United States Court of Appeals for the Federal Circuit

IMMUNOGEN, INC.,
Plaintiff-Appellant

v.

COKE MORGAN STEWART, ACTING UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND ACTING DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,
Defendant-Appellee

2023-1762

Appeal from the United States District Court for the Eastern District of Virginia in No. 1:20-cv-00274-TSE-LRV, Judge T. S. Ellis, III.

Decided: March 6, 2025

MICHAEL A. MORIN, Latham & Watkins LLP, Washington, DC, argued for plaintiff-appellant. Also represented by GABRIEL K. BELL, DAVID FRAZIER; YI SUN, San Diego, CA.

DANIEL KAZHDAN, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for defendant-appellee. Also represented by PETER J. AYERS,

MARY L. KELLY, WILLIAM LAMARCA, FARHEENA YASMEEN RASHEED; JESSICA D. ABER, MATTHEW JAMES MEZGER, Office of the United States Attorney for the Eastern District of Virginia, United States Department of Justice, Alexandria, VA.

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

LOURIE, *Circuit Judge*.

This case, arising from a civil action to obtain a patent under 35 U.S.C. § 145, returns to this court following a remand in *ImmunoGen, Inc. v. Hirshfeld*, No. 2021-1939, 2022 WL 885774 (Fed. Cir. Mar. 25, 2022) ("*ImmunoGen II*"). Following vacatur of the district court's grant of summary judgment in favor of the government, the case proceeded to a bench trial on the question whether ImmunoGen, Inc. is entitled to a patent for the invention claimed in U.S. Patent Application 14/509,809 ("the '809 application").[1] Determining that the claims of the application are "fatally indefinite and obvious," and that the claims are unpatentable under the doctrine of obviousness-type double patenting, the district court entered judgment in favor of the government, denying ImmunoGen's claim for entitlement to a patent. *ImmunoGen, Inc. v. Vidal*, 653 F. Supp. 3d 258, 307 (E.D. Va. 2023) ("*Decision*"). We affirm.

BACKGROUND

The '809 application, having a priority date of October 8, 2013, is directed to a dosing regimen for administering IMGN853 (*i.e.*, mirvetuximab soravtansine), a patented antibody drug conjugate ("ADC") used for treating certain ovarian and peritoneal cancers. Specifically, IMGN853 is

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[1] The '809 application published on May 14, 2015, as U.S. Patent Application Publication 2015/0132323.

a conjugate of (1) an antibody known as "huMov19," (2) a toxic maytansinoid payload known as "DM4," and (3) a charged chemical linker known as "charged sulfo-SPDB linker." *Decision*, 653 F. Supp. 3d at 269. The '809 application explains that, although IMGN853 exhibits promise as a cancer therapy, it can cause ocular toxicity in humans, resulting in keratitis and blurred vision. The inventors therefore set out to develop "a therapeutically effective dosing regimen [of IMGN853] that results in minimal adverse effects." '809 application, J.A. 209.

The '809 application contains three independent claims, of which claim 1 is representative:

> 1. A method for treating a human patient having an FOLR1-expressing ovarian cancer or cancer of the peritoneum comprising administering to the patient an immunoconjugate which binds to FOLR1 polypeptide,
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> wherein the immunoconjugate comprises an antibody or antigen-binding fragment thereof that comprises the variable light chain (VL) complementarity determining region (CDR)-1, VL CDR-2, VL CDR-3, variable heavy chain (VH) CDR-1, VH CDR-2, and VH CDR-3 of SEQ ID NOs: 6-9, 11, and 12, respectively, and a maytansinoid, and
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> wherein the immunoconjugate is *administered at a dose of 6 milligrams (mg) per kilogram (kg) of adjusted ideal body weight (AIBW) of the patient*.

J.A. 6574 (disputed "dosing limitation" emphasized).[2] It is undisputed that "[a] method of using IMGN853 to treat FOLR1-expressing ovarian cancer or peritoneum cancer was known in the art" at the time of the invention. J.A. 12176, ¶ 34. Accordingly, the patentability of the claims of the '809 application turns only on the dosing limitation.

