NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff-Appellant

v.

LUPIN LTD., LUPIN PHARMACEUTICALS, INC.,
Defendants-Appellees

2024-2297

Appeal from the United States District Court for the District of Delaware in No. 1:21-cv-00900-RGA, Judge Richard G. Andrews.

Decided: May 21, 2026

ZACHARY L. GARRETT, Venable LLP, New York, NY, argued for plaintiff-appellant. Also represented by JOHN D. MURNANE, JOSHUA ROTHMAN, ALICIA ALEXANDRA ROSE RUSSO; MEGAN S. WOODWORTH, Venable LLP, Washington, DC.

WILLIAM R. ZIMMERMAN, Knobbe, Martens, Olson & Bear, LLP, Washington, DC, argued for defendants-appellees. Also represented by JARED C. BUNKER, Irvine, CA; CAROL PITZEL CRUZ, Bellevue, WA.

Before HUGHES and CUNNINGHAM, *Circuit Judges,* and BURROUGHS, *District Judge*.†

HUGHES, *Circuit Judge*.

Otsuka Pharmaceutical Co., Ltd. appeals a final judgment of the United States District Court for the District of Delaware. The district court held that certain claims of U.S. Patent Nos. 8,273,735 and 8,501,730 were not infringed by Lupin Ltd. and Lupin Pharmaceuticals, Inc.'s manufacturing process incorporated in Abbreviated New Drug Application No. 216063. The court also held that certain claims of U.S. Patent No. 8,273,735 were invalid for obviousness. For the following reasons, we affirm.

I

Otsuka Pharmaceutical Co., Ltd. (Otsuka) is the owner of U.S. Patent Nos. 8,501,730 and 8,273,735 (collectively, patents-in-suit). Respectively, the patents-in-suit claim highly pure tolvaptan—a compound used to treat Autosomal Dominant Polycystic Kidney Disease (ADPKD)—and improved methods for synthesizing tolvaptan. While previous synthesis methods for tolvaptan led to the production of an impurity known as the dechlorinated impurity, the innovation of the patents-in-suit is that, by reducing the amount of a key hydrogenating reagent in the synthesis process—sodium borohydride—the amount of the dechlorinated impurity is reduced. Otsuka uses this innovation in manufacturing its ADPKD treatment JYNARQUE®.

In May 2021, Lupin Ltd. notified Otsuka that it had submitted an Abbreviated New Drug Application (ANDA)

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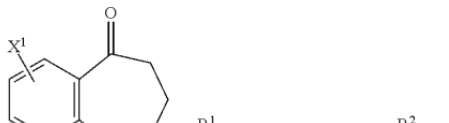
† Honorable Allison D. Burroughs, District Judge, United States District Court for the District of Massachusetts, sitting by designation.

to the Food and Drug Administration, seeking approval to market generic versions of JYNARQUE®. Otsuka then brought an action for infringement of the '730 patent against Lupin Ltd. and its wholly owned subsidiary Lupin Pharmaceuticals, Inc. (collectively, Lupin) under 35 U.S.C. § 271(a), (e)(2)(A), and (g). Later, Otsuka amended its complaint to also assert infringement of the '735 patent. Prior to and at trial, the issues were narrowed to include infringement and invalidity for obviousness.

Otsuka asserted claims 1, 2, 4, and 5 of the '730 patent and claims 7, 8, and 10 of the '735 patent against Lupin. The asserted claims of the '730 patent are all independent product-by-process claims, and they require reduction of a benzazepine compound in the presence of a hydrogenating agent. The claims further require that this hydrogenating agent be present in an amount of either 0.25–1 or 0.25–0.5 molar equivalent per 1 mole of benzazepine precursor compound. For example, claim 1 of the '730 patent recites:

> 1. A highly pure 7-chloro-5-hydroxy-1-[2-methyl-4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-1-benzazepine having a purity of more than 99.5%, or a salt thereof, which is produced by the process which comprises reducing a benzazepine compound of the formula (1):

(1)



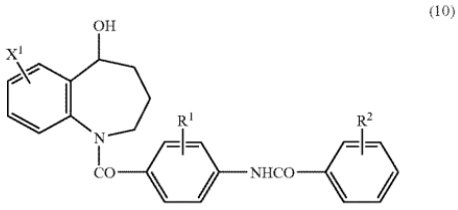
> wherein X^1 is a halogen atom, R^1 and R^2 are independently a lower alkyl group, or a salt

> thereof in the presence of a hydrogenating agent selected from the group consisting of lithium aluminum hydride, sodium borohydride, zinc borohydride, and diborane in an amount of 0.25 to 1 mole per 1 mole of the compound (1).

