Trials@uspto.gov
571-272-7822

Paper No. 52
Entered: March 5, 2018

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC., APOTEX CORP., APOTEX PHARMACEUTICALS HOLDINGS INC., AND APOTEX HOLDINGS, INC.,
Petitioner,

v.

OSI PHARMACEUTICALS LLC,
Patent Owner.

Case IPR2016-01284
Patent 6,900,221 B1

Before LORA M. GREEN, RAMA G. ELLURU, and ZHENYU YANG, *Administrative Patent Judges.*

GREEN, *Administrative Patent Judge.*

DECISION
Denying Patent Owner's Request for Rehearing
37 C.F.R. § 42.71

I. INTRODUCTION

OSI Pharmaceuticals LLC ("Patent Owner") filed a Request for Rehearing (Paper 51, "Reh'g Req.") of the Final Written Decision (Paper 49, "FWD") in which we concluded that Petitioner had shown by a preponderance of the evidence that claims 44–46 and 53 of U.S. Patent No. 6,900,221 B1 (Ex. 1001, "the '221 patent") are unpatentable under 35 U.S.C. § 103(a) over the combination of Schnur[1] and OSI's 10-K[2] or Gibbs.[3]

We grant Patent Owner's Request for Rehearing to the extent we reconsider the argument made by counsel at the oral hearing as to the level of ordinary skill in the art. For the reasons that follow, however, we deny Patent Owner's request to the extent that we decline to alter our determination that Petitioner has demonstrated by a preponderance of the evidence that claims 44–46 and 53 are unpatentable over the combination of Schnur and OSI's 10-K or Gibbs.

II. STANDARD OF REVIEW

When reconsidering a final written decision the Board reviews the decision to determine whether we misapprehended or overlooked a matter. *See* 37 C.F.R. § 42.71(d). Fed. Cir. 2004); *In re Gartside*, 203 F.3d 1305, 1315–16 (Fed. Cir. 2000). "The burden of showing that a decision should be modified lies with the party challenging the decision." Office Patent Trial

---

[1] Schnur et al., U.S. Patent No. 5,747,498, issued May 5, 1998 (Ex. 1009) ("Schnur").

[2] Annual Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 for the Fiscal Year Ended September 30, 1998, Commission File Number 0-15190, OSI Pharmaceuticals, Inc. (Ex. 1011) ("OSI's 10-K").

[3] J.B. Gibbs, "*Anticancer Drug Targets: Growth Factors and Growth Factor Signaling*," 105 J. CLIN. INV. 9–13 (2000) (Ex. 1010) ("Gibbs").

Practice Guide, 77 Fed. Reg. 48,756, 48,768 (Aug. 14, 2012). In its request for rehearing, the dissatisfied party must, in relevant part, "specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply." 37 C.F.R. § 42.71(d); Office Patent Trial Practice Guide, 77 Fed. Reg. at 48,768. We address Patent Owner's arguments with these principles in mind.

III. ANALYSIS

On rehearing, Patent Owner argues that we improperly relied on the expert opinions of Petitioner's expert, Dr. Giuseppe Giaccone, whose testimony, Patent Owner contends, "was not offered from the perspective of a person having ordinary skill in the art of the challenged claims of [the '221 patent]." Reh'g Req. 1. According to Patent Owner, because Dr. Giaccone did not testify as an ordinary artisan, the "expert testimony on which the Petition is grounded is irrelevant, [we] should reconsider [our] determination that claims 44-46 and 53 of the '221 patent (Ex. 1001) would have been obvious over" the combination of Schnur and OSI's 10-K or Gibbs. *Id.* Specifically, Patent Owner contends that "Petitioners' invalidity theory was . . . tied to Dr. Giaccone's heightened level of skill in the art requiring specialized training in thoracic oncology." *Id.* at 4.

