NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

ANACOR PHARMACEUTICALS, INC.,
Appellant

v.

FLATWING PHARMACEUTICALS, LLC,
Appellee

2019-2264, 2019-2265, 2019-2266, 2019-2267

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2018-00168, IPR2018-00169, IPR2018-00170, IPR2018-00171, IPR2018-01358, IPR2018-01359, IPR2018-01360, IPR2018-01361.

Decided: August 27, 2020

AARON P. MAURER, Williams & Connolly LLP, Washington, DC, for appellant. Also represented by DAVID I. BERL, ANTHONY SHEH.

PHILIP DALE SEGREST, JR., Husch Blackwell LLP, Chicago, IL, for appellee. Also represented by MARC WEZOWSKI; ERIC RAKESTRAW, St. Louis, MO.

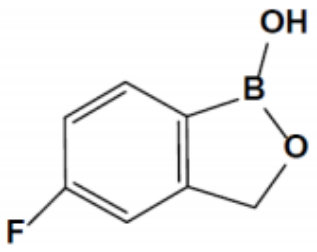
Before LOURIE, O'MALLEY, and CHEN, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Anacor Pharmaceuticals, Inc., ("Anacor") appeals from four final written decisions of the Patent Trial and Appeal Board (the "Board") holding all claims of U.S. Patents 9,549,938 (the "'938 patent"), 9,566,289 (the "'289 patent"), 9,566,290 (the "'290 patent"), and 9,572,823 (the "'823 patent") unpatentable as obvious. *FlatWing Pharm., LLC v. Anacor Pharm., Inc.*, No. IPR2018-00168, 2019 WL 2385219 (June 5, 2019); *FlatWing Pharm., LLC v. Anacor Pharm., Inc.*, No. IPR2018-00169, 2019 WL 2399836 (June 5, 2019); *FlatWing Pharm., LLC v. Anacor Pharm., Inc.*, No. IPR2018-00170, 2019 WL 2396792 (June 5, 2019); *FlatWing Pharm., LLC v. Anacor Pharm., Inc.*, No. IPR2018-00171, 2019 WL 2385222 (June 5, 2019) ("*Decision*"). Because the Board's factual findings are supported by substantial evidence and its conclusion of obviousness is correct, we *affirm*.

BACKGROUND

Anacor markets the compound tavaborole in the form of a topical solution called KERYDIN®, indicated for the treatment of onychomycosis, or fungal infection, of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*. KERYDIN® is administered on the toenail but penetrates through the nail to reach the site of infection on the nail bed. Tavaborole's structural formula is illustrated below:



J.A. 1502. The Food and Drug Administration approved KERYDIN® in 2014.

The four patents at issue share a specification that discloses a wide range of boron-containing compounds that are useful for the treatment of fungal infections. '823 patent Abstract. Example 13 indicates formulations of these compounds at concentrations of 10% w/v (weight/volume). '823 patent col. 186 ll. 20–42. Example 18 reports positive results from a nail penetrating study of tavaborole formulations at a concentration of 10% w/w. *Id.* at col. 189 l. 58–col. 193 l. 5. Example 20 discloses a prophetic study where tavaborole is applied to nail beds at concentrations of 1%, 2.5%, 5%, 7.5%, 10%, and 15% w/v, and inventors draw the conclusion that "[t]he optimal dose-response range for penetration into the human nail was determined to be between 1% and 15%." *Id.* at col. 193 l. 55–col. 194 l. 4. Claim 2 of the '823 patent is representative of all the claims at issue in this appeal, but, as it is dependent upon claim 1, both claims are shown as follows:

> 1. A method of delivering a compound, in a human, from a dorsal layer of a nail plate to a nail bed to treat onychomycosis caused by *Trichophyton rubrum* or *Trichophyton mentagrophytes*, the method comprising:
>
> > contacting the dorsal layer of the nail plate with a pharmaceutical composition comprising a compound that penetrates the nail plate, the compound being [tavaborole] or a pharmaceutically acceptable salt thereof, thereby treating onychomycosis due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*.
>
> 2. The method of claim 1, wherein the pharmaceutical composition is in the form of a topical solution *comprising 5% w/w of [tavaborole]*, and wherein

> the pharmaceutical composition further comprises ethanol and propylene glycol.