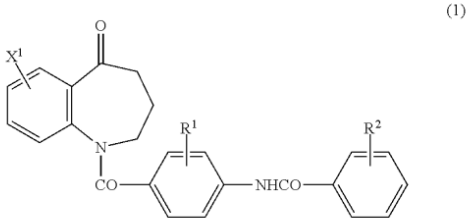
'730 Patent, 29:9–32.

Similarly, the asserted claims of the '735 patent are method claims, all of which also require the reduction of a benzazepine compound in the presence of a hydrogenating agent in an amount of either 0.25–1 or 0.25–0.5 molar equivalent per 1 mole of benzazepine compound. For example, claim 7, which depends from unasserted claim 6, recites (reproduced with claim 6 below for reference):

> 6. A process for producing a 2,3,4,5-tetrahydro-1H-1-benzazepine compound of the formula (10):



> wherein X^1 is a halogen atom, R^1 and R^2 are independently a lower alkyl group, or a salt thereof, which comprises reducing a benzazepine compound of the formula (1):



> wherein R^1, R^2 and X^1 are as defined above, or a salt thereof in the presence of a hydrogenating agent selected from the group consisting of lithium aluminum hydride, sodium borohydride, zinc borohydride, and diborane in an amount of 0.25 to 1 mole per 1 mole of the compound (1).
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> 7. The process according to claim 6, wherein the hydrogenating agent is sodium borohydride which is used in an amount of 0.25 to 1 mole per 1 mole of the compound (1).

'735 Patent, 31:61–32:36.

Lupin's ANDA submission incorporates Drug Master File (DMF) No. 036263, which describes the process by which Lupin intends to synthesize its generic tolvaptan ANDA product. Lupin's DMF indicates that its tolvaptan synthesis process also makes use of a reduction reaction like the one claimed by Otsuka, but where Otsuka's claimed process generally uses *1 molar equivalent or less* of hydrogenating agent such as sodium borohydride per 1 mole of precursor compound, Lupin's process uses *at least 1.2 molar equivalents* of sodium borohydride per 1 mole of precursor. *See, e.g.*, J.A. 2571–73. In Lupin's process, after this sodium borohydride has been added, two samples are taken, one after 15 minutes and one after 75 minutes. At each point, the sample is tested to see if no more than 0.05% of the original amount of precursor compound remains in the reaction mixture. If these tests indicate that 0.05% or less of the original amount of precursor compound remains, then Lupin quenches the reaction by adding water and hydrochloric acid. This destroys the chemical bonds in the sodium borohydride, preventing any further reaction. If these tests indicate that more than 0.05% of the amount of precursor compound remains, more sodium borohydride is added.

After a bench trial, the district court held that Lupin's DMF method for producing tolvaptan did not infringe the asserted claims of the patents-in-suit. Separately, the district court considered evidence of the invalidity of the patents-in-suit for obviousness over several pieces of prior art, ultimately concluding that "Lupin has shown by clear and convincing evidence that a POSA would have found the claimed invention [of the '735 patent] obvious." *Otsuka Pharm. Co. v. Lupin Ltd.*, No. 21-cv-00900, 2024 WL 3618123, at *11 (D. Del. July 31, 2024) (*Bench Trial Opinion*). The district court also found, however, that Lupin did not demonstrate the invalidity of the asserted '730 patent claims under its obviousness theory.

Otsuka appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II

On appeal, Otsuka challenges the district court's infringement conclusions, its conclusion that Lupin's expert at trial qualified as a skilled artisan, and its invalidity conclusions regarding the '735 patent. We address each argument in turn.

