Trials@uspto.gov
Tel: 571-272-7822

Paper 22
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

GILEAD SCIENCES, INC.,
Patent Owner.

Case IPR2014-00887
Patent 5,977,089

Before TONI R. SCHEINER, FRANCISCO C. PRATS, and CHRISTOPHER L. CRUMBLEY, *Administrative Patent Judges.*

PRATS, *Administrative Patent Judge*.

DECISION
Denying Petitioner's Request for Rehearing
of Decision Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.71

I. INTRODUCTION

Mylan Pharmaceuticals, Inc. ("Petitioner") filed a Request for Rehearing (Paper 21, "Req. Reh'g") of our Decision (Paper 16, "Dec.") denying review of claims 1–3 of U.S. Patent No. 5,977,089 (Ex. 1006, "the '089 patent"), as to all grounds advanced in the corrected Petition (Paper 5,

"Pet."). Petitioner requests rehearing by an expanded panel. Req. Reh'g 1–2. For the reasons that follow, we deny Petitioner's requests for rehearing and panel expansion.

II. STANDARD OF REVIEW

When rehearing a decision on a petition to institute an *inter partes* review, the Board "will review the decision for an abuse of discretion." 37 C.F.R. § 42.71(c). "An abuse of discretion occurs where the decision is based on an erroneous interpretation of the law, on factual findings that are not supported by substantial evidence, or represents an unreasonable judgment in weighing relevant factors." *Lacavera v. Dudas*, 441 F.3d 1380, 1383 (Fed. Cir. 2006) (citing *Star Fruits S.N.C. v. United States*, 393 F.3d 1277, 1281 (Fed. Cir. 2005)).

The party requesting rehearing has the burden of showing the decision should be modified, and "[t]he request must 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).

III. ANALYSIS

A. Subject Matter Allegedly Misapprehended or Overlooked

Claims 1–3 of the '089 patent, the claims under challenge, read as follows:

> 1. (R)-bis(POC)PMPA.
>
> 2. A composition comprising (R)-bis(POC)PMPA and a pharmaceutically acceptable carrier.

> 3. A method comprising orally administering to a patient infected with virus or at risk to viral infection a therapeutically effective amount of (R)-bis(POC)PMPA.

Ex. 1006, 60:55–60. In construing the challenged claims, we noted in our Decision that the term "POC" refers to the isopropoxycarbonyloxymethyl substituents attached to the phosphonyl residue of PMPA, and that "bis(POC)" refers to the fact that two isopropoxycarbonyloxymethyl moieties are attached to that phosphonyl group. Dec. 7.

In its Petition, Petitioner contended that the compound recited in each of the challenged claims, (R)-bis(POC)PMPA, is a prodrug composed of the known anti-HIV drug, tenofovir (also known as "PMPA"),[1] described in Tsai[2] and Srinivas,[3] conjugated to a known prodrug moiety, described in Cheng[4] and Kubo.[5] *See* Pet. 15–16, 18–28, 31–33, 34–36, 38–39. Petitioner contended that, based on the teachings in those references and the knowledge of persons of ordinary skill in the art, it would have been obvious to use the prodrug moieties described in Cheng and Kubo to create the claimed prodrug of tenofovir/PMPA. *See id.* at 28–31, 32–34, 39–40.

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[1] "PMPA" refers to 9-[(R)-2-(phosphonomethoxy)propyl]adenine.

[2] Che-Chung Tsai et al., *Prevention of SIV Infection in Macaques by (R)-9-(2-Phosphonylmethoxypropyl)adenine*, 270 SCIENCE 1197–99 (1995) (Ex. 1036).

[3] Ranga V. Srinivas et al., *Metabolism and In Vitro Antiretroviral Activities of Bis(Pivaloyloxymethyl) Prodrugs of Acyclic Nucleoside Phosphonates*, 37 ANTIMICROBIAL AGENTS & CHEMOTHERAPY 2247–50 (1993) (Ex. 1034).

[4] U.S. Patent No. 5,618,964 (issued April 8, 1997) (Ex. 1041).

[5] Keiji Kubo et al., *Nonpeptide Angiotensin I1 Receptor Antagonists. Synthesis and Biological Activity of Potential Prodrugs of Benzimidazole-7-carboxylic Acids*, 36 J. MED. CHEM. 2343–49 (1993) (Ex. 1043).