Patent Owner notes that in our Final Written Decision, we declined to adopt Petitioner's definition of the ordinary artisan, averring that we "rejected Petitioners' suggestion that the ordinary artisan 'would have the ability to infer facts from disclosures in the prior art directed to the development of drugs to treat lung cancer, and specifically [non-small cell lung cancer], and would not require every fact to be explicitly laid out in the

prior art.'" *Id.* at 5. Rather, we adopted Patent Owner's definition that the ordinary artisan would be "a medical oncologist who would hold an M.D. degree and would have completed several years of practice in the field of oncology." *Id.* at 5 (citing FWD 8–9).

Patent Owner asserts that even though we rejected Petitioner's definition of the ordinary artisan, we "did not consider whether doing so impacted how [we] should weigh Dr. Giaccone's other testimony." Reh'g Req. 5–6. Specifically, Patent Owner asserts that we erred in stating that both counsel had agreed at oral argument that the level of skill of the ordinary artisan should not affect the outcome of the proceeding. *Id.* at 6. Patent Owner contends that its counsel disputed that point, stating that

> although ***Patent Owner's*** expert had offered alternative opinions "under both definitions" (Tr., 37:10 (Paper 48)), the determination of the level of skill in the art could be outcome dispositive for ***Petitioners*** if Dr. Giaccone's definition of the level of skill in the art was not adopted because his opinions were offered exclusively from the perspective of someone with more than ordinary skill . . . .

Id. (citing Paper 48 ("Tr."), 37:12–18).

Patent Owner contends that our misapprehension of its counsel at oral argument affected our obviousness analysis, warranting rehearing. Reh'g Req. 7. That is, Patent Owner asserts, because Dr. Giaccone testified "from the perspective of someone with more than ordinary skill in the art," Dr. Giaccone more easily concluded that the claims of the '221 patent were rendered obvious over the combination of Schnur and OSI's 10-K or Gibbs. *Id.* at 9.

At trial, Petitioner advocated for the following definition of the level of skill of the ordinary artisan, relying on the testimony of its expert, Dr. Giaccone:

> A person of ordinary skill in the art relevant to the challenged claims of the '221 patent would have a medical degree and at least some specialized training in oncology, and more particularly, specialized training in thoracic oncology. (*See* **Ex. 1002** at ¶ 52.) A person of ordinary skill in the art would also have several years of clinical experience, and a substantive understanding and experience using the medications and therapies effective for treating various lung cancers at the relevant time. (*See* **1002** at ¶ 52.) A person of ordinary skill in the art may have collaborated with others having expertise in pharmaceutical formulation development and pharmaceutical drug development. (**Ex. 1002** at ¶ 51.)

Paper 3 ("Pet.") 13.

Patent Owner, however, relying on its expert, Dr. Bunn, argued that that the ordinary artisan "would be a medical oncologist who would hold an M.D. degree and would have completed several years of practice in the field of oncology." Paper 20 ("PO Resp.") 26 (citing Ex. 2021 ¶¶ 22–23).

In declining to adopt Petitioner's definition of skill of the ordinary artisan, we noted that the claims encompassed cancers other than non-small cell lung cancer, and, thus, found that "the ordinary artisan would be a medical oncologist who would hold an M.D. degree and would have completed several years of practice in the field of oncology." FWD 9. We did not just rely on Dr. Bunn's testimony as to the level of skill on the ordinary artisan, however, but noted that "the level of ordinary skill in the art in this proceeding is reflected by the prior art of record." *Id.* (citing *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001); *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995)).

In defining the level of ordinary skill, we also stated:

> [D]uring oral hearing, counsel for both parties opined that the outcome of the obviousness analysis would be the same under either parties' definition of the ordinary artisan. Tr. 22:3–8, 37:9–11. Thus, our analysis would be the same under either Petitioner's or Patent Owner's definition of the ordinary artisan.

FWD 9.

