United States Court of Appeals for the Federal Circuit

02-1447

NOVO NORDISK A/S
and NOVO NORDISK PHARMACEUTICALS, INC.,

Plaintiffs-Appellees,

v.

BIO-TECHNOLOGY GENERAL CORP.
and TEVA PHARMACEUTICALS USA, INC.,

Defendants-Appellants.

DECIDED: November 26, 2002

Before RADER, Circuit Judge, ARCHER, Senior Circuit Judge, and SCHALL, Circuit Judge.

SCHALL, Circuit Judge.

DECISION

Bio-Technology General Corp. ("BTG") and Teva Pharmaceuticals, Inc. ("Teva") appeal from the June 7, 2002 order of the United States District Court for the District of Delaware granting a preliminary injunction in favor of Novo Nordisk A/S and Novo Nordisk Pharmaceuticals, Inc. (collectively, "Novo") against BTG and Teva in Novo's suit against BTG and Teva for infringement of United States Patent No. 5,633,352 ("'352 patent"). Novo Nordisk A/S v. Bio-Technology Gen. Corp., 207 F. Supp. 2d 322, 324 (D. Del. 2002). Because we conclude that Novo failed to meet the requirement for a preliminary injunction of establishing a reasonable likelihood of success on the merits, we vacate and remand.

DISCUSSION

I.

We review the decision of a district court granting or denying a preliminary injunction under the abuse of discretion standard. Under that standard, we determine whether the district court "made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings." Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1350, 57 USPQ2d 1747, 1751 (Fed. Cir. 2001). In order to obtain a preliminary injunction, the moving party must show: "(1) a reasonable likelihood of success on the merits; (2) irreparable harm if an injunction is not granted; (3) a balance of hardships tipping in [the moving party's] favor; and (4) the injunction's favorable impact on the public interest." Id. Under our jurisprudence, in order to obtain a preliminary injunction, the movant must establish at the very least both of the first two factors, i.e., a likelihood of success on the merits and irreparable harm. Id. (citing Vehicular Techs. Corp. v. Titan Wheel Int'l, Inc., 141 F.3d 1084, 1088, 46 USPQ2d 1257, 1259-60 (Fed. Cir. 1998)). With regard to the requirement of a likelihood of success on the merits, the moving party must show, in light of the burdens that will inhere at trial, that (1) its patent was infringed, and (2) any challenges to the validity and enforceability of its patent "lack substantial merit." Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1366, 57 USPQ2d 1647, 1651 (Fed. Cir. 2001).

II.

The '352 patent issued in May of 1997. It claims priority to an application filed in December of 1983. Generally, the '352 patent describes the use of a genetically modified bacteria to produce human growth hormone ("hGH") that has an added extension of amino acids that are later cleaved off to produce "ripe" hGH. '352 patent, col. 1, l. 56 – col. 2, l. 6. In its pending suits Novo alleges that BTG and Teva's product Tev-Tropin™ infringes claim 1 of the '352 patent. After filing suit, Novo sought a preliminary injunction to enjoin BTG and Teva from selling Tev-Tropin™. Claim 1 of the '352 patent reads as follows:

1. Biosynthetic ripe human growth hormone free of contaminants from pituitary derived human growth

hormone.

'352 patent, col. 10, ll. 7-9.

The district court construed claim 1 in its preliminary injunction decision. It concluded that the term "biosynthetic" means that the human growth hormone must be made by recombinant techniques and that the term "ripe" is used to indicate that the product of the '352 patent has the 191 amino acid sequence that is identical to that of the human growth hormone produced by the human pituitary gland as well as the full biological activity of the human pituitary gland.[1] Novo Nordisk, 207 F. Supp. 2d at 325. For purposes of this appeal, neither party challenges the district court's claim construction.

III.

