UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INCYTE CORPORATION,
PETITIONER
v.
CONCERT PHARMACEUTICALS, INC.,
PATENT OWNER

PGR2021-00006
PATENT NO. 10,561,659

PETITIONER'S REQUEST FOR REHEARING UNDER 37 C.F.R. § 42.71

Contents

TABLE OF AUTHORITIES

Page(s)

Federal Cases

Federal Statutes

Regulations

Petitioner Incyte Corporation ("Petitioner") respectfully requests that the Patent Trial and Appeal Board ("Board") reconsider its Final Written Decision (Paper 68, "FWD") finding claims 1-7 and 9-21 of Concert Pharmaceuticals' ("Patent Owner") U.S. Patent No. 10,561,659 ("'659 patent") not unpatentable.

I. Legal Standard

A request for rehearing "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, a reply, or a sur-reply." 37 C.F.R. § 42.71(d). The Board will review the decision for an abuse of discretion "based on an erroneous interpretation of law, if a factual finding is not supported by substantial evidence, or if the decision represents an unreasonable judgment in weighing relevant factors." *Palo Alto Networks, Inc. v. Juniper Networks, Inc.*, IPR2013-00369, Paper 39, at 2-3 (PTAB Feb. 14, 2014); 37 C.F.R. § 42.71(c).

II. The Board's obviousness analysis is based on an erroneous interpretation of law and not supported by substantial evidence

Led to error by Patent Owner, the Board improperly required Petitioner to establish motivation to (1) "*select* Compound (I)"[1] from the Silverman Formula A compounds (FWD, 59) and (2) "*select*[] the disclosed compound with deuteration at *only* the 2- and 3-Y" positions over Silverman's Compound 127 (*id*. at 55, 58). The

[1] All emphasis added unless otherwise noted.

Board's finding that an "artisan would have found it obvious to use compounds of Formula A from Silverman to treat AA" (FWD, 50) was dispositive as "motivat[ion] to pursue [Compound (I)] as one of several potential treatment options" is sufficient as a matter of law. *Novartis Pharm. Corp. v. West-Ward Pharm. Int'l Ltd.*, 923 F.3d 1051, 1059 (Fed. Cir. 2019) ("*Novartis*") (quotations omitted); Paper 1 ("Pet.") 23-24, 35. The Board further overlooked and misapprehended argument and evidence that a POSA would have selected Compound (I) based on deuteration at ruxolitinib's metabolic hot spots.

A. The Board misapprehended the standard for motivation for methods of using a known compound

The Board applied an erroneous legal test for motivation to use a known compound. *See e.g.*, FWD, 58-59. Obviousness thereof requires only that "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention" and *does* "*not* require lead compound analysis." *Novartis* at 1059-60 (holding "district court erred in applying" the "heightened standard" of a lead compound analysis).

Unlike lead compound analysis, *Novartis* clearly states that motivation for using a known compound does *not* require petitioner to "prove that a person of ordinary skill would have selected [the claimed compound] over other prior art treatment methods." *Id.* (explaining the patent "does not claim the everolimus compound itself, but rather methods of using the compound"). Furthermore, it is

well settled that "'case law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation.'" *Novartis* at 1059 (quoting *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004)). Thus, logically, the prior art's disclosure of "a multitude of effective combinations does not render any particular formulation less obvious." *Celltrion, Inc. v. Genentech, Inc.*, IPR2017-01121, Paper 90, at 25 (PTAB Oct. 3, 2018), *aff'd*, *Genentech, Inc. v. Iancu*, 809 F. App'x 781, 783 (Fed. Cir. 2020) (finding method of treating malignant progressing tumor or cancer obvious) (quoting *Merck & Co., Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989)); *see also Ex Parte Alain H. Rook*, APPEAL 2015-004819, 2017 WL 2880141, at *4-*6 (PTAB June 16, 2017) (citing *Merck*, F.2d at 807 and affirming obviousness rejection of method of treating lymphoma over disclosure of claimed compound as one of "270 exemplified compounds" in a prior-art patent).