We acknowledge that during oral hearing, as to the level of ordinary skill, counsel for Patent Owner argued:

> In terms of the definition of a person of skill, since we touched on that, our expert used the same definition that had been applied previously by a District Court. We disagree that one would narrow the definition for each claim. The claims themselves address multiple cancers. So we don't believe the higher requirement of specialty in thoracic oncology is necessary.
>
> But even so, our expert, Dr. Bunn, has that expertise and he's opined under both definitions. So from our standpoint, the outcome should be the same, whichever definition is applied. But we'll note that their expert, Dr. Giaccone, only applied his definition, which is a higher standard. He did not offer an opinion under the more general definition that a court has previously adopted and that is consistent with the scope of the claim. So this, again, is another deficiency with their petition that we think could be dispositive if Dr. Giaccone's opinions were rejected as not applying the right standard.

Tr. 37:3–18.

We disagree with Patent Owner, however, that there is such a substantive difference between its definition of the ordinary artisan and Petitioner's that would cause us to make any different findings or come to any different conclusions in the case. Thus, to the extent we may have misapprehended the argument of Patent Owner's counsel at the oral hearing, we determine any such misunderstanding did not impact our fact finding or

analysis. And as noted above, we did not consider Dr. Giaccone's testimony in a vacuum, but in the context of the level of ordinary skill as evidenced by the prior art of record, as well as the other evidence made of record by the parties in this proceeding. In that regard, we note that Patent Owner in its Request for Rehearing does not point us to any argument it made in its papers that the definition of the ordinary skill is determinative of the outcome of any of the issues in this case.

Patent Owner contends also that our Final Written Decision "repeatedly referred to, cited, and credited the irrelevant testimony of Dr. Giaccone," and lists several places in our Final Written Decision where we relied on Dr. Giaccone testimony, as well as our reasons for that reliance. Reh'g Req. 8–9. Importantly, however, as discussed above, Patent Owner does explain how the difference between Petitioner's definition of the ordinary artisan and its definition would modify our fact-finding and analysis. For that reason alone, we decline to discount Dr. Giaccone's testimony or change our determination that the combination of Schnur and OSI's 10-K or Gibbs renders the challenged claims obvious. In the interest of completeness, however, we address each of those portions of the Final Written Decision identified by Patent Owner below.

> *[I]nterpret and evaluate the Gibbs reference and the testimony of Dr. Gibbs (FWD at 37-39 (Paper 49) (citing and quoting Giaccone Dep., 115:12-20 (Ex. 2020) ("We credit the testimony of Dr. Giaccone, who testified that the statement in Gibbs 'is a pretty strong and precise statement saying, there is activity in non-small cell lung cancer patients.'"))*

We acknowledge that we relied on the testimony of Dr. Giaccone relating to the Gibbs reference. *See* FWD 37–40. Specifically, in our Final Written Decision, in response to Patent Owner's argument (PO Resp. 53)

that the ordinary artisan would understand that when Gibbs referred to an "acceptable therapeutic index," the reference was only referring to ZD-1839, and not erlotinib (i.e. CP-358,774), we acknowledged that Dr. Gibbs, the author of the Gibbs reference, declared:

> Based on references 12 and 13, the abstracts from the 1999 ASCO and AACR Conferences, and my own personal recollection, my research at the time of my article did not identify any information suggesting that CP-358,774 exhibited anti-tumor activity in NSCLC. I was (and still am) not aware of any published abstracts or articles describing the clinical or preclinical response of a NSCLC tumor to CP-358,774 that were available as of the time my article was published, and I reviewed no such abstracts or articles in drafting my article.

FWD 38–39 (quoting Ex. 2022 ¶ 14).