Recognizing the requirements for the grant of a preliminary injunction, the district court considered first whether Novo had demonstrated a likelihood of success on the merits. In that regard, the court concluded that Novo had shown that Tev-Tropin™ infringed the '352 patent. In reaching that conclusion, the court pointed to the deposition testimony of BTG's and Teva's expert, Dr. Michael Wajnrajch, who admitted that Tev-Tropin™ is a 191 amino acid hGH, free from contaminants from pituitary derived human growth hormone. In addition, the court noted that BTG and Teva had produced "no persuasive evidence" on the infringement issue. Novo Nordisk, 207 F. Supp. 2d at 325.

In opposing the request for a preliminary injunction, BTG and Teva relied chiefly upon the contention that the '352 patent is anticipated by several patents owned by Genentech, Inc. ("Genentech"), specifically United States Patent Nos. 4,601,980 ("'980 patent"), 4,755,465, and 4,859,600. The district court concluded that BTG's and Teva's challenge to the validity of the '352 patent lacked substantial merit. As far as all three patents were concerned, the court stated that the patents had already been considered by the Patent and Trademark Office ("PTO") during the prosecution and reexamination of the '352 patent. Novo Nordisk, 207 F. Supp. 2d at 325. The court also relied upon two additional considerations, both relating to the '980 patent.

The '980 patent, which issued in July of 1986, and which claims priority to an application filed in July of 1979, claims a process for making human growth hormone. Claim 2 of the patent reads as follows:

2. A method for producing human growth hormone which method comprises culturing bacterial transformants containing recombinant plasmids which will, in a transformant bacterium, express a gene for human growth hormone unaccompanied by the leader sequence of human growth hormone or other extraneous protein bound thereto, and isolating and purifying said expressed human growth hormone.

'980 patent, col. 14, ll. 2-10. In Novo Nordisk of North America, Inc. v. Genentech, Inc., 77 F.3d 1364, 37 USPQ2d 1773 (Fed. Cir. 1996), we held that "properly construed, claim 2 of the '980 patent is a process for the direct expression of met-hGH or hGH." 77 F.3d at 1371, 37 USPQ2d at 1779 (emphasis added). (Met-hGH is comprised of the 191 amino acid molecule produced by the human growth hormone gene, with one additional amino acid, methionine ("met"), added to the N-terminus.) In Bio-Technology General Corp. v. Genentech, Inc., 80 F.3d 1553, 38 USPQ2d 1321 (Fed. Cir. 1996)("BTG I"), we ruled that "the production of hGH must also be considered to be within the literal scope of claim 2." 80 F.3d at 1560, 38 USPQ2d at 1326.

In the district court, BTG and Teva argued that, in addition to the production of met-hGH, the '980 patent enables the ripe or mature hGH (i.e. met-free hGH). Thus, they claimed that the '980 patent (claim 2) anticipates the '352 patent. Responding to the validity challenge, Novo argued that the '980 patent may not serve as an anticipating reference because it is not enabled. See Bristol-Myers Squibb v. Ben Venue Laboratories, Inc., 246 F.3d 1368, 1378-79, 58 USPQ2d 1508, 1515 (Fed. Cir. 2001) (holding that a prior art reference anticipated certain claims of one of the patents at issue only after a discussion of several other references that showed that the anticipatory reference was enabled); In re Donohue, 766 F.2d 531, 533, 226 USPQ619, 621 (Fed. Cir. 1985) ("[E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it is not enabling." (citing In re Borst, 345 F.2d 851, 855, 145 USPQ 554, 557 (C.C.P.A. 1962))). BTG and Teva answered this response by citing prior litigation in which Genentech sued BTG for infringement of the '980 patent and (i) a jury rejected BTG's defense that the '980 patent was invalid because it was not enabled; and (ii) we reversed the trial court's grant of judgment as a matter of law ("JMOL") in favor of BTG on the validity issue. See Bio-Technology General Corp. v. Genentech, Inc., 267 F.3d 1325, 60 USPQ2d 1430 (Fed. Cir. 2001) ("BTG II"). The district court rejected BTG's and Teva's reliance on Genentech's prior suit against BTG: "The Federal Circuit's decision in BTG II does not demonstrate, as argued by BTG, that the '980 patent is enabled, but only that BTG failed to carry its burden to prove by clear and convincing evidence that the '980 patent is not enabled." Novo Nordisk, 207 F. Supp. 2d at 325. In addition, pointing to an interference proceeding between Novo and BTG involving the '352