Ex Parte William L. Pridgen is illustrative. APPEAL 2018-002182, 2019 WL 7169728 (PTAB Nov. 25, 2019). There, the claims covered methods of treating fibromyalgia with specific doses of famciclovir and meloxicam. *Id*. at *1. One prior art reference (Payne) "disclose[ed] that fibromyalgia is caused by cytomegalovirus" while the other (Maziasz) disclosed "120 'suitable combinations'" of compounds, including the claimed combination, for treating cytomegalovirus. *Id*. at *3-*4. The Board found that "[i]t would have been obvious to *select any one of the combinations*

of compounds disclosed" and explained that "even if some of Mazaisz's compositions were better at treating [cytomegalovirus] than others… that does not render the choice of any one of the compositions non-obvious." *Id*. at *4-5 (citing *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012)).

First, contrary to this established Federal Circuit precedent and the PTAB's application thereof, Patent Owner argued that "nothing in Silverman itself [] would impel a POSA *to select Compound 111* from among all of the compounds disclosed" (Paper 37 ("POR"), 45) and "[n]othing in Silverman points to Compound 111 as a logical choice for further development" (*id*., at 47). Patent Owner's arguments were expressly premised on "select[ing]" a lead compound as the threshold for obviousness. *Id*. at 45 (quoting *UCB, Inc. v. Accord Healthcare, Inc.*, 890 F.3d 1313, 1328-29 (Fed. Cir. 2018)) (addressing lead compound analysis)); *id*. at 47 (citing *Altana Pharma AG v. Teva Pharms USA, Inc.*, 566 F.3d 999, 1007-08 (Fed. Cir. 2009) (same)).

Relying on Patent Owner's mischaracterization of the legal standard, the Board erred by requiring Petitioner "to show by a preponderance of the evidence that a skilled artisan would have been motivated *to select Compound (I)* for use *from among the genus* of compounds falling within Formula A." FWD, 59. Under *Novartis*, ***the question is not*** "would you select a particular compound from a genus of 60 plus compounds," as Patent Owner asserted (FWD, 57 (quoting Tr., 50:2-19).

The question is "whether a person of ordinary skill would have been motivated to modify the prior art disclosing use of [ruxolitinib] to treat [alopecia areata] with the prior art disclosing [Compound (I)]." *Novartis* at 1060.

Applying the correct legal test, the question of motivation was "answered affirmatively" (*id.*) when the Board found that:

> [1] the ordinarily skilled artisan would have found deuteration to provide potential metabolic stability vis-à-vis ruxolitinib, and would also have recognized that Formula A of Silverman… included the embodiment identified as Compound (I) of the '659 patent [and]
>
> [2] the artisan would have found it obvious to use compounds of Formula A from Silverman to treat AA based on Silverman's teaching that deuterated Formula A compounds could be used to treat diseases beneficially treated by ruxolitinib and Xing's success in treating AA with ruxolitinib.

FWD, 49-50. That these findings *also* support the use of other deuterated ruxolitinib analogs is of no moment. *Cf.* FWD, 59 ("cannot sufficiently support… why Compound (I) is the only one of the similar compounds it selected") (alteration in original)). "Compound (I) is not novel" (Pet., 1) and thus obviousness here does not require that "person of ordinary skill would have selected [Compound (I)] *over* other prior art compounds" (*Novartis* at 1060).

The Board's rejection of "Petitioner's argument that motivation can be found where the skilled artisan would have been motivated to pursue one compound as one