A

We begin with Otsuka's challenge to the district court's infringement conclusions. "Following a bench trial, we review the district court's conclusions of law de novo and its fact-findings for clear error." *Merck Sharp & Dohme Corp. v. Amneal Pharms. LLC*, 881 F.3d 1376, 1384 (Fed. Cir. 2018). Infringement is a question of fact reviewed for clear error after a bench trial. *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1367 (Fed. Cir. 2023). "A factual finding is clearly erroneous when, despite some supporting evidence, we are left with a definite and firm conviction that the district court was in error." *Packet Intel. LLC v. NetScout Sys., Inc.*, 965 F.3d 1299, 1305 (Fed. Cir.

2020) (quoting *Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1186 (Fed. Cir. 2014)).

Otsuka's primary infringement argument on appeal is that the district court adopted a "practical completion" construction for the claim term "amount" but applied a different and contradictory "absolute completion" construction in determining that Lupin's DMF process does not infringe. Under the proper understanding of "amount," Otsuka claims that Lupin infringes because the reaction is practically complete before 1 molar equivalent of hydrogenating agent is added to the reaction mixture.

During claim construction, the parties disputed how to construe the term "amount" in the asserted claims. While Lupin offered a construction of "amount" that would make the relevant amount of hydrogenating agent the *total* amount added into the reaction chamber, *see* J.A. 136, 25:1–4, the district court disagreed, finding that the claim language itself required that the claimed amount of hydrogenating agent be "the amount while the reaction is taking place," *see* J.A. 138–39, 27:22–28:9. Later, in post-trial briefing, the parties presented conflicting visions of when the reduction reaction actually takes place. While Otsuka argued that the claim term referred to "the amount of hydrogenating agent added before the reduction reaction reaches 'practical completion' or is 'complete in a practical sense,'" *Bench Trial Opinion*, 2024 WL 3618123, at *6 (quoting J.A. 1987), Lupin argued that "so long as unreacted ketone precursor and sodium borohydride are present, the reaction will continue to proceed," *id.* (quoting J.A. 2025). The district court agreed with Otsuka, finding that Lupin's proposed construction was directed to the "theoretical possibility" of "absolute completion" of the reaction. *Id.* The district court therefore noted that it understood "the reduction reaction to be 'taking place' until it reaches some point of practical completion." *Id.*

Having decided that the "amount" of hydrogenating agent was the amount present until the claimed reduction reached "practical completion," the district court determined that Otsuka failed to show infringement for two reasons. First, the district court found that, even if Otsuka was correct that practical completion is reached when "so little precursor ketone remains that no further reduction is observed," Otsuka did not adduce evidence that showed that the reaction was practically complete by the time the amount of precursor compound fell to 0.05% of its original level, the point at which Lupin decides to end the reaction by initiating the quenching step. *See id.* at *7 (quoting J.A. 1985). Second, the district court determined that, even if Lupin's reaction *did* reach practical completion at the 0.05% precursor level, Otsuka failed to demonstrate that "no more than 1 molar equivalent of sodium borohydride or less has been added by that point." *Id.*

Assuming without deciding that practical completion is reached when Otsuka claims it is—that is, when the amount of precursor compound has fallen to 0.05% of its original level—we agree with the district court that Otsuka has failed to prove infringement of the patents-in-suit by Lupin's DMF process. Otsuka offers two main pieces of evidence to suggest infringement of the patents-in-suit: (1) two experiments performed by Lupin while developing its DMF process, Experiments 109 and 115, which Otsuka contends show practical completion before 1 molar equivalent of sodium borohydride is added; and (2) testimony from its expert Dr. William Roush that the details of Lupin's DMF process indicate that the reduction reaction will be complete long before the addition of 1 molar equivalent of sodium borohydride. Ultimately, neither persuades us that the district court clearly erred.

First, as the district court found, the underlying data for Experiments 109 and 115 "contained anomalies that might be accounted for by some unspecified 'margin of error' or a lack of 'appropriate quality control.'" *Id.* (citations

omitted). For example, as per the testimony from Otsuka's expert Dr. Roush, after the full amount of hydrogenating reagent was added in Experiment 115, the precursor molecule appeared to be regenerating, despite this being impossible based on the reaction's chemistry. *See* J.A. 324, 88:7–16; J.A. 354–56, 118:3–120:25. While Otsuka attempts to convince us that these experiments nonetheless could form a reliable basis for Dr. Roush's infringement opinions, we do not find clear error in the district court's decision to not rely on experimental data that is, by Dr. Roush's own admission, flawed.