After a patent examiner rejected the claims of the '809 application and the Patent Trial and Appeal Board ("the Board") affirmed, ImmunoGen brought suit in the U.S. District Court for the Eastern District of Virginia, seeking a judgment pursuant to 35 U.S.C. § 145 that would declare ImmunoGen's entitlement to a patent for the claimed invention. At summary judgment, the government argued that the claims are unpatentable because (1) the claimed "AIBW" renders the claims indefinite; (2) the dosing limitation renders the claims obvious over the asserted prior art; and (3) the claims are unpatentable under the doctrine of obviousness-type double patenting. The district court agreed with the government that, as a matter of law, there was no genuine dispute of material fact as to any of those issues and entered judgment in the government's favor. *ImmunoGen, Inc. v. Iancu*, 523 F. Supp. 3d 773, 799 (E.D. Va. 2021) ("*ImmunoGen I*"). We vacated and remanded, observing that "the district court resolved numerous factual disputes against non-movant ImmunoGen, an error that [was] fatal to its ultimate ruling." *ImmunoGen II*, 2022 WL 885774, at *1.

Following remand, the case proceeded to a three-day bench trial. Based on the evidence presented, the district

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[2] The claims at issue at trial were 242, 252–55, 258–65, 300, 317–25, 329–30, 341–49, and 354. *Decision*, 653 F. Supp. 3d at 272; ImmunoGen Br. 12 n.5. However, because all claims recite the dosing limitation at issue, the parties cite claim 1 as representative. We do the same.

court again determined that the claims are "fatally indefinite." *Decision*, 653 F. Supp. 3d at 289. The district court explained that the '809 application "fails to define AIBW . . . anywhere in its claims." *Id.* That the claims did not define the term was particularly important because the district court found that the intrinsic and extrinsic evidence established that there are various formulas for AIBW from which a person of ordinary skill in the art could have chosen. *See id.* Accordingly, the court determined that the claims fail to inform a person of ordinary skill in the art with reasonable certainty of the scope of the invention. *See id.* at 285, 289. The court further determined that the claims are unpatentable as obvious over ImmunoGen's own prior art that discloses treatment of ovarian and peritoneal cancers with IMGN853 using "total body weight," or "TBW," dosing, and other prior art disclosing AIBW dosing for other compounds. Specifically, it found that a person of ordinary skill in the art would have been motivated to arrive at the claimed dosing limitation because "(i) the problem of ocular toxicity was known, (ii) skilled artisans understood that changing the dose was a possible solution for adverse side effects such as ocular toxicity, and (iii) the prior art disclosed AIBW dosing as a potential means to eliminate or ameliorate ocular toxicity." *Id.* at 300. In the court's view, even the unpredictability of immunoconjugates was insufficient to overcome that obviousness determination. *Id.* The court entered judgment on those bases.[3]

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[3] As noted above, the government further challenged the patentability of the claims under the doctrine of obviousness-type double patenting, which the district court resolved in its favor. *See id.* at 306–07. On appeal, the parties agree that that issue rises and falls with the issue of obviousness, ImmunoGen Br. 2; Gov't Br. 21, so they do not brief it separately. We therefore do not address it further.

ImmunoGen timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(C).

DISCUSSION

ImmunoGen argues that the district court erred in each of its indefiniteness and obviousness analyses. Because we affirm the district court's judgment on obviousness grounds, as discussed below, we need not address indefiniteness.

I

"Obviousness is a question of law, which we review *de novo*, with underlying factual questions, which we review for clear error following a bench trial." *Honeywell Int'l, Inc. v. United States*, 609 F.3d 1292, 1297 (Fed. Cir. 2010). "A finding is 'clearly erroneous' when although there is evidence to support it, the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed." *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948); *accord Galderma Lab'ys, L.P. v. Lupin Inc.*, 122 F.4th 902, 907 (Fed. Cir. 2024). "If the district court's account of the evidence is plausible in light of the record viewed in its entirety, the court of appeals may not reverse it even though convinced that had it been sitting as the trier of fact, it would have weighed the evidence differently." *Anderson v. City of Bessemer City*, 470 U.S. 564, 573–74 (1985).

