United States Court of Appeals for the Federal Circuit

IMPAX LABORATORIES INC., ASTRAZENECA AB, ASTRAZENECA UK LIMITED,
Plaintiffs-Appellees

v.

LANNETT HOLDINGS INC., LANNETT COMPANY INC.,
Defendants-Appellants

2017-2020

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-00984-RGA, 1:14-cv-00999-RGA, Judge Richard G. Andrews.

Decided: June 28, 2018

JAMES F. HURST, Kirkland & Ellis LLP, Chicago, IL, argued for plaintiffs-appellees. Also represented by MARCUS EDWARD SERNEL.

JOSEPH F. POSILLICO, Fox Rothschild, LLP, Philadelphia, PA, argued for defendants-appellants. Also represented by FRANK T. CARROLL; MICHAEL W. GLYNN, New York, NY.

Before LOURIE, DYK, and TARANTO, *Circuit Judges.*

LOURIE, *Circuit Judge.*

Lannett Holdings Inc. and Lannett Co. Inc. (together, "Lannett") appeal from the decision of the United States District Court for the District of Delaware concluding, after a bench trial, that claims 4, 11, 12, and 14 of U.S. Patent 6,760,237 ("the '237 patent") and claims 6 and 14–16 of U.S. Patent 7,220,767 ("the '767 patent") were not shown to be invalid, *see Impax Labs., Inc. v. Lannett Holdings Inc.*, 246 F. Supp. 3d 1024 (D. Del. 2017) ("*Opinion*"), entering judgment in favor of Impax Laboratories Inc. ("Impax"), AstraZeneca AB, and AstraZeneca UK Limited (together, "AstraZeneca"), and entering an injunction against Lannett pursuant to 35 U.S.C. § 271(e)(4), *see Impax Labs. Inc. v. Lannett Holdings Inc.*, No. 1:14-cv-00984-RGA (D. Del. Apr. 17, 2017), ECF No. 174; J.A. 1–4. For the reasons that follow, we affirm.

BACKGROUND

Triptans are selective serotonin receptor agonists, developed in the early 1980s. The first triptan to be marketed was sumatriptan under the name Imitrex®, which first became available in the U.S. in an injection form in 1993. In 1995, sumatriptan became available in an oral tablet form and later, in 1997, in an intranasal form as Imitrex® (sumatriptan) Nasal Spray ("NS"). Zolmitriptan is another triptan, which first became available in the U.S. in an oral tablet form in 1999 under the name Zomig®. At that time, there were several other triptans that were either on the market or under development.

AstraZeneca owns and Impax is the exclusive licensee of the '237 and '767 patents,[1] which relate to formulations

[1] At the district court, Lannett alleged lack of standing and ownership issues regarding the '237 and

of zolmitriptan for intranasal administration. The claims at issue in this appeal are directed to pharmaceutical formulations, intranasal administration devices, or aqueous solutions, of zolmitriptan. '237 patent col. 5 l. 4–col. 6 l. 22; '767 patent col. 5 l. 8–col. 6 l. 25.

Claim 4 of the '237 patent depends from claim 2, which in turn, depends from claim 1. Claims 1, 2, and 4 of the '237 patent read as follows:

> 1. A pharmaceutical formulation suitable for intranasal administration which comprises zolmitriptan and a pharmaceutically acceptable carrier wherein the pH of the formulation is in the range 4.5 to 5.5.
>
> 2. A pharmaceutical formulation according to claim 1 wherein the pH of the formulation is 5.
>
> 4. A pharmaceutical formulation according to claim 2 wherein the formulation is buffered.

'237 patent col. 5 ll. 4–9, 12–13.

Similarly, claims 6 and 15 of the '767 patent read:

> 6. A pharmaceutical formulation suitable for intranasal administration which comprises zolmitriptan and a pharmaceutically acceptable carrier wherein the pH of the formulation is in the range 3.5 to 5.5, wherein the formulation is buffered by a mixture of citric acid and disodium phosphate.

'767 patents among different AstraZeneca entities and their effect on the licensing agreement between Impax and AstraZeneca. *Opinion*, 246 F. Supp. 3d at 1028–30. However, Lannett no longer challenges standing on appeal.

> 15. An aqueous solution of zolmitriptan in a buffer at a pH of less than 6.0.