In finding that the above testimony of Dr. Gibbs was entitled to little weight in determining whether the Gibbs reference was referring to CP-358,774 when referring to "good anti-cancer activity" and "an acceptable therapeutic index," we cited the Gibbs reference itself, which explicitly discloses:

> The EGF receptor is also the target for the development of inhibitors of the intracellular tyrosine kinase domain. ZD-1839 and *CP-358,774*, competitive inhibitors of ATP binding to the receptor's active site, *are currently in clinical trials* (12, 13). Their mechanism of action has led to some concern about safety, given the variety and physiological significance of protein kinases and other enzymes that bind ATP. *However, these compounds appear to have good anti-cancer activity in preclinical models, with an acceptable therapeutic index, particularly in patients with non-small cell lung cancer.*

Id. at 39 (quoting Ex. 1010, 10). That is, Gibbs refers to two compounds, ZD-1839 and CP-358,774, and refers to compounds in the plural in stating that the compound*s* have anticancer activity. *See id.* Thus, we found that

"the clear inference [of the Gibbs reference] is that erlotinib has anti-cancer activity against non-small cell lung cancer." *Id.*

In that regard, we credited the testimony of Dr. Giaccone, noting that Dr. Giaccone

> testified that the statement in Gibbs "is a pretty strong and precise statement saying, there is activity in non-small cell lung cancer patients." Ex. 2020, 115:12–20. In addition, Dr. Giaccone testified further that statement by Dr. Gibbs would have been based on the information he had at the time, and that as Dr. Gibbs was a reputable pharmacologist, and as the statement was made in "a peer-reviewed journal of high impact," he would have trusted that Dr. Gibbs "was saying something very important." Ex. 2020, 115:12–20.

Id.

The testimony of Dr. Giaccone, therefore, was consistent with the express statements made in the Gibbs reference, in contrast to the testimony of Dr. Gibbs, who testified that he was an experienced editor, and that he never attempted to correct or retract that statement made in the Gibbs reference. *Id.* at 39–40 (quoting Ex. 1049, 29:18–30:16).

We determine, therefore, that any misapprehension of Patent Owner's argument as to the level of skill of the ordinary artisan at the oral hearing does not change our determination that the ordinary artisan would not read the above discussed statements of the Gibbs reference as only applying to ZD-1839.

> *[S]uggest that erlotinib was a preferred compound and that Gibbs or OSI 10-K would have pointed to the use of erlotinib, from the compounds of Schnur, for the treatment of NSCLC (FWD at 16-18 (Paper 49) (citing Giaccone Decl. ¶¶ 93, 102-107 (Ex. 1002)))*

The portion of our Final Written Decision to which Patent Owner is referring is an overview of Petitioner's challenge on which we instituted trial, and not our analysis of that challenge. In presenting that overview, we merely noted the evidence that Petitioner relied on in support of its challenge, which evidence included the Declaration of Dr. Giaccone.

As we note above, however, Patent Owner's Request for Rehearing does not point out how Dr. Giaccone's statement of the level of skill in the art impacts our fact-finding and the analysis of the challenge. In addition, as also noted above, we relied on additional evidence as the level of ordinary skill, that is, the prior art of record as well as other evidence made of record by the parties. Finally, we note that we do not discern such a difference as the level of skill in the art defined by Petitioner, which we declined to adopt, and that as defined by Patent Owner, that it would change our fact-finding and analysis of the challenge.

> *[S]uggest that individuals working at pharmaceutical companies would have reviewed documents similar to the OSI 10-K (FWD at 20-21 (Paper 49) (citing Giaccone Dep., 75:18-76:16, 78:9-80:5 (Ex. 2020)))*

We acknowledge that we relied on the testimony of Dr. Giaccone in finding that "an ordinary artisan would have looked to OSI's 10-K to determine what drugs and treatments pharmaceutical companies were working on at the time of invention." FWD 21. Specifically, we noted, as argued by Petitioner (Paper 33 ("Reply") 10), "Dr. Giaccone testified that his peers working at pharmaceutical companies routinely reviewed documents similar to OSI's 10-K to learn of the development status of potentially competing products, and Dr. Giaccone even gave an example of [an ordinary artisan], who at the relevant time would likely have reviewed

OSI's 10-K." FWD 20–21 (citing Ex. 2020, 75:18–76:16, 78:9–80:5). We noted further, however, that the testimony of Dr. Giaccone was corroborated by the testimony of Patent Owner's fact witness, Dr. Gibbs. Dr. Gibbs, "who at the time of the Gibbs reference relied upon by Petitioner, worked as a senior director of cancer research at Merck Research Laboratories," testified "'competitor data could be made available,' and that is something he would review as 'it related to [his] project.'" *Id.* at 21 (citing Ex. 1049, 19:3–12, 20:19–21:1).