To determine whether a particular claimed invention would have been obvious over cited prior art, a factfinder must consider, among other things, whether "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and [whether] the skilled artisan would have had a reasonable expectation of success in doing so." *Novartis Pharms. Corp. v. W.-Ward Pharms. Int'l Ltd.*, 923 F.3d 1051, 1059 (Fed. Cir. 2019). "The presence or absence of a motivation to combine references in an obviousness determination is a

pure question of fact." *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014) (quoting *Alza Corp. v. Mylan Lab'ys, Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006)). "The presence or absence of a reasonable expectation of success is also a question of fact." *Id.*

II

ImmunoGen first argues that the district court erred in its motivation-to-combine analysis because it was undisputed that at the time of the invention, a person of ordinary skill in the art would not have known that IMGN853 caused ocular toxicity in humans. According to ImmunoGen, because "[t]here was no motivation to solve the problem of ocular toxicity," the claimed dosing limitation could not have been obvious. ImmunoGen Br. 34. We disagree.

As an initial matter, although ImmunoGen is correct that "[w]here a problem was not known in the art, the solution to that problem may not be obvious," *Forest Lab'ys, LLC v. Sigmapharm Lab'ys, LLC*, 918 F.3d 928, 935 (Fed. Cir. 2019), it does not follow that a claimed solution to an unknown problem is *necessarily* non-obvious. *See* ImmunoGen Br. 35. Indeed, the Supreme Court has made clear that "[i]n determining whether the subject matter of a patent claim [was] obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 419 (2007); *id.* at 420 ("Under the correct analysis, *any* need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." (emphasis added)); *see Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 97 F.4th 915, 929 (Fed. Cir. 2024) ("[A]lthough identifying a recognized problem or need in the prior art is one way to demonstrate motivation . . . the motivation analysis is not limited by the problem or need recognized by the inventors."); *Alcon Rsch., Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1368 (Fed. Cir.

2012) ("We have repeatedly held that the motivation to modify a prior art reference to arrive at the claimed invention need not be the same motivation that the patentee had."). Accordingly, that the *specific* problem the inventors of the '809 application purported to solve via the claimed dosing regimen was unknown does not necessarily mean that the dosing regimen itself was not obvious. We therefore do not find ImmunoGen's argument on this point persuasive.

In any event, after expressly acknowledging that the prior art does not "specifically disclose[] that IMGN853 caused ocular toxicity in humans," *Decision*, 653 F. Supp. 3d at 278, the district court proceeded to explain that because ocular toxicity was "a well-known adverse event in the administration of immunoconjugates that contain as a toxic payload the maytansinoid known as DM4," *id.* at 268 (footnote omitted), and because IMGN853 includes that DM4 payload, *id.*, a person of ordinary skill in the art "would [have] underst[oo]d the potential risk of ocular toxicity and would [have] monitor[ed] for ocular toxicity when testing IMGN853 in humans," *id.* at 269. *See id.* at 292. As the district court found, experts for each of ImmunoGen and the government agreed that "even though rabbits did not experience ocular toxicity when given IMGN853, preclinical results do not always translate to clinical safety when the same drug is tested in humans." *Id.* at 269 (footnote omitted). We therefore see no clear error in the district court's findings that a person of ordinary skill in the art, despite not *knowing* of IMGN853's ocular toxicity, would have nonetheless been motivated to monitor for those side effects when administering the drug to humans.

Next, ImmunoGen argues that the district court clearly erred in finding that a person of ordinary skill in the art would have been motivated to try AIBW dosing as a dosing methodology for IMGN853 to eliminate ocular toxicity. In that regard, the district court found that it would have been obvious "to experiment with changing the dosing

methodology to reduce toxicity while preserving the therapeutic effects" of IMGN853 because drug toxicities, including those associated with the DM4 payload, are "usually dose-related." *Id.* at 278 (quoting J.A. 13150). And it found that AIBW was a known dosing methodology for both large and small anticancer drugs. *Id.* at 279, 291. Further still, the district court found that the prior art discloses the use of AIBW "to reduce ocular toxicity in patients receiving the [antibiotic] drug ethambutol" and that, prior to the critical date, "researchers were motivated to try AIBW dosing in order to reduce toxic side effects in a clinical study on a radioimmunoconjugate." *Id.* at 279. The district court therefore concluded that, based on the evidence, a person of ordinary skill in the art would have understood AIBW to be a "potential solution for ocular toxicity" and that it would have been obvious "to experiment with AIBW in attempting to eliminate or ameliorate the toxicities associated with IMGN853." *Id.* at 294. Again, we see no clear error in these findings.