'767 patent col. 5 ll. 23–27, col. 6 ll. 21–22.

Other formulation claims of the '237 and '767 patents at issue include similar limitations with regard to pH ranges and buffering, and some formulation claims include additional limitations relating to sterility. '237 patent col. 5 l. 4–col. 6 l. 22; '767 patent col. 5 l. 8–col. 6 l. 25. These additional limitations are not at issue on appeal.

AstraZeneca owns the New Drug Application ("NDA") for Zomig® (zolmitriptan) Nasal Spray, 2.5 mg/spray and 5 mg/spray, approved by the U.S. Food and Drug Administration ("FDA") for treatment of migraine. The '237 and '767 patents are listed in connection with Zomig® Nasal Spray in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the "Orange Book."

In 2012, AstraZeneca and Impax entered into an agreement for distribution, license, development, and supply of the Zomig® products. The agreement granted to Impax an exclusive license to AstraZeneca's patents covering the Zomig® products, including the '237 and '767 patents, in return for the payment of $130 million and additional payments at varying royalty rates, including 40% on the nasal spray. *Opinion*, 246 F. Supp. 3d at 1039; J.A. 2204–05.

In June 2014, Lannett notified AstraZeneca that it had filed an Abbreviated New Drug Application ("ANDA"), seeking approval for a generic version of Zomig® Nasal Spray, making a certification according to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV certification"), alleging noninfringement and/or invalidity of the '237 and '767 patents.

In July 2014, Appellees filed suit against Lannett in the District of Delaware for infringement of the '237 and '767 patents pursuant to 35 U.S.C. § 271(e)(2)(A). In December 2015, the district court issued its claim construction opinion and order. The court agreed with Appellees that the preamble of "[a] pharmaceutical formulation suitable for intranasal administration" is limiting. *Impax Labs. Inc. v. Lannett Holdings Inc.*, 2015 WL 7737309, at *2–3 (D. Del. 2017) ("*Claim Construction Opinion*"); *see also Impax Labs. Inc. v. Lannett Holdings Inc.*, No. 1:14-cv-00984-RGA (D. Del. Dec. 8, 2017), ECF No. 64 ("*Claim Construction Order*"); J.A. 9–10. The court also adopted Appellees' construction of "zolmitriptan" as meaning its chemical name and structure, declining to adopt Lannett's proposed construction that would include "ionic and covalently bonded forms thereof that preserve the pharmaceutical activity of the structure." *Claim Construction Opinion*, 2015 WL 7737309, at *3–4. The court, however, agreed with Lannett regarding the construction of the word "buffer," adopting the "functional definition" proposed by Lannett, *id.* at *4–7; J.A. 9, and adopted the parties' agreed-upon constructions of "disodium phosphate" and "pH of the formulation is 5," J.A. 10.

In September 2016, a four-day bench trial was held on the issues of infringement and validity. Following the bench trial, the parties stipulated that Lannett's product described in its ANDA with a target pH of 5, if approved by the FDA, will infringe the '237 and '767 patents. *Impax Labs. Inc. v. Lannett Holdings Inc.*, No. 1:14-cv-00984-RGA (D. Del. Sept. 29, 2016), ECF No. 137.

In March 2017, the district court issued its decision on validity, holding that Lannett failed to prove by clear and convincing evidence that the asserted claims were invalid. *Opinion*, 246 F. Supp. 3d at 1030. The court first made factual findings on the teachings of the prior art references, namely, sumatriptan NS, International Publication No. WO 99/64044 ("Marquess"), U.S. Patent 6,326,401

and its counterpart French Publication No. FR 2773489 (together, "Chauveau"),[2] and Stewart Tepper & Alan Rapoport, *The Triptans: A Summary*, 12(5) CNS Drugs 403–417 (Nov. 1999) ("Tepper & Rapoport"). *Id.* at 1032–34.