patent, the district court stated, "the fact that BTG initiated an interference in order to take claim 1 of the '352 patent from Novo tends to support the fact that claim 1 is valid over the prior art." Novo Nordisk, 207 F. Supp. 2d at 325 (footnote omitted).

Having determined that Novo had shown a reasonable likelihood of success on the merits with regard to both patent infringement and validity, the district court presumed irreparable harm. Novo Nordisk, 207 F. Supp. 2d at 325. Addressing the public interest and balance of equities requirements for a preliminary injunction, the court concluded that both factors weighed in favor of granting the injunction. Novo Nordisk, 207 F. Supp. 2d at 326. BTG and Teva timely appealed the district court's grant of the preliminary injunction. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

IV.

BTG's and Teva's principal argument on appeal is that, in granting Novo's request for a preliminary injunction, the district court erred in concluding that Novo had established a reasonable likelihood of success on the merits of its infringement suit.[2] In making this argument, BTG and Teva focus exclusively on the validity issue. In that regard, they contend that the district court erred in concluding that their challenge to the validity of the '352 patent, based upon the '980 patent, lacked substantial merit. They base their contention on the fact that they presented to the district court testimony of three of Genentech's experts from the Genentech-BTG trial. These experts, Dr. Sidney Altman of Yale University, Professor James Manley of Columbia University, and Dr. Steven Hughes of the National Cancer Institute, testified that the '980 patent enables the production of ripe or mature hGH. BTG and Teva also base their contention on the fact that, in BTGII, we sustained the verdict of the jury that BTG had failed to prove "by clear and convincing evidence that the '980 patent did not enable a scientist skilled in the art in 1979 to make any mature human growth hormone of 191 amino acids." BTGII, 267 F.3d at 1329, 60 USPQ2d at 1433. Referring to the expert testimony from the Genentech-BTG trial and our decision in BTGII, BTG and Teva argue that the district court ignored substantial evidence of invalidity relating to the '352 patent. They also argue that the district court erred

in relying on (i) the fact that the '980 patent was before the PTO and (ii) BTG's participation in an interference involving the '352 patent.

Novo responds by arguing that BTG and Teva have not raised a substantial question regarding the validity of the '352 patent. Novo maintains that it has shown a reasonable likelihood of success on the merits with respect to the validity issue because the PTO found the subject matter of the '352 patent patentable over the '980 patent. As far as BTGII is concerned, Novo asserts that BTG's and Teva's reliance on the prior litigation between Genentech and BTG is misplaced. Novo states that the "Federal Circuit did not rule that the '980 patent in fact necessarily enabled the production of mature hGH, much less that it anticipated Claim 1 of the 352 patent[,] which was not before the Court." Novo points out that, in BTGII, we simply ruled that BTG had failed to prove by clear and convincing evidence that the '980 patent did not enable the making of mature hGH. Finally, Novo argues that, because it participated in the interference proceeding involving the '352 patent, BTG is estopped from challenging the patent's validity.

V.