Second, Dr. Roush's separate testimony that Lupin's DMF process is practically complete before the addition of 1 molar equivalent of hydrogenating agent, based on his "vast experience performing sodium borohydride reactions," similarly fails to persuade us that the district court clearly erred. J.A. 312, 76:15–16. Otsuka claims that Dr. Roush's expertise, combined with certain details about Lupin's DMF process, demonstrates that the DMF reaction will proceed quickly and run to completion before even 0.5 molar equivalents of hydrogenating agent are added. But Dr. Roush's DMF conclusions also meaningfully rely on data from Lupin's Experiments 109 and 115. *See, e.g.*, J.A. 1993 (characterizing Dr. Roush's testimony as "based on Experiments 109/115, and taking into account the differences in process parameters between Experiments 109/115 and the DMF process"). And we find no clear error in the district court's conclusion that these experiments, on their own or in combination with Dr. Roush's expertise, shed little light on when the reduction reaction in Lupin's DMF process is practically complete. For one, record evidence from both experts supports the district court's conclusion that Experiments 109 and 115 were performed under different conditions than the DMF process. *See, e.g.*, J.A. 327, 91:23–25 (Dr. Roush); J.A. 432–33, 196:13–197:5 (Dr. Dichtel). Further, notwithstanding Dr. Roush's testimony that these differences should be

immaterial, *see* J.A. 327–34, 91:23–98:13, Dr. Dichtel testified that these differences *would* be material and impact any potential infringement conclusions resulting from the extrapolation of these experiments to the DMF process, *see* J.A. 432–33, 196:13–197:24.

Considering the totality of the evidence before the district court, we do not find clear error in its conclusion that "Otsuka fail[ed] to prove by a preponderance of the evidence that the reduction reaction in Lupin's tolvaptan synthesis process reaches completion before more than 1 molar equivalent of sodium borohydride has been added." *Bench Trial Opinion*, 2024 WL 3618123, at *7.

B

We next turn to Otsuka's argument that the district court's infringement and invalidity analyses were flawed because Lupin's expert Dr. Dichtel does not qualify as a person having ordinary skill in the art. Otsuka notes that the district court's own definition of the skilled artisan in this case is someone who "ha[s] a relevant doctorate degree and 'at least two years of experience in the synthesis, research, and development of medicinal compounds.'" Appellant Br. 49 (citing *Bench Trial Opinion*, 2024 WL 3618123, at *3). Otsuka then argues that because Dr. Dichtel lacks the requisite experience, his testimony should not have been admitted.

Otsuka presented these same arguments to the district court after trial. Ultimately, however, the district court did not entertain the merits of Otsuka's arguments, finding that because Otsuka did not timely object to Dr. Dichtel's testimony before or during trial, it had not preserved any challenge to the admissibility of Dr. Dichtel's testimony. *Bench Trial Opinion*, 2024 WL 3618123, at *5 (citing Fed. R. Evid. 103(a)).

We review procedural issues not unique to patent law, such as forfeiture, under the law of the regional circuit. *See*

Innogenetics, N.V. v. Abbott Lab'ys, 512 F.3d 1363, 1371 (Fed. Cir. 2008). The Third Circuit "review[s] for abuse of discretion a district court's determination that a party forfeited an argument by failing to raise it earlier in the proceedings." *Harbor Bus. Compliance Corp. v. Firstbase.io, Inc.*, 152 F.4th 516, 527 (3d Cir. 2025). If an argument is found to be forfeited, it is reviewable only in "truly 'exceptional circumstances.'" *Id.* at 529 (citation omitted).