Petitioner contended that Balzarini[6] disclosed that the (R) enantiomer of PMPA had a much higher in vitro anti-HIV activity than the (S) enantiomer, and that an ordinary artisan, therefore, would have developed the (R) form of PMPA in favor of the (S) form. *Id.* at 40–41.

In the Request for Rehearing, Petitioner contends that, in declining to institute review, we "misapprehended the relevant law governing a proper obviousness inquiry," and, contrary to *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 415 (2007), erroneously "adopted a rigid approach, while misapprehending the predictability of the art and the basis for the expert testimony." Req. Reh'g 3. Petitioner contends that, to demonstrate obviousness under *KSR*, it only needed to identify a finite number of identified predictable solutions leading to an anticipated success in solving a problem in the prior art. *Id.* at 4. Petitioner contends that, in failing to conclude that its Petition made a showing of obviousness, our Decision "effectively cast aside *KSR* and the approach embraced by the Supreme Court for conducting a proper obviousness inquiry." *Id.*

Petitioner does not persuade us that we misapprehended or overlooked the relevant law governing a proper obviousness inquiry. Indeed, we expressly noted *KSR*'s emphasis on "an expansive and flexible approach" to the obviousness analysis. Dec. 9 (citing *KSR*, 550 U.S. at 415). We also expressly noted the Supreme Court's reaffirmation, nonetheless, of the importance of determining "whether there was an apparent reason to

[6] J. Balzarini et al., *Differential Antiherpesvirus and Antiretrovirus Effects of the (S) and (R) Enantiomers of Acyclic Nucleoside Phosphonates: Potent and Selective In Vitro and In Vivo Antiretrovirus Activities of (R)-9-(2-Phosphonomethoxypropyl)-2,6-Diaminopurine*, 37 ANTIMICROBIAL AGENTS & CHEMOTHERAPY 332–38 (1993) (Ex. 1044).

combine the known elements *in the fashion claimed* by the patent at issue." *Id.* (citing *KSR*, 550 U.S. at 418 (emphasis added)).

Our Decision further noted the post-*KSR* analysis regarding the obviousness of chemical compounds set out by our reviewing court:

> Applying *KSR* to the question of obviousness of a chemical compound based on structural similarity, the Court of Appeals for the Federal Circuit stated that "it remains necessary to identify some reason that would have led a chemist to modify a known compound *in a particular manner* to establish prima facie obviousness of a new claimed compound." *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007) (emphasis added). Thus, consistent with the principles enunciated in *KSR*, establishing that a chemical compound would have been obvious requires "a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention." *Id.* at 1356 (internal quotations omitted).

Id. at 9–10; *see also Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1292 (Fed. Cir. 2012) (accord).

Petitioner does not explain convincingly how applying the inquiry regarding the obviousness of chemical compounds mandated by the Court of Appeals for the Federal Circuit demonstrates that we misapprehended or overlooked law relevant to the obviousness challenges presented in the Petition. Nor does Petitioner explain convincingly how we misapprehended or overlooked how the flexible approach emphasized in *KSR* is inconsistent with the requirement for a showing of how or why an ordinary artisan would have been prompted to modify tenofovir/PMPA with the specific isopropoxycarbonyloxymethyl substituents required by the challenged claims.

Petitioner contends that our Decision "misapplies the law of analogous art" in holding that Cheng "was not shown to be relevant to the proposed modification because Cheng teaches modifying a different molecule." Req. Reh'g 5 (citing Dec. 11). Petitioner contends that our Decision makes the same error in its treatment of Srinivas and Kubo. *Id.* at 6 (citing Dec. 12–13).

Petitioner does not direct us, however, to any specific discussion in our Decision stating that Cheng, Kubo, and Srinivas were either irrelevant or non-analogous art. Nor does Petitioner direct us to the specific teachings in those references we misapprehended or overlooked.

Rather, in evaluating Cheng, we noted that the reference described derivatized drug molecules that differed significantly from the proposed lead compound, tenofovir/PMPA, as to structure and therapeutic activity. Dec. 11. We noted also that Petitioner had not directed us to a specific teaching in any cited reference suggesting that Cheng's strategy would have been viewed as generically applicable for improving the biovailability of any drug having a phosphonic acid moiety, regardless of the drug's therapeutic activity or chemical structure. *Id.* at 11–12. Perhaps most importantly, we noted also that, although Petitioner had directed us to the abstract and Examples 1–3 of Cheng as evidence that the particular substituent required by the challenged claims was known in the art, none of Cheng's examples used that substituent, and the generic formula in Cheng's abstract encompassed numerous substituents having structures varying significantly from the claim-recited substituent. *Id.* at 12. Accordingly, we found that Petitioner had not explained adequately why an ordinary artisan would have been prompted to select the particular isopropoxycarbonyloxymethyl

substituent required by the challenged claims from among the many prodrug moieties described in Cheng. *Id.*