of several potential treatment options" (FWD, 58-59) repeats the district court's error in *Novartis*. *See Novartis* at 1060. There, the challenged claims covered a method of treating renal cell carcinoma with everolimus, mTOR inhibitor; one prior art reference disclosed temsirolimus (another mTOR inhibitor) was effective against solid tumors and a second disclosed everolimus among a list of structurally and functionally-related mTOR inhibitors. *Novartis* at 1054, 1056-57. Here, the claims cover a method of treating AA with Compound (I); Xing teaches that ruxolitinib is effective to treat AA and Silverman discloses a group of structurally and functionally-related compounds, including Compound (I), "used to treat diseases beneficially treated by ruxolitinib…." FWD, 49-50. Indeed, the case for obviousness here is stronger than *Novartis*, where temsirolimus and everolimus had "different binding affinities" *Novartis* at 1061. Here, by contrast, "replacement of hydrogen by deuterium would not be expected to affect the biochemical potency and selectivity of the drug as compared to the original chemical entity." Pet., 35 (quoting EX1002, 2:15-20); *see* Pet., 35-37; Paper 44 ("Rep."), 25-26.

Second, misdirected by Patent Owner's argument that "the POSA would have selected one of [Compounds 103, 107, and 127]… *rather than* Compound 111[I]" (POR, 45), the Board further erred by requiring Petitioner to show a POSA would have "selected the disclosed compound with deuteration at *only* the 2- and 3-Y positions" (FWD, 58). "The prior art's mere disclosure of more than one alternative

does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed." *In re Fulton*, 391 F.3d at 1201. Even if Compound 127, for example, was preferred—a proposition unsupported by the record—that does not undermine the motivation for using Compound (I). Rep., 20-21 (citing *Novartis* at 1059 and *In re Mouttet*, 686 F.3d at 1333–34). "[O]bviousness does not require that the motivation be the *best* option, only that it be a *suitable* option from which the prior art did not teach away." *Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1328 (Fed. Cir. 2017) (emphasis in original; internal quotation omitted).

Third, to that extent the Board read the Petition as arguing that "Compound (I) is the only one of the compounds" obvious from Silverman (FWD, 59), the Board misapprehended Petitioner's position. The Petition established that a POSA would have been motivated to pursue Compound (I) as "one of several potential treatment options" and "to use [ruxolitinib's] deuterated analog—*particularly* Compound (I)—to achieve at least equally efficacious treatment of AA" as ruxolitinib. Pet., 34-35 (quoting *Novartis* at 1060) (citing EX1007 ¶126 ("a POSA would have been motivated to use *a deuterated analog of ruxolitinib*")); Pet., 38 ("The motivation to use *deuterated ruxolitinib* for this reason was specifically addressed in *Silverman*") (citing EX1007 ¶129 ("motivated *the use of a deuterated analog of ruxolitinib* in place of ruxolitinib")); *see also* Rep., 20-21 (citing EX1120 ¶¶53-54 (explaining

"one would have been *motivated to use any of the compounds* disclosed in *Silverman*" and "*all of the compounds in Silverman* would have been expected to work as ruxolitinib substitutes")). Whether a POSA *also* would have been motivated to use other compounds is a "separate and independent" issue. *Hospira, Inc. v. Genentech, Inc.*, IPR2017-00731, Paper 29, at 13 (PTAB Oct. 26, 2017).

B. The Board overlooked substantial argument and evidence for selecting Compound (I) specifically

Although unnecessary to find obviousness, the Board also overlooked the Petition's argument that "*a POSA would have been motivated* to use Compound (I) in place of ruxolitinib to treat AA by potential improvements in *metabolic properties resulting from deuterium substitution at ruxolitinib's metabolic hot spots*." Pet., 37; *cf*. FWD, 58 ("Petitioner did not argue this as a basis for… motivation in selecting Compound (I), but merely noted that resultant metabolic stability would have been expected") (quoting Pet., 34 n.8)). Patent Owner did not even dispute the principle of substituting deuterium at ruxolitinib's metabolic hotspots. *Compare* Pet., 37, 40, 62 *with* Paper 11, 33-37, 43-44 *and* POR, 43-47 *and* Paper 51 ("Sur-Rep."), 14; *Shopify, Inc. v. DDR Holdings, LLC*, IPR2018-01011, Paper 36, at 3-6 (PTAB Oct. 26 2020) (granting request for rehearing where Board overlooked "unrebutted" evidence).