Moreover, we note that Patent Owner also relied on the testimony of Dr. Giaccone in arguing that the ordinary artisan would not have looked to OSI's 10-K. *See* P.O. Resp. 33. In particular, Patent Owner contended that "Petitioner's expert, Dr. Giaccone, admitted that before this proceeding, he had never relied on or heard of a 10-K, testifying that it is not a scientific publication, and that it does not contain scientific data." FWD 20 (citing Ex. 2020, 77:21–78:8, 81:17–20, 75:15–17, 86:11–14, 81:17–20).

We determine, therefore, that our determination that the ordinary artisan would have looked to OSI's 10-K is consistent with the evidence of record, including the testimony of Dr. Giaccone and Dr. Gibbs.

[I]dentify the structure of erlotinib (FWD at 18-19 (Paper 49) (citing Giaccone Decl. ¶¶ 28-29 (Ex. 1002)))

We cited our Decision on Institution in determining that that the Petition had sufficiently established that CP-358,774 and erlotinib are the same compound. FWD 18. In particular, we noted that the Petition had pointed us to paragraph 28 of Dr. Giaccone's Declaration, and in paragraph

29 of that Declaration, Dr. Giaccone cited Moyer,[4] which specifically defines "CP-358,774" as "[6,7-Bis(2-methoxy-ethoxy)-quinazolin-4-yl]-(3-ethynylphenyl) amine." *Id.* at 19 (citing Decision on Institution 16). We also cited *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F. 3d 1359, 1365 (Fed. Cir. 2015) for the proposition that "[a]rt can legitimately serve to document the knowledge that skilled artisans would bring to bear in reading the prior art identified as producing obviousness." Thus, our reliance on Dr. Giaccone's Declaration to support our finding that CP-358,774 and erlotinib are the same compound is supported by prior art of record, specifically Moyer.

> *[S]uggest that erlotinib did not satisfy a long-felt need for improved treatments for non-small cell lung cancer ("NSCLC") patients (FWD at 42 (Paper 49) (citing Giaccone Reply Decl. ¶¶ 8-10 (Ex. 1053)))*

In responding to Patent Owner's argument that long-felt need supported the patentability of the challenged claims, we acknowledged that Petitioner cited paragraphs 8 to 10 of Dr. Giaccone's Reply Declaration (Ex. 1053) in support of its contention that "erlotinib did not satisfy a long-felt need as it does not treat nearly 90% of patients with non-small cell lung cancer." FWD 42 (citing Reply 19).

In finding that Patent Owner's evidence of long-felt need was weak, however, we noted that "[a]ll types of objective evidence of nonobviousness must be shown to have a nexus to the claimed invention." *Id.* at 42–43 (citing *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (nexus

[4] Moyer et al., *Induction of Apoptosis and Cell Cycle Arrest by CP-358,774, an Inhibitor of Epidermal Growth Factor Receptor Tyrosine Kinase*. 57 CANCER RESEARCH 4838–4848 (1997) (Ex. 1016) ("Moyer").

generally); *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996) (commercial success); *Rambus Inc. v. Rea*, 731 F.3d 1248, 1256 (Fed. Cir. 2013) (long-felt need)). In particular, we stated that the challenged claims were not limited to the treatment of patients with non-small cell lung cancer, but included treatment of mammals, and that the challenged claims did not require a clinical effect. *Id.* at 43. In addition, we noted that Patent Owner acknowledged in its Response that "the FDA required it to change its label as it is only effective in treating approximately 10% of patients with non-small cell lung cancer." *Id.*

Therefore, our finding that the evidence of long-felt need is weak relied primarily on a lack of nexus. *Id.* at 42. To the extent we relied on the testimony of Dr. Giaccone that erlotinib was only approved for treatment of subset of non-small cell lung cancer, that testimony is supported by Patent Owner's admission that "Tarceva is currently approved for the treatment of a subset of NSCLC patients," as well as the evidence that Patent Owner relied upon to support that statement. PO Response 12 (citing Ex. 2030, 1; Ex. 2021 ¶¶ 41, 102–107; Ex. 2023 ¶ 7).