In evaluating Srinivas, we noted the reference's disclosure that derivatizing PMPA with "bis(pom)" esters, a substituent different from that required by the challenged claims, resulted in prodrugs with improved antiviral activity. *Id.* at 12–13. In evaluating Kubo, we noted the reference's selection of a cyclohexyloxy substituent, also a substituent different from that required by the challenged claims, in the preparation of a prodrug of a nonpeptide angiotensin II (AII) receptor antagonist, based on reported adverse effects of using pom-derivatized prodrugs. *Id.* at 13. We found, however, that Petitioner had not adequately explained why those references' teachings of derivatizing drugs with substituents different from those required by the challenged claims would, nonetheless, have prompted an ordinary artisan to derivatize tenofovir/PMPA with the particular isopropoxycarbonyloxymethyl substituent required by the challenged claims. *Id.* at 13–14.

Accordingly, because we evaluated Cheng, Kubo, and Srinivas by comparing their teachings to the specific compound required by each of the challenged claims, Petitioner does not persuade us that we misapplied the law of non-analogous art as to those references.

In its Request for Rehearing, Petitioner avers that Cheng's derivatization strategy would have been applicable to any drug compound having a phosphonic acid moiety. *See* Req. Reh'g 5–8. Petitioner does not direct us, however, to any specific evidence that we may have misapprehended or overlooked, in the prior art or otherwise, supporting that premise. That Petitioner disagrees with our ultimate evaluation of the

teachings in the cited references does not persuade us that we misapprehended or overlooked any evidence Petitioner advanced to show obviousness.

Petitioner also contends that we erred by requiring express motivation in Kubo to modify tenofovir/PMPA with the particular isopropoxycarbonyloxymethyl substituent required by the challenged claims. Req. Reh'g 6–7 (citing Dec. 13). Petitioner contends that "[l]imiting Kubo to its preferred embodiment highlights how unreasonably rigid the Board's approach has been in this case." *Id.* Petitioner contends:

> As the Petition fully explained, Kubo provides the motivation to select the particular isopropoxycarbonyloxymethyl substituent required by the challenged claims, and the expert testimony explains how those in the art had the knowledge and experience to understand and benefit from the collective disclosures of the cited references. The decision overlooks that the universe of prodrugs taught by Kubo is small and focused. Kubo prepares only eight carbonate prodrugs, with isopropoxy as one of the four alkyl moieties in all of the eight. The biological characteristics reported by Kubo for the isopropoxy moiety and the cyclohexyloxy moiety are nearly identical. Kubo teaches the selection of a small number of pro-moieties, among which is the isopropoxy. One of ordinary skill faced with a conceptually identical problem would include the isopropoxy among the test set. Thus, Kubo provides sufficient motivation to substitute the isopropoxy moiety.

Id. at 7.

Petitioner does not identify specifically, however, where in its Petition it presented any of the above-quoted contentions regarding the isopropoxy substituent described in Kubo, such that we may have misapprehended or

overlooked them. Petitioner did identify compound 10k, which includes the isopropoxy substituent, in one claim chart. Pet. 36.

Nonetheless, in contending that Kubo provided motivation to modify tenofovir/PMPA to arrive at the specific compound required by the challenged claims, Petitioner repeatedly pointed to Kubo's selection of a "poc" derivatized compound for clinical development. *Id.* at 13, 28–30, 32, 34, 40. As noted above, and in our Decision, Kubo selected the cyclohexyloxy-derivatized compound for clinical development, rather than the isopropoxy compound. Dec. 13; Ex. 1043, 2346 (Kubo). Accordingly, as explained in our Decision, we are not persuaded that Kubo's teaching of derivatizing drugs different from the tenofovir/PMPA required by the challenged claims, with prodrug substituents different from those recited in the claims, would have prompted an ordinary artisan to derivatize tenofovir/PMPA with the particular isopropoxycarbonyloxymethyl substituent required by the challenged claims. Dec. 13–14.