The district court then determined that Lannett failed to prove that claim 4 of the '237 patent and claim 15 of the '767 patent were anticipated by Marquess or Chauveau, as neither of the references disclosed all the limitations of the claims. *Id.* at 1034–35. The court also determined that Lannett failed to prove by clear and convincing evidence that the claims at issue would have been obvious over the prior art. *Id.* at 1035–44. In reaching the nonobviousness conclusion, the court found that: (1) the prior art, including Chauveau, taught away from formulating zolmitriptan for intranasal administration because zolmitriptan was known to be active, not by itself, but through its more potent metabolite, 183C91; (2) the prior art at the time failed to teach that zolmitriptan by itself, as contrasted with its metabolite, would have been effective; and (3) a skilled artisan would not have been motivated to make with a reasonable expectation of success nasal formulations of zolmitriptan. *Id.* at 1036–39; *see also id.* at 1032 n.3. The court also found that sumatriptan does not have an active metabolite and that "[o]nly two other triptans, eletriptan and almotriptan, have active metabolites, but their metabolites 'don't really contribute at all to the efficacy of those drugs.' Zolmitriptan stands alone in the class of triptans as having an active, more potent metabolite." *Id.* at 1033 (quoting Appellees' expert, Dr. Alan Rapoport) (citation omitted).

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[2] As counterparts of each other, the two Chauveau references' disclosures are substantially identical. In this opinion, references to Chauveau will be based on the U.S. patent unless otherwise noted.

The district court also considered evidence of objective indicia of nonobviousness. *Id.* at 1039–43. It found that the 2012 agreement between Impax and AstraZeneca supported a showing of nonobviousness, but found any further secondary considerations evidence inconclusive. *Id.* Ultimately, after noting that "[t]he question of obviousness is a close one," the court determined that Lannett had failed to meet its burden of proving invalidity by clear and convincing evidence. *Id.* at 1043–44. Following the decision on the issue of validity, the court entered final judgment and an injunction in favor of Appellees. J.A. 1–4.

Lannett timely appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

As an initial matter, we note that Lannett no longer argues anticipation as a defense and does not challenge the district court's claim constructions on appeal. Also, Lannett's invalidity arguments relying on International Publication No. WO 98/02186 ("Penkler") and European Publication No. EP 0636623 ("Robertson"), which were not raised or developed either before the district court or on appeal in its opening brief, are waived. *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319–20 (Fed. Cir. 2006). We further note that because the court's nonobviousness decision applied commonly to all of the challenged claims, the court did not and needed not make separate decisions on the validity of the claims at issue. *Opinion*, 246 F. Supp. 3d at 1030–31, 1032 n.2. Similarly, on appeal, the parties do not make separate arguments on validity,[3] and thus all of the claims at issue rise and fall

[3] In its opening brief, Lannett appears to suggest that the district court's nonobviousness conclusion with respect to claim 15 was in error because claim 15 merely

together with the issue of whether it would have been obvious to make zolmitriptan into a nasal spray.

We proceed to the obviousness issue, the sole issue on appeal, based on the prior art references and arguments properly before us. On appeal from a bench trial, we review a district court's conclusions of law *de novo* and its findings of fact for clear error. *Golden Blount, Inc. v. Robert H. Peterson Co.*, 365 F.3d 1054, 1058 (Fed. Cir. 2004). A factual finding is only clearly erroneous if, despite some supporting evidence, we are left with the definite and firm conviction that a mistake has been made. *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948); *see also Polaroid Corp. v. Eastman Kodak Co.*, 789 F.2d 1556, 1559 (Fed. Cir. 1986) ("The burden of overcoming the district court's factual findings is, as it should be, a heavy one.").

A party challenging the validity of a patent must establish invalidity by clear and convincing evidence. *See Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011). Clear and convincing evidence should "place[] in the fact finder 'an abiding conviction that the truth of [the] factual contentions are highly probable.'" *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (quoting *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984)) (second alteration in original).

Obviousness is a question of law based on underlying factual findings relating to "the scope and content of the

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requires an "aqueous solution." Appellant's Br. 25–26. However, beyond this oblique reference in its opening brief, Lannett does not separately argue invalidity of claim 15 until its reply brief. *Id.*; Reply Br. 5–7. We therefore find Lannett's separate invalidity arguments regarding claim 15 waived. *SmithKline Beecham*, 439 F.3d at 1319–20.

prior art," "differences between the prior art and the claims at issue," "the level of ordinary skill in the pertinent art," and "secondary considerations," such as "commercial success, long felt but unsolved needs, [and] failure of others." *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1047–48 (Fed. Cir. 2016) (en banc) (internal quotation marks omitted) (quoting *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007)).