We determine, therefore, that any misapprehension of Patent Owner's argument as to the level of skill of the ordinary artisan at the oral hearing does not change our determination that Patent Owner's evidence of long-felt need is weak.

> *[D]iminish OSI's evidence of the failure of others in developing treatments for NSCLC (FWD at 44 (Paper 49) (citing Giaccone Reply Decl. ¶ 11 (Ex. 1053)))*

In our Final Written Decision, we merely noted that Petitioner relied on paragraph 11 of Dr. Giaccone's Reply Declaration (Ex. 1053) in addressing Patent Owner's argument that the failure of others supported the

patentability of the claims. FWD 44 (quoting Reply 20). Rather, in our analysis, similarly to long-felt need, we noted that "the claims do not require treatment of humans, much less regulatory approval, Patent Owner has failed to establish that the long felt need for FDA approved drugs to treat non-small cell lung cancer has the required nexus to the challenged claims." *Id.* at 44–45.

We determine, therefore, that any misapprehension of Patent Owner's argument as to the level of skill of the ordinary artisan at the oral hearing does not change our determination that Patent Owner's evidence as to the failure of others is weak.

> *[S]uggest that Tarceva's commercial success is not probative (FWD at 47-48 (Paper 49) (citing Giaccone Reply Decl. ¶ 10 (Ex. 1053)))*

In our Final Written Decision, we noted that Petitioner was arguing

> that the sales of Tarceva "were not driven by its actual treatment of cancer, but instead an overly broad approval by FDA that was subsequently revoked." *Id.* That is, Petitioner argues, "on October 18, 2016[,] FDA eliminated the original label and limited the patient population to those who tested positive for epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations, which only accounts for about 10% of the NSCLC patient population. " *Id.* at 23 (citing Ex. 1048, 23:9–26:6, 99:22–101:13; Ex. 1053 ¶ 10; Ex. 1051, 3–4).

FWD 47–48. Dr. Giaccone's Reply Declaration (Exhibit 1053) was only cited as evidence on which Petitioner was relying to support its argument that FDA limited the patient population that could be treated using Tarceva. In our analysis as to commercial success, however, we did not rely on the fact that the FDA had had limited the patient population in declining to find that the purported commercial success supported the patentability of the

claims, rather, we relied on the presence of a blocking patent to Tarceva. *Id.* at 49.

Specifically, in determining that the purported commercial success did not support the patentability of the claims, we noted that "erlotinib was previously known and patented." *Id.* (citing Exhibit 1009 (Schnur)). That is, we were persuaded by Petitioner's argument that "the blocking patent would have deterred others from exploring the commercial potential of Tarceva, and thus, that blocking patent to Tarceva limits the applicability of other evidence of commercial success." *Id.*

We determine, therefore, that any misapprehension of Patent Owner's argument as to the level of skill of the ordinary artisan at the oral hearing does not change our determination that that Patent Owner's evidence of the purported commercial success of Tarceva is also weak.

IV. ORDER

Accordingly, it is hereby:

ORDERED that Patent Owner's Request for Rehearing is *denied*.

For PETITIONER:

Blake Coblentz
Aaron Lukas
COZEN O'CONNOR PC
Wcoblentz@cozen.com
ALukas@cozen.com

For PATENT OWNER:

Emily Whelan
Jonathan Roses
Kevin Yurkerwich
WILMER CUTLER PICKERING HALE AND DORR LLP
emily.whelan@wilmerhale.com
jonathan.roses@wilmerhale.com
kevin.yurkerwich@wilmerhale.com