Petitioner contends that we overlooked Dr. McCutchan's testimony. Req. Reh'g 8. We are not persuaded. That our Decision did not expressly reiterate every contention made by Petitioner and its supporting witnesses does not demonstrate that we overlooked those contentions. Petitioner advanced Dr. McCutchan's testimony to show the state of the art, and to establish that tenofovir/PMPA would have been considered a suitable anti-HIV lead compound for further modification. Pet. 9–10, 16–23. As noted above, however, we determined that Petitioner had not shown a reasonable likelihood of prevailing in its obviousness challenges because it had not explained adequately how or why an ordinary artisan would have been prompted to derivatize tenofovir/PMPA with the particular

isopropoxycarbonyloxymethyl substituent required by the challenged claims. Dec. 13–16. Thus, our Decision in essence assumed that an ordinary artisan would have selected tenofovir/PMPA as a lead compound, as Dr. McCutchan testified, but found, for other reasons, that Petitioner had not shown a reasonable likelihood of prevailing in showing the obviousness of the challenged claims.

Petitioner contends that we reordered its presentation of the prior art, and considered the references individually, rather than in combination. Req. Reh'g 8. Petitioner then reiterates the contentions it made in its Petition. *Id.* at 9–10.

Petitioner's reordering argument fails to direct us, with any particularity, to any specific contention that we misapprehended, overlooked, or failed to address. We considered the obviousness rationales Petitioner presented when making our obviousness determinations. *See* Dec. 7–10, 14–15. That Petitioner disagrees with our ultimate conclusion of obviousness does not demonstrate that we misapprehended or overlooked its arguments. Moreover, as to the presentation order of the references, our reviewing court's predecessor has noted that, generally, it is "of no significance, but merely a matter of exposition, that the [unpatentability assertion] is stated to be on A in view of B instead of on B in view of A." *In re Bush*, 296 F.2d 491, 496 (CCPA 1961).

In sum, for the reasons discussed, Petitioner does not persuade us that we misapprehended or overlooked any point of fact or law presented in the Petition.

B. Request for Expanded Panel

Petitioner requests expansion of the panel pursuant to the Board's Standard Operating Procedure 1. Req. Reh'g 1 (citing BPAI SOP 1 (Rev. 13) 2009, § III (A)(2)).[7] Petitioner contends that our Decision "represents an extreme departure from the norms of obviousness that have led to an erroneous result in this case and will surely be cited as precedent by future patent owners to circumvent the Supreme Court's decision in *KSR*, thereby leading to further confusion and error in subsequent Board reviews." *Id.* Petitioner, thus, "requests that a member of the panel suggest to the Chief Judge that it would be advantageous to expand the panel due to the broader and potentially far-reaching implications of this case." *Id.* at 2.

As discussed above, Petitioner does not persuade us that we misapprehended or overlooked the proper obviousness analysis required under *KSR* and other controlling case law. Moreover, the version of SOP 1 cited by Petitioner states expressly that "[i]t does not create any legally enforceable rights." BPAI SOP 1, 1 (Rev. 13). Accordingly, we are not persuaded that SOP 1 gives parties to Board proceedings a right to suggest panel expansion, as Petitioner here avers. *See AOL, Inc. v. Coho Licensing LLC*, Case IPR2014-00771, slip op. at 2–3 (PTAB March 24, 2015) (Paper 12) (informative) (sole authority for panel designation and expansion resides with Chief Administrative Patent Judge, delegated from Director). In any event, the panel informed the Chief Judge of Petitioner's request, and the Chief Judge declined to expand the panel.

[7] Revision 14 of SOP 1 issued after Petitioner requested rehearing. http://www.uspto.gov/sites/default/files/documents/SOP1%20-%20Rev.%2014%202015-05-08.pdf.

IV. CONCLUSION

Having considered its Request for Rehearing, Petitioner does not persuade us, for the reasons discussed, that our Decision misapprehended or overlooked any point of law or fact advanced in the Petition, such that the Decision can be considered an abuse of discretion. For the reasons discussed, we also deny Petitioner's request for panel expansion.

V. ORDER

For the reasons given, it is hereby ORDERED that Petitioner's request for panel expansion and Request for Rehearing are *denied*.

For PETITIONER:

Peter R. Munson, Esq.
Lorelei P. Westin, Ph.D., Esq.
Matthew Argenti, Esq.
WILSON SONSINI GOODRICH & ROSATI PC
pmunson@wsgr.com
lwestin@wsgr.com
margenti@wsgr.com

For PATENT OWNERS:

Gary Frischling, Esq.
Keith Orso, Esq.
David McPhie, Esq.
IRELL & MANELLA LLP
gfrischling@irell.com
korso@irell.com
dmcphie@irell.com