'823 patent col. 317 l. 51–col. 318 l. 53 (emphasis added).[1]

Previously, the Board held claims of two related patents—U.S. Patents 7,582,621 (the "'621 patent") and 7,767,657—unpatentable as obvious in two final written decisions. *See Coal. for Affordable Drugs X LLC v. Anacor Pharm., Inc.*, No. IPR2015-01776 (P.T.A.B. Feb. 23, 2017), Paper 70; *Coal. for Affordable Drugs X LLC v. Anacor Pharm., Inc.*, No. IPR2015-01780 (P.T.A.B. Feb. 23, 2017), Paper 70; *Coal. for Affordable Drugs X LLC v. Anacor Pharm., Inc.*, No. IPR2015-01785 (P.T.A.B. Feb. 23, 2017), Paper 70. In relevant part, the Board concluded that the claims were obvious in view of two published patent applications, WO1995/033754 ("Austin") and U.S. Patent App. Pub. 2002/0165121 ("Brehove"). Austin is directed to the use of organoboron compounds (including tavaborole) as fungicides for industrial uses and teaches that tavaborole shows antifungal activity against several fungi. J.A. 3214–15 (Example 64). Brehove discloses topical compositions of organoboron compounds and results from an *in vitro* test showing inhibition of a common fungus, J.A. 3231 (¶¶[0030–33]), and *in vivo* tests showing nail penetration and antifungal activity for compositions of organoboron compounds formulated in petroleum jelly or mineral oil at 10% or 25% concentration, J.A. 3231–32 at ¶¶[0034–38].

Anacor appealed to this court in that case only with respect to claim 6 of the '621 patent, which was directed to a method of treating onychomycosis by administration of a

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[1] The Board held all claims of each patent unpatentable. Anacor appeals here only with respect to claims 3, 5, and 6 of the '938 patent; claims 10 and 12–15 of the '289 patent; claims 2, 5, 6, 8, and 11 of the '290 patent; and claim 2 of the '823 patent. Appellant Br. 4.

"therapeutically effective amount" of a tavaborole composition. This court affirmed. *See Anacor Pharm., Inc. v. Iancu*, 889 F.3d 1372, 1385 (Fed. Cir. 2018). We rejected Anacor's argument that a skilled artisan would not have expected tavaborole to be effective against multiple fungi species. We concluded that substantial evidence supported the Board's finding of a reason to combine Austin and Brehove because the "structural and functional similarities" between tavaborole and Brehove's compounds provided a reason to expect a similar tavaborole composition to be useful for treating onychomycosis. *Id.*

Meanwhile, FlatWing Pharmaceuticals, LLC ("FlatWing"), petitioned for *inter partes* review of the four patents at issue here on the ground of obviousness. The Board issued final written decisions concluding that the challenged claims—which further limit the claimed compositions to those formulated at a concentration of 5% by weight—would have been obvious over a combination of Austin, Brehove, and U.S. Patent 6,224,887 ("Samour"), which discloses topical formulations of other antifungal compounds, such as econazole, at concentrations of 5% by weight. *Decision*, 2019 WL 2385222, at *6. The Board found that Austin, Brehove, and Samour each teach antifungal compositions at concentration ranges that overlap 5%, *id.* at *7, that a skilled artisan would have been able to make the claimed composition of tavaborole using known techniques, and that formulation of tavaborole, even as a boron-containing compound, would not have been unpredictable, *id.* at *11–13. And it rejected Anacor's argument that Samour teaches away from a 5% concentration, as Samour does not "criticize or otherwise discourage the use of 5% w/w of antifungal agent." *Id.* at *9.

Anacor timely appealed from each of the Board's decisions. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

We review the Board's legal determinations *de novo*, *In re Elsner*, 381 F.3d 1125, 1127 (Fed. Cir. 2004), but we review the Board's factual findings underlying those determinations for substantial evidence, *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). A finding is supported by substantial evidence if a reasonable mind might accept the evidence as adequate to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938).

The sole issue presented in this appeal is obviousness. Obviousness is a question of law that "lends itself to several basic factual inquiries," *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966) (citing *Great Atl. & Pac. Tea Co. v. Supermarket Equip. Corp.*, 340 U.S. 147, 155 (1950)), including the scope and content of the prior art, the level of ordinary skill in the art, differences between the prior art and the claimed invention, and any relevant secondary considerations, *id.* at 17–18. The Supreme Court has held that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Instead, there must have been "an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *Id.* at 417–18. Such a reason exists if the claimed invention "simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement." *Id.* (internal quotation marks and citation omitted).

Anacor argues that the Board erred in determining that the claimed composition would have been obvious as the product of routine optimization. It asserts that the mere existence of screening techniques for assessing an antifungal composition's efficacy and nail penetration is insufficient evidence that it would have been obvious to formulate the claimed composition, as organoborons are

quite reactive. Appellant Br. 28–31. Anacor also contends that skilled artisans would have been discouraged from creating a 5%-tavaborole composition because Samour teaches away from a 5%-econazole composition in favor of a 10%-econazole composition.

Flatwing responds that the Board reasonably found that Samour teaches successful nail penetration with a 5% econazole composition, and since tavaborole is a smaller molecule than econazole, a skilled artisan would have expected that a similar tavaborole composition would perform as well or better. Flatwing adds that there is a clear relationship between antifungal concentration and nail penetration, making tavaborole concentration a result-effective variable, and merely selecting a concentration from a known range is obvious. Flatwing also denies Anacor's teaching-away claim.

