma Global FZE (collectively, the "Defendants") submitted Abbreviated New Drug Applications ("ANDAs") to the FDA, seeking approval to engage in the commercial manufacture, use, or sale of generic versions of Actonel® 150 mg tablets. In response, the Plaintiffs sued each of the Defendants in the United States District Court for the District of Delaware, asserting that the Defendants' ANDA filings infringed the '938 and '634 patents under 35 U.S.C. § 271(e)(2).

While the Actonel® ANDA litigation was pending, the United States District Court for the District of New Jersey granted summary judgment of invalidity for obviousness in an ANDA litigation involving another bisphosphonate oral drug: ibandronate dosed monthly at 150 mg and marketed by Roche under the Boniva® brand name. *Opinion*, 2014 WL 1285656, at *1–2. Specifically, the New Jersey court held that claims 1–8 of the '634 patent, which are directed to monthly oral administration of 150 mg of ibandronate, would have been obvious in view of several prior art references, and we later affirmed that decision. *Hoffmann-La Roche Inc. v. Apotex Inc.*, No. 07-4417, 2012 WL 1637736, at *1 (D.N.J. May 7, 2012), *aff'd*, 748 F.3d 1326 (Fed. Cir. 2014), *reh'g & reh'g en banc denied*, No. 13-1128, ECF No. 87 (Fed. Cir. July 11, 2014).

In the Delaware court, the Defendants similarly moved for summary judgment of obviousness of the claims directed to monthly administration of 150 mg of risedronate. The district court granted the motion on March 28, 2014, holding that the asserted claims would have been obvious in view of the cited prior art, which included: (1) *Update: Bisphosphonates*, Lunar News, Winter 2000, at 32 ("Lunar News"); (2) Schofield *et al.*, U.S. Patent Application Publication 2003/0118634 ("Schofield"); (3) Riis *et al.*, *Ibandronate: A Comparison of Oral Daily Dosing Versus Intermittent Dosing in Postmenopausal Osteoporosis*, 16 J. Bone & Mineral Research 1871 (2001) ("Riis"); (4) Delmas *et al.*, *Bisphosphonate Risedronate Prevents Bone Loss in Women With Artificial Menopause Due to Chemotherapy of Breast Cancer: A Double-Blind, Placebo-Controlled Study*, 15 J. Clinical Oncology 955 (1997) ("Delmas"); (5) Zegels *et al.*, *Effect of High Doses of Oral Risedronate (20 mg/day) on Serum Parathyroid Hormone Levels and Urinary Collagen Crosslink Excretion in Postmenopausal Women With Spinal Osteoporosis*, 28 Bone 108 (2001) ("Zegels"); and (6) Daifo-

tis *et al.*, U.S. Patent 6,432,932 ("Daifotis"). *Opinion*, 2014 WL 1285656, at *3–6.

In particular, the district court examined the summary judgment opinion of the New Jersey court, which relied on eight prior art references, including Daifotis, Riis, and Schofield, to invalidate the claims at issue there. *Id.* at *2–3. The district court then reviewed the record before it relating to risedronate, including the prior art, expert declarations, and proffered evidence of secondary considerations. *Id.* at *3. The court found that Lunar News, Schofield, Riis, Delmas, Zegels, and Daifotis disclosed the three limitations of the asserted claims: (1) oral administration of risedronate for the treatment of osteoporosis, (2) once monthly, and (3) at a dose of 150 mg. *Id.* at *7. The court also found that the prior art, viewed as a whole, would have suggested the efficacy and safety of the claimed dosing regimen. *Id.* The court determined that the Plaintiffs' expert declarations and the proffered evidence of secondary considerations failed to raise any genuine issue of material fact. *Id.* The court therefore concluded that the Defendants had proven by clear and convincing evidence that the asserted claims would have been obvious and that "[n]o reasonable finder of fact could conclude otherwise." *Id.* at *3, *7.

The district court entered final judgment on April 1, 2014. The Plaintiffs timely appealed, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).*

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* The Plaintiffs filed eight actions in the district court, separately asserting the two patents against the four ANDA filers, Teva, Apotex, Mylan, and Sun Pharma, and the district court consolidated those actions into one lead case. After the court entered final judgment in each of the eight actions, the Plaintiffs filed several copies of an identical notice of appeal. That notice listed just five of