On appeal, Lannett contends that the district court erred in concluding that the claims at issue would not have been obvious, based on an erroneous finding that the prior art taught away from nasal formulations of zolmitriptan. According to Lannett, the court improperly disregarded express teachings in the prior art. Lannett also argues that the court erred in finding that the 2012 agreement, which encompassed the entire Zomig® franchise, including matters unrelated to the patents at issue, supported its conclusion of nonobviousness. Lannett alleges that it made a strong showing of obviousness, and therefore, even accepting the district court's findings of teaching away and objective indicia of nonobviousness, the court still erred in its ultimate conclusion of obviousness.

Appellees respond that the district court did not err because it correctly found that a skilled artisan would not have been motivated to make nasal formulations of zolmitriptan or had a reasonable expectation of success in doing so. Appellees contend that the court's finding of teaching away was not clearly erroneous, and, at any rate, Lannett failed to prove obviousness by clear and convincing evidence. According to Appellees, the court's factual findings, including those relating to secondary considerations, were supported by record evidence and based on credibility determinations concerning the parties' experts, and such evidence should not be reweighed on appeal.

We find no reversible error in the district court's decision that Lannett failed to prove invalidity of the asserted claims by clear and convincing evidence. The court's decision was supported by its underlying factual findings, which we do not find clearly erroneous. Because the question of the level of ordinary skill in the art is undisputed, we proceed to the remaining parts of the obviousness analysis.

I

A

Lannett contends that the prior art expressly discloses nasal formulations of zolmitriptan, and it faults the district court for failing to consider the prior art "as a whole." Appellant's Br. 31. Lannett argues that prior art references, in particular, Chauveau,[4] expressly disclosed

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[4] Lannett alludes to Tepper & Rapoport as supporting the similar proposition that the prior art taught nasal formulations of zolmitriptan, without making any particular invalidity argument based on Tepper & Rapoport. Appellant's Br. 17–18. Thus, we find any invalidity argument relying on Tepper & Rapoport waived, *SmithKline Beecham*, 439 F.3d at 1319–20; at any rate, we find no clear error in the district court's finding that the statement that a zolmitriptan nasal spray being "under development" in Tepper & Rapoport was a mere "passing reference," *Opinion*, 246 F. Supp. 3d at 1034. "[U]nder development" does not mean developed, with an expectation of success. Lannett also similarly alludes to Marquess for the same proposition without making any particular invalidity argument based on Marquess. Appellant's Br. 18–19. Similarly, any invalidity argument based on Marquess is waived. *SmithKline Beecham*, 439 F.3d at 1319–20. Moreover, the court correctly found that Marquess did not disclose the claimed nasal formulation

using zolmitriptan in a nasal spray. Lannett urges that the court's discounting of Chauveau's express mention of zolmitriptan in connection with nasal formulations constituted clear error. We disagree.

Chauveau is generally directed to formulating an active ingredient using capryl caproyl macrogol glycerides (a version of which is marketed under the name Labrasol®) for oromucosal administration of the active ingredient. Chauveau col. 2 ll. 5–16, col. 3 ll. 18–21. As the district court noted, Chauveau discusses that its teachings can be applied to formulations for buccal, nasal, or pharyngeal administration, among which the nasal route is preferred. *Id.* col. 1 ll. 5–6, col. 2 ll. 27–29, col. 3 ll. 60–67, col. 5 ll. 8–15. Chauveau's teachings seek to provide pharmaceutically effective formulations for active ingredients that would be degraded by oral administration, particularly in the gastrointestinal tract. *Id.* col. 1 ll. 10–31, 48–52. The court found that Chauveau "offers a laundry list of potential active ingredients," including "over twenty-five categories or examples of medications." *Opinion*, 246 F. Supp. 3d at 1033 (citing Chauveau col. 2 l. 38–col. 3 l. 14). At the end of the list, Chauveau states that "[t]he active substance can also be, in particular, an antimigraine active substance, such as a triptan, such as sumatriptan or zolmitriptan." Chauveau col. 3 ll. 12–14. The example formulations described in Chauveau include IS 159 (tryptamine-5-O-carboxymethyl-tyrosyl-glycinamide) as the active ingredient, but not zolmitriptan. *Id.* col. 4 ll. 10–28, col. 5 l. 47–col. 9 l. 18.