We agree with Flatwing. As an initial matter, we reject Anacor's teaching-away argument. Samour discloses several small experiments to determine the effect of econazole concentration on nail penetration. J.A. 3279–82 (Examples 4–9). The results indicate that 10%-econazole compositions provide greater nail penetration than the 5%-econazole compositions, but the effect is modest overall and depends on other variables, such as excipients. J.A. 3281–82 (Tables 11–14) (showing 5%-econazole compositions achieving nail penetration between 1.067 and 2.176 μg/mg and 10%-econazole compositions between 1.984 and 2.166 μg/mg). Samour finds "no significant benefit" from increasing the concentration to 20% econazole, J.A. 3281 col. 24 ll. 54–56, concludes that the "especially preferabl[e]" range of concentrations is "from about 5 to 20%," J.A. 3275 col. 12 ll. 25–26, and ultimately claims compositions with concentrations of 1 to 10% econazole, J.A. 3285 col. 32 ll. 26–33.[2]

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[2] While Anacor protests the Board's decision to cite Samour's claims, as that portion of Samour was not

Thus, Samour's teachings barely even suggest a "preference for an alternative" approach, *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009) (citation omitted)—let alone discourage a skilled artisan from pursuing a 5%-antifungal composition, as is required for a reference to teach away, *see, e.g.*, *United States v. Adams*, 383 U.S. 39, 52 (1966). The Board's finding is therefore amply supported by substantial evidence.

The remainder of Anacor's challenge fares no better. As the Board found, the references teach all elements of the claimed invention. *See Decision*, 2019 WL 2385222, at *6–7. Austin teaches that tavaborole is an effective antifungal agent outside the clinical context, J.A. 3214–15, and Brehove and Samour each suggest methods of formulating different antifungal compounds in topical compositions to achieve nail penetration. J.A. 3231–32, 3281–82. Each reference suggests compositions with a range of concentrations overlapping 5%, and Samour discloses several 5%-econazole topical compositions that attained nail penetration. J.A. 3281–82 (Examples 9–10).

Yet Anacor argues that tavaborole would have presented special challenges as an organoboron molecule, and a skilled artisan would not have simply used the formulation techniques in Brehove and Samour to create the claimed 5%-tavaborole composition.

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specifically cited in Flatwing's petition or expert testimony, the Board was entitled to do so because the entirety of Samour was before it as evidence, both parties discussed Samour's claims at the hearing, and Samour's claims are cumulative in view of its multiple experiments showing nail penetration with a 5%-econazole composition. *See In re NuVasive*, 841 F.3d 966, 971 (Fed. Cir. 2016) ("[T]he Board is not limited to citing only portions of the prior art specifically drawn to its attention . . . .").

We find Anacor's arguments unpersuasive. The Board reasonably credited testimony from Flatwing's expert that the claimed composition could have been made according to well-known formulation techniques, and tavaborole's potential reactivity as an organoboron compound would not have been an important consideration. *Decision*, 2019 WL 2385222, at *10 (declining to credit Anacor's expert's testimony because he did not consider the rate of tavaborole hydrolysis or oxidation in a topical composition). And the existence of the Brehove reference describing *in vivo* inhibition of a common fungus with organoboron compositions—formulated in either mineral oil or petroleum jelly—is especially damaging to Anacor's arguments.

As the Board noted, the inventors evidently did not consider formulating organoborons a great challenge, as the specification does not offer any guidance beyond citation of well-known guides to pharmaceutical formulation. *See* '823 patent col. 161 ll. 19–29 ("Those skilled in the art will recognize various synthetic methodologies that may be employed to prepare non-toxic pharmaceutical formulations incorporating the compounds described herein."), col. 186 ll. 40–42 ("The preparation of these formulations is well known in the art and is found in references such as *Remington: The Science and Practice of Pharmacy* . . . ."); *cf. Lincoln Eng'g Co. v. Stewart-Warner Corp.*, 303 U.S. 545, 550 (1938) ("If this were so vital an element in the functioning of the apparatus, it is strange that all mention of it was omitted."). Thus, the Board did not err in determining that creating a tavaborole topical composition would have been obvious.

Furthermore, there is no dispute that a skilled artisan would have appreciated that concentration is a result-effective variable, Reply Br. 2, such that one could optimize nail penetration by routine experimentation within a predictable range of concentrations. *Decision*, 2019 WL 2385222, at *7, *10 (crediting Flatwing's expert's testimony that tavaborole's lower molecular weight would

indicate its suitability for diffusion across the nail at lower concentrations). We conclude, as the Board did, that the selection of 5% as the concentration of a tavaborole composition would have been obvious to a skilled artisan. *See In re Aller*, 220 F.2d 454, 456 (CCPA 1955) ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." (collecting cases)).

CONCLUSION

We have considered Anacor's further arguments but find them unpersuasive. For the foregoing reasons, the decisions of the Board are

AFFIRMED