As argued in the Petition, deuterating at metabolic hotspots was well known in the art and provided motivation to select Compound (I) over the other compounds

in Silverman even in the absence of the 2015 Uttamsingh Declaration. *E.g.*, Pet., 37, 40, 62. Substantial evidence—not addressed in the Decision—supports this conclusion, including:

- Patent Owner's marketing materials which explained the strategy of deuterating at "metabolic 'hotspots'" to produce "more favorable pharmacokinetics" including "improved metabolic stability" (EX1034, 4-5 (Pet., 40));
- Prior art identifying ruxolitinib's metabolic hotspots as the eight positions (*i.e.*, 2- and 3-Y, EX1002, 3:7-12) at which Compound (I) is deuterated (Pet., 40 (citing EX1055, 6, 8); *accord Incyte Corp. v. Concert Pharm.*, *Inc.*, IPR2017-01256, Paper 119, at 8, 23-24, 27 (PTAB Apr. 8, 2019) (EX1176) (finding, based on Concert Backgrounder (EX1034) and Shilling (EX1055), claims to Compound (I) obvious where a POSA would have been motivated to deuterate "ruxolitinib compounds at their metabolic 'hot spots'… to achieve… improved safety, tolerability, and efficacy"); and
- Prior art demonstrating that "[r]eplacing hydrogen with deuterium at metabolically active sites can result in a slower metabolism… [t]his approach has been shown to be effective for a number of pharmacological agents" (Pet., 39-40 (quoting EX1036, 1)); (EX1007 ¶153 n.221 (quoting EX1053, 3)) ("we therefore replaced the hydrogen atoms at [nintedanib's major metabolic pathways] with deuterium").

Regarding Patent Owner's argument that a POSA would have selected Compound 127—which has a ninth deuterium at a position not subject to metabolism (EX1002, 3:7-12; FWD, 56-57)—over Compound (I), the Board did not address Dr. Ortiz De Montellano's admission that deuteration at a non-metabolic hot spot, *i.e.*, Compound 127's additional ninth position, "would probably not be relevant" (Rep., 21 (quoting EX1171, 40:18-41:5). *See also* Pet., 42-43 (citing EX1007 ¶168) ("At positions not subject to metabolism, the default would have been to simply leave the molecule unmodified."); *Genzyme Therapeutic Prod. Ltd. P'ship v. Biomarin Pharm. Inc.*, 825 F.3d 1360, 1366 (Fed. Cir. 2016) (explaining reply evidence "is to be expected in *inter partes* review").

In sum, Petitioner respectfully submits that the Board erred in requiring Petitioner to show a reason to select Compound (I) from Silverman *and* preferentially select it over Compound 127. § II.A. Even if required, the Board overlooked unrebutted evidence that a POSA would have selected Compound (I) based on deuteration at ruxolitinib's metabolic hotspots. § II.B.

III. The Board's application of AIA- 35 U.S.C. § 102(b) is based on an erroneous interpretation of law, improper procedure, and not supported by substantial evidence

The Board, misled by Patent Owner's arguments, misapprehended the legal standards and burdens for Patent Owner to establish a § 102(b) exception for the 2015 Uttamsingh Declaration (EX1045, 390-417). The Board also misapprehended

the law and facts in finding Dr. Uttamsingh to be an inventor based on her alleged "singling [Compound (I)] out for future development" (FWD, 36), which is neither supported by the record nor legally sufficient to establish inventorship. The Board should reverse its findings in the FWD and consider the excluded material.

A. The Board misapplied the framework for 35 U.S.C. 102(b)

Patent Owner bears the burden of production to establish a § 102(b) exception for the 2015 Uttamsingh Declaration. *In re Magnum Oil Tools Int'l, Ltd*., 829 F.3d 1364, 1376 (Fed. Cir. 2016). The Board misapprehended this legal standard by improperly adopting a presumption for correct inventorship from *Acromed Corp. v. Sofamor Danek Group, Inc.*, which was expressly based on "a presumption of validity [under] 35 U.S.C. § 282." 253 F.3d 1371, 1379 (Fed. Cir. 2001); FWD, 34. But presumptions based on § 282 do not apply in PGR proceedings. *Taiwan Semiconductor Mfg. Co., Ltd. v. DSS Tech. Mgt., Inc.*, IPR2014-01030, Paper 28, at 6 (PTAB Nov. 30, 2015); *RF Controls, LLC, v. A-1 Packaging Sols., Inc.*, IPR2014-01536, Paper 10, at 8 (PTAB Mar. 30, 2015). The Board thus erred in "accord[ing] the presumption that Dr. Uttamsingh is a properly named joint inventor…." FWD, 37-38.