Lannett is correct that in an obviousness analysis, prior art should be viewed as a whole. *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350,

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of zolmitriptan according to the court's construction of "zolmitriptan," which is unchallenged on appeal. *Opinion*, 246 F. Supp. 3d at 1034–35.

1358 (Fed. Cir. 2007). However, Chauveau, as a whole, is not about intranasal formulations of zolmitriptan, which is barely mentioned. It is about formulations of a wide variety of compounds with capryl caproyl macrogol glycerides. Zolmitriptan is mentioned once, with no further mention in an example or claim. Moreover, properly viewing the prior art as a whole, the district court here made additional findings beyond the fact that zolmitriptan was barely mentioned in Chauveau. Specifically, the court found that the prior art taught that zolmitriptan has a "unique attribute" in that its "[f]irst pass metabolism results in an active metabolite, 183C91, which is two to eight times more powerful than zolmitriptan itself." *Opinion*, 246 F. Supp. 3d at 1036–37. The court credited Appellees' expert, Dr. Rapoport, who provided his opinion on the state of the prior art in support of this finding. *Id.* The court also noted that Lannett's expert did not dispute the relevance of zolmitriptan's active metabolite in considering whether to develop zolmitriptan formulations. *Id.* at 1037. It is also undisputed that sumatriptan does not have an active metabolite. *See id.* at 1033.

Lannett nevertheless argues that the district court erred in finding that the effectiveness of zolmitriptan "relied on" its active metabolite, Appellant's Br. 41–45, and puts forth arguments to discount the significance of zolmitriptan's active metabolite. In particular, Lannett argues that triptans are specifically designed to act as serotonin receptor agonists, which, by itself, would rebut the contention that zolmitriptan was understood to be ineffective without the contribution of its metabolite. We disagree, particularly because Lannett's contentions are without any evidentiary support beyond its attorney arguments concerning factual issues. *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1406–07 (Fed. Cir. 2014) (rejecting a conclusory obviousness argument without evidentiary support).

Contrary to Lannett's contentions, the district court found that zolmitriptan's more potent, active metabolite was actually thought to be significant for its efficacy by a person of skill in the art at the time. Specifically, the court credited Appellees' evidence of expert testimony and studies and found that a skilled artisan would have expected delayed or lower therapeutic effectiveness from zolmitriptan if administered nasally because it would have been "absolutely counterintuitive to make a nasal spray when you have an active metabolite which is more potent . . . than the drug itself." *Opinion*, 246 F. Supp. 3d at 1037 (quoting Dr. Rapoport); J.A. 667. As such, the court found that "because of zolmitriptan's reliance on its active metabolite, the prior art failed to teach that zolmitriptan by itself would be effective." *Id.* The court thus found zolmitriptan's acting through its metabolite not only relevant, which was substantially undisputed, but also significant for a skilled artisan to consider regarding whether to make intranasally administered zolmitriptan.

In view of the totality of the record evidence of the state of the prior art, we cannot find that the district court clearly erred in its findings. Far from disregarding the prior art's discussion of zolmitriptan, the court specifically considered and acknowledged that zolmitriptan was mentioned in connection with nasal formulations and sprays. However, the court also properly considered additional record evidence to make findings on the state of the prior art as a whole.

Both parties put forth evidence of various factors a person of ordinary skill in the art would have considered. Ultimately, the district court found that a skilled artisan would not have been motivated to make a zolmitriptan nasal spray with a reasonable expectation of success. *Opinion*, 246 F. Supp. 3d at 1038–39; *see id.* at 1043–44. "The presence or absence of a motivation to combine references in an obviousness determination is a pure

question of fact," and "[w]hat a reference teaches and whether it teaches toward or away from the claimed invention are questions of fact." *Par Pharm., Inc. v. TWi Pharm., Inc.*, 773 F.3d 1186, 1196–97 (Fed. Cir. 2014) (citation and internal quotation marks omitted). In particular, the court here found that "a skilled artisan would look to any of the other triptans before looking to zolmitriptan to develop a pharmaceutical product that would not take advantage of first pass metabolism." *Opinion*, 246 F. Supp. 3d at 1037.