Nevertheless, ImmunoGen argues on appeal that "[j]ust because AIBW preexisted the '809 application, that does not mean it would [have] be[en] obvious to try—particularly when no ADC had ever been dosed using AIBW before." ImmunoGen Br. 39. In ImmunoGen's view, the district court "simply plucked AIBW dosing out of [a] multitude of possibilities without explaining the required motivation for selecting this particular dosing methodology." *Id.* at 40. We disagree.

The district court's findings, which are not clearly erroneous, reasonably support the conclusion that AIBW dosing, though never used for ADCs, would have been within the range of knowledge of a person of ordinary skill in the art when confronted with dosing-induced toxicities, and particularly when confronted with dosing-induced ocular toxicity. AIBW dosing was a well-known methodology that had been implemented on drugs both smaller and larger than IMGN853 and had been used to specifically reduce

ocular toxicity. Furthermore, the primary prior-art reference relied upon by the district court and parties, U.S. Patent Application Publication 2012/0282282 ("Lutz '282")—ImmunoGen's own publication which discloses IMGN853 and the relationship between the DM4 payload and ocular toxicity—discloses that "[t]he dosing regimen and dosages of [the disclosed ADCs] will depend on the particular cancer being treated, the extent of the disease and other factors familiar to the physician of skill in the art *and can be determined by the physician*." Lutz '282, ¶ 252 (emphasis added); *id.* ("One of skill in the art can review the [Physician's Desk Reference] . . . to determine dosing regimens and dosages of the [disclosed ADCs]."). ImmunoGen's argument that a person of ordinary skill in the art would not have been motivated to try AIBW dosing with IMGN853 is unpersuasive.

We turn now to the question whether the district court clearly erred in determining that a person of ordinary skill in the art would have been motivated to select the claimed dose of 6 mg/kg AIBW with a reasonable expectation of success. By way of background, this case requires familiarity with three different weight-based dosing methodologies: total body weight, ideal body weight, and AIBW. Total body weight, or "TBW," is a patient's actual body weight. Ideal body weight, or "IBW," is "an estimate of weight corrected for sex and height, and optionally frame size." '809 application, J.A. 157 ¶ 69. Finally, AIBW "refers to a size descriptor that accounts for sex, total body weight, and height." *Id.*, J.A. 158 ¶ 71. As the district court found, as of the '809 application's critical date, "there were many ways to define AIBW, all of which involved a variation of the following generic formula, wherein 'CF' stands for 'correction factor'":

$$\text{AIBW} = \text{IBW} + \text{CF}(\text{weight in kg} - \text{IBW})$$

Decision, 653 F. Supp. 3d at 274; *see* '809 application, J.A. 158 ¶ 71 (using 0.4 for CF). To put those three

measurements into useful context, "patients who weigh exactly their ideal body weight receive an *identical* dose of IMGN853 when dosed based on either AIBW or TBW." *Decision*, 653 F. Supp. 3d at 283.

With that understanding in mind, the district court found that Lutz '282 discloses dosing IMGN853 at around 6 mg/kg of TBW of the patient and that a 2013 abstract from the American Society of Clinical Oncology discloses that IMGN853 had been tested on humans at a dose of 5 mg/kg TBW. *Id.* at 275–76. Therefore, given that AIBW dosing was well known in the prior art, *id.* at 294, the district court concluded that a person of ordinary skill in the art "would start with doses of around 5 mg/kg or 6 mg/kg AIBW and then determine the precise dose based on routine optimization." *Id.* Indeed, as the district court found, "for patients who weigh exactly their ideal body weight, a dose of 6 mg/kg AIBW is identical to a dose of 6 mg/kg TBW," which is expressly disclosed as a suitable dose in Lutz '282. *Id.* at 297; *see id.* at 298 (noting expert witnesses' agreement that a patient at her ideal body weight "will receive the same amount of IMGN853 regardless [] whether she is dosed based on TBW or AIBW."). Thus, ImmunoGen's argument that "[i]t is particularly perverse to suggest that Lutz '282's dose of 6 mg/kg TBW would have led to the dose of 6 mg/kg AIBW," ImmunoGen Br. 49, falls short because, in at least some cases, 6 mg/kg AIBW is identical to 6 mg/kg TBW, as disclosed in Lutz '282. *See Decision*, 653 F. Supp. 3d at 297 (explaining that the '809 application "in effect seeks to cover a dose that was already disclosed in the prior art.").