Even if a presumption for correct inventorship applied, Petitioner elicited testimony from Dr. Uttamsingh that she did not invent *any* subject matter claimed in the '659 patent. *See* Rep., 8-9. Dr. Uttamsingh testified that she did not conceive of

any of the claimed subject matter, which was described in the provisional application that, as admitted by Dr. Uttamsingh and reflected in the provisional cover sheet, was invented by Dr. Wagner. EX1172, 19:14-25:21, 75:7-11; 37 C.F.R. § 1.41(c); Rep., 8-9; FWD, 31 (finding written description support in an earlier provisional). To the extent a "burden of production" had shifted to Petitioner (FWD, 34), this evidence meets that burden to show that Dr. Uttamsingh is not an inventor. The signed oath and face of the patent (Sur-Rep., 7-8; FWD 35) are not contrary evidence; they are no more than a presumption already overcome by Petitioner's evidence. *See Safco Prods. Co. v. Welcom Prods., Inc.*, 799 F. Supp. 2d 967, 989 (D. Minn. 2011) (presumption, such as listing on patent face, is not evidence in support of a finding); *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1258-59 (Fed. Cir. 2004) ("[T]he presumption [of validity] is one of law, not fact, and does not constitute 'evidence' to be weighed against the challenger's evidence." (citation omitted)). Given that Patent Owner did not produce *evidence* of conception or contribution to the *claimed* subject matter to rebut Petitioner's showing (*infra* § III.B), the Board erred in "finding that Petitioner has not carried its burden to overcome the presumption that Dr. Uttamsingh is a properly named inventor of the '659 patent." FWD, 38.

B. The Board misapplied the law of inventorship as Dr. Uttamsingh did not conceive of or contribute to any claimed subject matter

The Board further erred in concluding that "Dr. Uttamsingh's contribution to the claimed subject matter of the '659 patent included her work in identifying the

metabolic stability of Compound 111/(I) relative to other compounds disclosed in Silverman, thus singling this compound out for future development." FWD, 36. Even if Dr. Uttamsingh did identify Compound (I) for unspecified future testing, that still would not make her an inventor because it is not a contribution to the claimed use of Compound (I) to treat hair loss, as required for inventorship.

First, although the Board's conclusion tracks Patent Owner's argument that Patent Owner "relied on this type of [metabolic] data" in "selecting the deuterated compound for development and determining its dose" (Sur-Rep., 7), ***there is no evidence*** establishing this alleged reliance and Patent Owner's attorney argument "carries no weight." *Sandoz, Inc. v. Abbvie Biotech. Ltd.*, IPR2017-01823, Paper 16, at 15-16 (PTAB Feb. 9, 2018). Dr. Uttamsingh's testimony that the data were developed from a "fairly standard" and "industry-wide" assay (EX1172, 28:16-29:6, 48:17-49:7) also contradicts the Board's finding that Dr. Uttamsingh "helped develop" the assay (FWD, 35). *Compare* EX1045, 406 *with* EX1132, 4 *and* EX1133, 5 (Dr. Uttamsingh using the same assays in declarations supporting alleged patentability of other drugs). Nor is there evidence that *Dr. Uttamsingh* "singl[ed]… out," selected, or emphasized Compound (I) for some further development (FWD, 36); rather, she, at most, supervised measuring properties untethered from any specific use and submitted declarations as a "routine practice." EX1172, 36:18-38:8. EX1132, 2 ("During my tenure at Concert I have supervised the testing of over 250

different deuterated compounds and their undeuterated counterparts in various assays performed with Human Liver Microsomes (HLM). The deuterated compounds that I have been involved in testing in *in vitro* assays were based on over 50 different undeuterated compounds."); EX1133, 2 (same).