Based on the record before us, we do not find that the court clearly erred in concluding that at the time, zolmitriptan's known significant reliance on its active metabolite would have, on balance, dissuaded a person of skill in the art from making nasal formulations of zolmitriptan. *See, e.g.*, *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 1349–50 (Fed. Cir. 2000) (no clear error in the district court's finding that a person of skill in the art, on balance, would not have made the claimed invention); *Intendis GmbH v. Glenmark Pharm. Inc.*, 822 F.3d 1355, 1366–67 (Fed. Cir. 2016) (no clear error when the district court found that a person of skill in the art would have pursued other formulations).

B

The district court also considered evidence of secondary considerations, including the 2012 license agreement between Impax and AstraZeneca covering the Zomig® products for which Impax paid $130 million. The court found that this 2012 agreement favored Appellees as it found a nexus between the agreement and the '237 and '767 patents. However, it found that Appellees' other evidence of secondary considerations was inconclusive.

Lannett argues that the district court's analysis is unsupported by any evidence, as the court, without any support, did its own nexus analysis. We disagree. The court found that the patents covering the oral formula-

tions of zolmitriptan expired in only a little more than one year after the effective date of the 2012 agreement, but the patents covering the nasal formulations of zolmitriptan, *i.e.*, the '237 and '767 patents, were not set to expire until 2021. *Opinion*, 246 F. Supp. 3d at 1039. Based on the timing of the 2012 agreement as it related to the various formulation patents and the sales data presented to the court, it found that "a portion of the $130 million had to be based on expected profits from Zomig nasal spray." *Id.* at 1040. Also, contrary to Lannett's suggestion, the court did rely on corroborating evidence showing a nexus between the patents at issue and the licensing, including Impax's press release stating that Impax "look[s] to build sales of the Zomig® nasal spray dosage form." *Id.* (quoting the press release); J.A. 2405. Thus, there was adequate nexus between the intranasal patents and $130 million. To the extent that Lannett invites us to analyze the 2012 agreement and reweigh evidence, we decline to do so. In view of other underlying factual findings discussed above, it is sufficient for us to find that the court did not clearly err in finding that the 2012 agreement is at least in part attributable to the patents at issue.

II

We finally consider whether the district court reached a legally erroneous conclusion of nonobviousness. The court called this case indeed a "close one." *Opinion*, 246 F. Supp. 3d at 1043. The court stated that, on the one hand, as a "promising migraine treatment," various aspects of zolmitriptan "would have been encouraging to a skilled artisan motivated to make an anti-migraine nasal spray better than Imitrex." *Id.* On the other hand, the court stated that "zolmitriptan had a known, powerful metabolite, the creation of which would be delayed and diminished by nasal administration" of zolmitriptan, which "would point a skilled artisan away from including zolmitriptan in a nasal spray." *Id.* The court found

Appellees' experts more credible than Lannett's and ultimately was not convinced that Lannett had shown that the patents were invalid. *Id.* at 1044. We are unconvinced that the court erred in that judgment.

Contrary to Lannett's suggestion, it has not shown a "strong" case of obviousness and has not proven obviousness by clear and convincing evidence. *Procter & Gamble*, 566 F.3d at 994. We are not left with a firm conviction that the district court erred in its underlying factual findings, as discussed above. Indeed, the court weighed the evidence before it and made findings for and against both Appellees and Lannett. We do not and should not reweigh evidence or make factual findings anew on appeal. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 838 (2015) ("A district court judge who has presided over, and listened to, the entirety of a proceeding has a comparatively greater opportunity to gain that familiarity than an appeals court judge who must read a written transcript or perhaps just those portions to which the parties have referred.").

Ultimately, we agree that this case was close. But, we defer to the district court in its fact findings, including what Chauveau discloses and the state of the prior art as a whole. And we are especially persuaded by the testimony of Appellees' expert, Dr. Rapoport, on which the district court relied, who opined that it would have been "absolutely counterintuitive" to make an intranasal formulation of zolmitriptan, given that its activity primarily came from its metabolite, and the agreement between AstraZeneca and Impax covering the intranasal product and its patents for which the latter paid $130 million. We therefore conclude that the district court did not commit reversible error in its nonobviousness conclusion.

The district court did not clearly err in its underlying factual findings, and we agree with the district court that Lannett failed to prove by clear and convincing evidence

that the claims of the '237 and '767 patents are invalid. We have considered all the other arguments raised in the briefs, but have not been persuaded that the district court erred in its conclusions.

CONCLUSION

For the foregoing reasons, we affirm the judgment of the district court.

AFFIRMED