In further proceedings in the district court, BTG will have the burden of proving by clear and convincing evidence that the '980 patent anticipates the '352 patent. Moreover, in carrying that burden, BTG will have to ward off Novo's argument that the '980 patent is not enabled. Needless to say, we express no views on the ultimate determination of the validity issue in this case. At this point, our sole task is to determine whether the district court erred in granting Novo's request for a preliminary injunction. We are constrained to hold that it did. We reach that holding because we conclude that the district court erred as a matter of judgment by failing to give proper weight to (i) the testimony of Genentech's expert witnesses in the Genentech-BTG trial and (ii) our decision in BTG II. "In resisting a preliminary injunction, . . . one need not make out a case of actual invalidity. Vulnerability is the issue at the preliminary injunction stage, while validity is the issue at trial." Amazon.com, 239 F.3d at 1359, 57 USPQ2d at 1758. We think that the testimony of Genentech's experts and our decision in BTG II indicate, at least at this stage of the case, that the '352 patent is vulnerable to BTG's and Teva's validity

challenge.

Dr. Hughes testified that "the '980 patent shows a process wherein the initial gene expression product is met-hGH, and some of the methionine may be removed intracellularly to produce mature hGH." BTGII, 267 F.3d at 1330, 60 USPQ2d at 1433. Dr. Hughes went on to describe the process described in BTG's hGH New Drug Application to the Food and Drug Administration (at issue in the BTGII litigation), testifying that "about 6.2% of the met is removed intracellularly and the other 93.8% of the met stays on, so there is a mixture of met-hGH and met-less hGH in this material…" Id. Professor Manley testified that "the processes described in the '980 patent and in BTG's New Drug Application are 'remarkably similar,' that both initially produce met-hGH, and that intracellular cleavage 'almost certainly' produced the 6.2% mature hGH reported by BTG." Id. Professor Altman agreed with the two other Genentech experts; he stated that "at the time of filing of the '980 patent one of skill in this field would be able to 'use the '980 process and separate out from that mature human growth hormone to treat children.'" BTGII, 267 F.3d at 1330, 60 USPQ2d at 1433-34. The jury verdict in the Genetech-BTG trial indicates that the jury credited the testimony of the Genentech experts.

In BTGII, after the district court granted JMOL in favor of BTG, we sustained the jury's finding that BTG had failed to prove by clear and convincing evidence that the '980 patent was not enabled. The evidence from the Genentech-BTG trial and our decision in BTG II compel us to conclude that Novo has not established that BTG's and Teva's challenge to the validity of the '352 patent lacks substantial merit. See Helifix Ltd. v. Blok-Lok, Ltd., 208 F.3d 1339, 1351, 54 USPQ2d 1299, 1307 (Fed. Cir. 2000) (affirming the denial of a preliminary injunction and vacating a grant of interlocutory summary judgment where there was conflicting evidence in the record which made the grant of summary judgment of invalidity impossible, but which nevertheless was sufficient support for the denial of a preliminary injunction). In the face of the testimony of Genentech's experts and our decision in BTGII, we do not think that the fact that the '980 patent was before the PTO in the prosecution of the '352 patent and during the subsequent interference involving the '352 patent provides an adequate basis for us to affirm the decision of the district court. The presumption of a patent's validity created by 35 U.S.C. § 282 "does not relieve a patentee who moves for a preliminary injunction from carrying the normal burden of demonstrating that it will likely succeed on all disputed liability issues at trial, even when the issue concerns the patent's validity." New England Braiding Co. v. A.W. Chesterton Co., 970 F.2d 878, 882, 23 USPQ2d 1622, 1625 (Fed. Cir. 1992). If the alleged infringer raises a substantial question concerning validity by asserting an invalidity defense that the patentee is unable to prove "lacks substantial merit," then the preliminary injunction should not issue. Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361, 1364, 42 USPQ2d 1001, 1003 (Fed. Cir. 1997). We hold that is the case here.[3]

For the foregoing reasons, the grant of a preliminary injunction in favor of Novo is vacated. The case is remanded to the district court for further proceedings.

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[1] We understand the district court to mean that the 191 amino acid product exhibits the full biological activity of the growth hormone produced by the human pituitary gland.

[2] Because we conclude that determination of this issue disposes of the appeal, we do not consider the additional arguments raised by BTG and Teva.

[3] Since it was not a basis for the district court's decision, we decline to reach the matter of judicial estoppel.