Second, even if Dr. Uttamsingh did contribute "work in identifying" unclaimed metabolic stability of Compound (I) (FWD, 36), that is not an inventive contribution to the claimed use of treating hair loss. *See Gen. Elec. Co. v. Wilkins*, 750 F.3d 1324, 1332 (Fed. Cir. 2014) (inventor of universal power supply was not an inventor of claim reciting particular use thereof); *BJ Servs. Co. v. Halliburton Energy Services, Inc.*, 338 F.3d 1368, 1373-74 (Fed. Cir. 2003) (inventor of polymer did not contribute to and was not inventor of specific method of using the polymer). Contrary to the Board's findings, Dr. Uttamsingh twice confirmed that the idea to use Compound (I) to treat hair loss was *not* hers. EX1172, 19:14-22, 21:15-20; Rep., 8-9.

The Board's reasoning is further inconsistent with the record. Any "work in identifying" unclaimed metabolic properties of Compound (I) (FWD, 36) would also require Dr. Uttamsingh be an inventor of the provisional application that claimed substantially the same subject matter. *See* FWD, 23-33. But, per Dr. Uttamsingh's admissions, she is not. EX1172, 19:14-25:21, 75:7-11; Rep., 8-9. Likewise, the provisional application identified Dr. Wagner as the sole inventor. EX1127, 3, 6; 37

C.F.R. § 1.41(c) ("inventorship of a provisional application is the inventor or joint inventors set forth in the cover sheet"). Patent Owner did not produce any evidence that the provisional's inventorship was *incorrect*, whereas Petitioner produced evidence that Dr. Uttamsingh is not an inventor of any claim of the '659 patent. Rep., 8-9.

The Board also misapprehends *Pannu v. Iolab Corp.*, 155 F.3d 1344 (Fed. Cir. 1998). FWD, 36-37. Although *Pannu* states that an inventor need not contribute to "every claim," a joint inventor must nevertheless contribute to what is actually *claimed*. *Pannu*, 155 F.3d at 1351; *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1359 (Fed. Cir. 2004). Dr. Uttamsingh testified that she did not have the idea of using Compound (I) to treat hair loss or any other subject matter claimed. EX1172, 19:14-25:21, 75:7-11; Rep., 8-9. That Dr. Uttamsingh is not a patent attorney or that some admissions referenced corresponding limitations in the provisional is irrelevant to her admission that each claim limitation in the '659 patent was conceived of by Dr. Wagner. Neither the Board nor Patent Owner identified any claim element to which Dr. Uttamsingh contributed.

Because the Board misapprehended the law and facts, it erred in excluding the subject matter in the Uttamsingh 2015 Declaration. The Board should reverse and consider that excluded subject matter.

Date: June 10, 2022

Respectfully submitted,

/Mark J. Feldstein/

Mark J. Feldstein, Reg. No. 46,693
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, LLP

Counsel for Petitioner
Incyte Corporation

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing **Petitioner's Request for Rehearing Under 37 C.F.R. § 42.71** was served electronically via email on June 10, 2022, directed to counsel of record for the Patent Owner at the following:

Marta E. Delsignore
Daniel P. Margolis
GOODWIN PROCTER LLP
The New York Times Building
620 Eighth Avenue
New York, NY 10018-1405
mdelsignore@goodwinprocter.com
dmargolis@goodwinprocter.com

Daryl L. Wiesen
Emily L. Rapalino
Gerard J. Cedrone
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
dwiesen@goodwinlaw.com
erapalino@goodwinlaw.com
gcedrone@goodwinlaw.com
DG-ConcertPGR@goodwinlaw.com

Patent Owner has consented to service by email.

Date: June 10, 2022

By: /William Esper/
William Esper
Case Manager and PTAB Coordinator
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, LLP