DISCUSSION

We apply regional circuit law, here the law of the Third Circuit, when reviewing a district court's grant of a motion for summary judgment. *Teva Pharm. Indus. Ltd. v. AstraZeneca Pharm. LP*, 661 F.3d 1378, 1381 (Fed. Cir. 2001). The Third Circuit "review[s] an order granting summary judgment de novo, applying the same standard" used by the district court. *Azur v. Chase Bank, USA, Nat'l Ass'n*, 601 F.3d 212, 216 (3d Cir. 2010) (quotation omitted). Summary judgment is appropriate when, drawing all justifiable inferences in the nonmovant's favor, "there is no genuine dispute as to any material fact

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the eight cases in the caption (a captioning confusion in which the district court took part), and copies were recorded in the dockets of those five actions, including the lead case. The caption did not list, and copies were not recorded in the dockets of, the three actions in which the Plaintiffs asserted the '634 patent against Apotex, Mylan, and Sun Pharma. On appeal, the Defendants argue that we lack jurisdiction to review the judgment on the '634 patent as to those Defendants. We disagree. Rule 3(c)(1) of the Federal Rules of Appellate Procedure requires a notice of appeal to "designate the judgment, order, or part thereof being appealed." In the lead case below, the Plaintiffs timely filed a notice of appeal in which they expressly appealed from the March 2014 summary judgment, an appealable "judgment" for purposes of Rule 54(a) of the Federal Rules of Civil Procedure. In its March 2014 decision, the district court granted summary judgment of invalidity of the asserted claims in both patents as to all defendants. On these particular facts, we conclude that the Plaintiffs have perfected their appeal in all eight consolidated actions and that we have jurisdiction to review the invalidity judgment on the '634 patents as to all of the Defendants.

and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).

Obviousness is ultimately a question of law premised on underlying issues of fact, including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the pertinent art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence such as commercial success, long-felt need, and the failure of others. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 427 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Monarch Knitting Mach. Corp. v. Sulzer Morat GmBH*, 139 F.3d 877, 881 (Fed. Cir. 1998). A patent claim is invalid as obvious if an alleged infringer proves that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious at the time of invention to a person having ordinary skill in the art. 35 U.S.C. § 103(a) (2006). Patents are presumed to be valid, and overcoming that presumption requires clear and convincing evidence. 35 U.S.C. § 282; *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. __, 131 S. Ct. 2238, 2242 (2011).

The Plaintiffs argue that the district court erred in granting summary judgment of invalidity because there was a genuine dispute of material fact as to whether a person of ordinary skill in the art would have reasonably expected that dosing 150 mg of risedronate once monthly would be safe and effective. According to the Plaintiffs, researchers would not have been able to predict the bioavailability of risedronate or its retention in the bone over the month-long dose-free interval. The Plaintiffs also assert that there was a long felt need for and skepticism of others toward the claimed monthly regimen. Finally, the Plaintiffs argue that our recent decision affirming the New Jersey court's invalidity judgment in the Boniva® litigation does not control this case because ibandronate

and risedronate are different compounds and the record here contains additional evidence of nonobviousness.

The Defendants respond that there is no genuine dispute that the prior art taught monthly administration of risedronate for the treatment of osteoporosis, suggested a dose of 150 mg, and provided a person of ordinary skill in the art with a motivation to pursue that regimen and with a reasonable expectation of success. According to the Defendants, the Plaintiffs' arguments, their expert declarations, and their proffered evidence of secondary considerations fail to raise any genuine issue of material fact to preclude summary judgment of invalidity. The Defendants also maintain that our decision affirming the summary judgment of invalidity in the Boniva® litigation supports a conclusion of obviousness in this case.

We agree with the Defendants that the district court did not err in granting summary judgment that the asserted claims would have been obvious over the considered prior art. There is no dispute that the asserted claims are directed to a method of treating osteoporosis, which requires the following limitations: (1) oral administration of risedronate, (2) once monthly, and (3) at a dose of 150 mg. The district court correctly determined that the cited prior art references disclosed or suggested each of those limitations and provided an express motivation to pursue the claimed monthly regimen and a reasonable expectation of success in doing so. *See Opinion*, 2014 WL 1285656, at *3, *6.

As of May 2002, the priority date of the asserted patents, the FDA had approved several oral regimens of bisphosphonates for the treatment of osteoporosis, including risedronate dosed daily at 5 mg and alendronate dosed daily at 5 mg or weekly at 35 mg. Lunar News, an article published in 2000, reviewed the clinical efficacy of risedronate and stated that "risedronate ha[d] met all standards for efficacy and should receive FDA approval in

the USA for prevention and treatment of osteoporosis in spring 2000." J.A. 9498. The prior art thus indisputably disclosed the first limitation of the asserted claims: oral administration of risedronate for treating osteoporosis.