As the district court aptly recognized, to hold otherwise "would prevent doctors from practicing what is already disclosed in the prior art for patients at their ideal body weight." *Decision*, 653 F. Supp. 3d at 298. We have explained that if "the disclosure is sufficient to show that *the natural result flowing* from the operation as taught would result in the performance of the questioned function, it

seems to be well settled that the disclosure should be regarded as sufficient." *PAR Pharm.*, 773 F.3d at 1195 (quoting *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981)). That is the case here. A doctor dosing a patient at his or her IBW with IMGN853 at a dose of 6 mg/kg TBW would necessarily be dosing that patient at 6 mg/kg AIBW, as claimed. This would be true regardless whether a doctor *knew* of AIBW dosing.

ImmunoGen's final challenge is that, even if a person of ordinary skill in the art would have been motivated to use AIBW dosing to eliminate ocular toxicity with a reasonable expectation of success, the district court clearly erred because it "d[id] not actually hold that a skilled artisan had a reasonable expectation of success that a *6 mg/kg AIBW dose* would solve ocular toxicity," which ImmunoGen argues is unpredictable. ImmunoGen Br. 50–51 (emphasis added). But ImmunoGen's framing of the reasonable-expectation-of-success analysis is inapt. As noted above, the obviousness inquiry is generally agnostic to the particular motivation of the inventor. *See KSR Int'l*, 550 U.S. at 419. That means that in this case the district court was not required to determine that a person of ordinary skill in the art would have had a reasonable expectation of eliminating ocular toxicity using a 6 mg/kg AIBW dose; indeed, the claims are silent as to any ocular toxicity problem. Instead, the inquiry merely required the district court to determine whether the evidence established that a person of ordinary skill in the art would have had a reasonable expectation that dosing a human at 6 mg/kg AIBW would have been effective in treating ovarian and peritoneal cancers, as claimed. *See Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021) ("The reasonable-expectation-of-success analysis must be tied to the scope of the claimed invention.").

Here, as noted above, the district court found that the prior art teaches that a dose of 6 mg/kg TBW is suitable for administering IMGN853 to humans for the treatment of

ovarian and peritoneal cancers, therefore providing "parameters" for the claimed AIBW dosing. *Decision*, 653 F. Supp. 3d at 299. Because those parameters "provided 'direction as to which of many possible choices is likely to be successful,'" the district court found that a person of ordinary skill in the art would have had a reasonable expectation of success. *Id.* (quoting *In re Cyclobenzaprine*, 676 F.3d 1063, 1071 (Fed. Cir. 2012)). That was not clearly erroneous. What is more, given the fact that the AIBW dosing would be the same as the TBW dosing for a patient at his or her IBW, and the fact that Lutz '282 expressly teaches "method[s] to overcome ocular toxicity of DM4-containing antibody drug conjugates at a range of dosages," Lutz '282, ¶ 272, including 6 mg/kg TBW, there is no need to further establish a reasonable expectation of success in this case. Lutz '282 clearly discloses this limitation and provides that it would have been reasonable to expect success in dosing IMGN853 at 6 mg/kg AIBW, at least for a patient at his or her IBW. *See Hewlett-Packard Co. v. Mustek Sys., Inc.*, 340 F.3d 1314, 1326 (Fed. Cir. 2003) ("[A] prior art product that sometimes, but not always, embodies a claimed method nonetheless teaches that aspect of the invention.").

We therefore conclude that the district court did not clearly or legally err in holding that the claims of the '809 application would have been obvious. The claims are therefore unpatentable.

CONCLUSION

We have considered ImmunoGen's remaining arguments and find them unpersuasive. For the foregoing reasons, the district court's judgment denying ImmunoGen's claim for entitlement to a patent is affirmed.

AFFIRMED