Under the law of the Third Circuit, a party who fails to object to errors at trial forfeits the right to complain about those alleged errors later. *United States v. Rivas*, 493 F.3d 131, 136 (3d Cir. 2007). And while Otsuka is correct that it argued Dr. Dichtel was not a skilled artisan in an elliptical fashion in its opening statement, *see, e.g.*, J.A. 244–45, 8:3–9:21 ("[W]e think Dr. Dichtel is straying from his expertise."), it did *not* object at trial when Dr. Dichtel stated that he felt comfortable opining on the patents-in-suit from the perspective of a skilled artisan, *see* J.A. 445–46, 209:21–210:12. Nor did Otsuka file a *Daubert* motion seeking to exclude Dr. Dichtel as an expert before trial. On these facts, we cannot find that the district court abused its discretion in finding that Otsuka forfeited its challenges to Dr. Dichtel's status as a skilled artisan. We therefore uphold the district court's finding without reaching the merits of this issue.

C

Finally, we consider Otsuka's arguments that the district court erred in invalidating the asserted claims of the '735 patent for obviousness. "Obviousness is a question of law based on underlying facts, and '[o]n appeal from a bench trial, this court reviews the district court's conclusions of law de novo and findings of fact for clear error.'" *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1372 (Fed. Cir. 2017) (quoting *Prometheus Lab'ys, Inc. v. Roxane Lab'ys, Inc.*, 805 F.3d 1092, 1097 (Fed. Cir. 2015)). The underlying factual determinations within the

obviousness analysis include: "(1) the scope and content of the prior art; (2) differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art; and (4) secondary considerations such as commercial success, long felt but unsolved needs, and failure of others." *Incept LLC v. Palette Life Scis., Inc.*, 77 F.4th 1366, 1371 (Fed. Cir. 2023).

In its bench trial opinion, the district court first concluded that a skilled artisan would have been motivated to select Kondo,[1] a reference which teaches a process for small-scale synthesis of tolvaptan, as a starting point in seeking to achieve the claimed invention. Next, the district court found that within the Kondo process, a skilled artisan would have been motivated to specifically select the reduction step for modification based on testimony from Dr. Dichtel. The district court then concluded that a skilled artisan would have been motivated to reduce the amount of sodium borohydride used in Kondo's reduction step before going on to find that a skilled artisan would also be motivated to reach the claimed invention either in light of his or her background knowledge or in light of two other pieces of prior art. After establishing this motivation to combine, the district court also found a reasonable expectation of success in developing the invention claimed by the asserted claims of the '735 patent. Finally, the district court considered various secondary considerations of nonobviousness and concluded that these considerations did not overcome the strong evidence in favor of obviousness.

On appeal, Otsuka primarily attacks the court's motivation analysis, arguing that Dr. Dichtel's focus on

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[1] Kazumi Kondo et al., *7-Chloro-5-hydroxy-1-[2-methyl-4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1*H*-1-benzazepine (OPC-41061): A Potent, Orally Active Nonpeptide Arginine Vasopressin V_2 Receptor Antagonist*, 7 Bioorganic & Med. Chemistry 1743, 1743–54 (1999).

Kondo—and, specifically, Kondo's reduction step—is indicative of hindsight bias that should have rendered his testimony not credible. Otsuka also argues that the district court erred by dismissing its secondary consideration evidence, specifically evidence of unexpectedly high tolvaptan purity and yield over Kondo.

We are unpersuaded that the district court clearly erred in its analysis of the skilled artisan's motivation to start with and modify Kondo. While Otsuka argues that Dr. Dichtel focused solely on Kondo, reflecting hindsight bias, Dr. Dichtel testified that he "did [his] own literature search" and looked at several other tolvaptan-synthesis references in addition to Kondo, but that he considered Kondo to be a particularly promising reference. *See* J.A. 544–45, 308:21–309:13. So too does Otsuka's argument downplay evidence, credited by the district court, that a separate, non-prior-art reference, Zard,[2] referred to Kondo as a standard method for synthesizing tolvaptan at the time of the claimed invention. *See* J.A. 677–78, 441:18–442:21. While Otsuka is correct that Zard acknowledged "major obstacle[s]" with Kondo's process, *see* J.A. 618–19, 382:4–383:10, considering all of the evidence, we do not find that these considerations undermine the district court's conclusion that "Lupin . . . presented clear and convincing evidence that a POSA would have recognized Kondo as a viable starting point," *Bench Trial Opinion*, 2024 WL 3618123, at *12. *See In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012) (recognizing that even "inferior combination[s]" of prior art may be appropriately considered in obviousness inquiry).