In addition, the district court correctly found that the prior art taught once-monthly dosing of risedronate, the second limitation of the asserted claims. It was well recognized that daily oral dosing of bisphosphonates resulted in adverse esophageal and gastrointestinal side effects, which were somewhat mitigated by weekly dosing. Appellants' Br. 13. Specifically discussing risedronate and alendronate, Lunar News provided that "[w]eekly, or even monthly, dosing if done properly could foster long-term compliance as well as minimiz[e] side-effects." J.A. 9498. Schofield likewise taught that "[e]quivalent doses [of bisphosphonates] can be given every other day, twice a week, weekly, biweekly, or monthly." J.A. 11696, at [0037]. The prior art thus expressly suggested monthly dosing of risedronate.

The prior art also established a reasonable expectation that once-monthly dosing of risedronate could successfully treat osteoporosis. The district court correctly found that Riis, Delmas, and Zegels disclosed that "bisphosphonates were effective treatments for osteoporosis, even when dosed in intervals exceeding two weeks," and that "risedronate . . . [wa]s effective in preventing bone loss even when given at long intervals." *Opinion*, 2014 WL 1285656, at *4. Delmas, a reference not considered by the United States Patent and Trademark Office during the prosecution of the patents at issue, described a study observing an increase in bone mineral density in patients treated with 30 mg of risedronate every day for 2 weeks, followed by a 10-week period of no treatment, and with that 12-week cycle repeated eight times over 2 years. Delmas thus demonstrated that risedronate could be efficacious even with a dose-free interval of up to 10 weeks. Zegels and Riis similarly described studies on

intermittent dosing of risedronate or ibandronate with dose-free intervals longer than a month. Accordingly, any serious doubt about the efficacy of a monthly regimen of risedronate based on its bone retention profile would have been put to rest. As longer dosing intervals suit patient convenience and compliance, the prior art therefore provided express motivation to pursue a monthly dosing regimen.

Furthermore, the record shows that there would have been a reasonable expectation of success in pursuing the 150 mg monthly dose, the third limitation of the asserted claims. Riis presented evidence, through a study on intermittent dosing of ibandronate, that "a total dose administered over a defined period provides equivalent results irrespective of the dosing schedule." *Opinion*, 2014 WL 1285656, at *4 (quotation marks omitted); *see also* J.A. 11921 ("These results confirm previous preclinical findings indicating that the efficacy of ibandronate depends on the total oral dose given rather than on the dosing schedule."). Zegels similarly taught that the total amount of risedronate, rather than the dosing frequency, "would be more important . . . in terms of the impact on bone metabolism." J.A. 11934. Notably, in Delmas, the total dose given during the 12-week cycle was equivalent to a daily dose of 5 mg. The prior art thus suggested that, in setting the dose for a once-monthly regimen, one could extrapolate from a known effective daily dose to achieve an equivalent total dose over one month.

As indicated, the FDA had approved a 5 mg daily dose of risedronate for the treatment of osteoporosis. Moreover, both Schofield and Daifotis taught an equivalent once weekly dose of 35 mg of risedronate. J.A. 9638; J.A. 11697, at [0042]. Accordingly, a person skilled in the art looking to select a monthly oral dose of risedronate would have reasonably expected success in administering a dose of 150 mg (5 mg/day times 30 days/month). Indeed, the Plaintiffs' own expert testified that risedronate was

known to exhibit a linear bioavailability from 2.5 mg to 50 mg, and that linear scaling of risedronate to a higher dose was merely unknown. While it is true that, as of May 2002, the highest single dose of risedronate that had actually been tested in a patient was 50 mg, obviousness does not require absolute certainty or a guarantee of success. *In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988) ("Obviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success."). The district court therefore did not err in concluding that the asserted claims would have been obvious in view of the prior art.

The Plaintiffs' arguments do not support a contrary conclusion. The Plaintiffs rely on the testimony of their experts and assert that there was uncertainty regarding the safety and efficacy of a once-monthly regimen of 150 mg of risedronate and that there was a long-felt need for and skepticism of others toward the claimed regimen. However, lack of certainty does not preclude a conclusion of obviousness. Therefore, upon a careful review of the record as a whole, and drawing all justifiable inferences in the Plaintiffs' favor, we agree with the district court that the Plaintiffs fail to raise any genuine issue of material fact to preclude summary judgment. We therefore conclude as a matter of law that the asserted claims would have been obvious.

CONCLUSION

We have considered the Plaintiffs' remaining arguments and find them unpersuasive. For the foregoing reasons, we conclude that the asserted claims would have been obvious in view of the cited references and therefore *affirm* the judgment of the district court.

AFFIRMED