Similarly, we find no clear error in the district court's analysis of the skilled artisan's motivation to modify the reduction step of Kondo specifically. As the district court

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[2] U.S. Patent Application Publication No. 2007/0185323.

noted, both experts agreed that many of the steps of Kondo would have been considered for modification, including the reduction step. *See* J.A. 546–48, 310:13–312:16 (Dr. Dichtel); J.A. 665, 429:7–16 (Dr. Roush). And Dr. Dichtel presented significant testimony about why a skilled artisan would have sought to modify Kondo's reduction step, including cost savings, improvement of the reaction's safety profile, post-processing simplification, and knowledge that the hydrogenating agent was already being used in molar excess. *See, e.g.*, J.A. 457–63, 221:1–227:12. This evidence, tethered to the chemical realities of the reaction, is a far cry from the conclusory expert testimony our case law rejects. *Cf. TQ Delta LLC v. CISCO Sys., Inc.*, 942 F.3d 1352, 1361–62 (Fed. Cir. 2019). We therefore decline to find clear error in the district court's choice to credit this testimony.

Lastly, we fail to find reversible error in the district court's conclusions regarding secondary considerations of non-obviousness. Otsuka purports to demonstrate both high yield and high purity by relying in part on a declaration from one of its chemists, Hirotaka Yukawa. *See* J.A. 4106–16. However, in analyzing purity, the Yukawa declaration compares the claimed methods not to Kondo itself, but to a process that uses *double* Kondo's amount of hydrogenating agent. *Compare* J.A. 449–50, 213:21–214:9 (reflecting that Kondo uses 1.5 molar equivalents of hydrogenating agent), *with* J.A. 4111 (indicating that Yukawa's process used "3 fold molar amount of [sodium borohydride] per 1 mole of the [precursor molecule]"). The district court did not therefore clearly err by failing to credit the Yukawa declaration as accurately reporting the results of Kondo's purity. *See Bench Trial Opinion*, 2024 WL 3618123, at *21. Nor do we find clear error in the district court's conclusion that this difference in concentration of hydrogenating agent was material because "Otsuka's internal documents report the presence of a dechlorinated impurity when using 2 molar equivalents of sodium borohydride . . . but not

when using 1.5 molar equivalents as disclosed in Kondo." *Id.* at *10, *21. While Otsuka argues that this interpretation of the evidence of record rests on a misinterpretation of Otsuka's internal documents, we do not find clear error in the district court's contrary conclusion, based on testimony from Dr. Dichtel that the court explicitly found "more credible." *Id.* at *21.

Regarding unexpectedly high yield, it appears that the district court overlooked evidence from Dr. Dichtel's testimony, Kondo itself, and the Yukawa declaration reporting that the yield of Kondo's process using 1.5 molar equivalents of hydrogenating agent was 30%, as opposed to the claimed process's 82–93% yield. Nonetheless, we conclude that any error in evaluating this secondary consideration is harmless. After all, "weak secondary considerations generally do not overcome a strong prima facie case of obviousness." *Genentech, Inc. v. Sandoz Inc.*, 55 F.4th 1368, 1378 (Fed. Cir. 2022) (citation modified). And we have already declined to disturb the district court's findings underpinning the prima facie case. Accordingly, any evidence introduced of unexpected yield "is not sufficient to overcome the strong case of obviousness as a matter of law." *Adapt Pharma Operations Ltd. v. Teva Pharms. USA, Inc.*, 25 F.4th 1354, 1375 (Fed. Cir. 2022). We therefore affirm the district court's obviousness determinations regarding the asserted claims of the '735 patent.

III

We have considered the parties' remaining arguments and find them unpersuasive. For the foregoing reasons, we affirm the district court's judgment of non-infringement of the patents-in-suit, its determination that Otsuka forfeited its skilled-artisan arguments, and its judgment that the asserted claims of the '735 patent are invalid for obviousness.

AFFIRMED