No. 21-1939

IN THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IMMUNOGEN INC.,

Plaintiff-Appellant

v.

KATHERINE K. VIDAL,

Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, in Her Official Capacity,

Defendant-Appellee

On Appeal from the United States District Court for the Eastern District of Virginia, Civ. No. 1:20-cv-00274 (Hon. T.S. Ellis III, U.S. District Judge)

PETITION FOR PANEL REHEARING

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INTRODUCTION

First and most importantly, the USPTO believes the Court's decision, concluding that ImmunoGen's claims to a known way of fine-tuning a known dose of a drug (by substituting adjusted ideal body weight for actual weight, which in some instances are identical) are not legally obvious, misapprehended some of the USPTO's arguments, and suggests the Court applied an incorrect legal standard. Though the USPTO respects this Court's time and files motions for rehearing sparingly, this decision impacts the USPTO's mission to not only incentivize and protect the investment essential for bringing life-saving and life-altering drugs to market, but to also ensure our patent laws are not misused to delay getting generic, biosimilar, and more affordable versions of those drugs into the hands of Americans who need them.

The USPTO appreciates that the Court is only remanding this case, but that was true in *KSR* as well. The government there explained that the "further proceedings on remand are themselves a product of the Federal Circuit's rigid rule," and "[t]hose costly proceedings are unnecessary." U.S. Certiorari-Stage Amicus Br. 16-17, *KSR Int'l Co. v. Teleflex Inc.*, No. 04-1350, 2006 WL 1455388 (May 25, 2006).

This kind of unnecessary remand is particularly problematic for pharmaceutical patents. There is a well-documented problem of drug manufacturers receiving numerous follow-on patents for trivial modifications that end up delaying generic

drugs' entry to the market.[1] This drives up the prices of life-saving and life-altering drugs and results in many Americans not having access the drugs they need. As the House of Representatives' Majority Staff Report shows, brand drug companies often bank on the fact that it will take years to find patents invalid while they maintain market exclusivity because generic drug companies cannot launch their products during the 30-month Hatch Waxman stay.[2] Making it harder for district courts to grant summary judgment exacerbates this problem.

Part of the reason drug manufactures are able to get these patents—which they are unable to get in other countries—is that they are often able to create factual issues by pointing to unpredictability in the art. The USPTO believes Judge T.S. Ellis III of the U.S. District Court for the Eastern District of Virginia, in upholding the USPTO's decision not to issue a patent on this follow-on drug, correctly rejected the unpredictability arguments here. The USPTO believes the Court misapprehended or overlooked some of the USPTO's arguments. Moreover, by finding certain disputed

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[1] *See generally* Staff of H.R. Comm. on Oversight & Reform, 117th Cong., Rep. on Drug Pricing Investigation 84 (Dec. 10, 2021), https://oversight.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf ("*Drug Pricing Investigation*"). The report specifically and repeatedly complains about "dosing patents." *See id.* at 79, 83, 84, 110, 117, 174; *see* E.O. on Promoting Competition in the American Economy (July 9, 2021) (Drug patents "have been misused to inhibit or delay—for years and even decades—competition from generic drugs and biosimilars, denying Americans access to lower-cost drugs.").

[2] *See Drug Pricing Investigation* at 84.

facts to be material, the Court may have implicitly adopted a legal standard inconsistent with *KSR* and this Court's precedent—one that might allow a patent on any follow-on pharmaceutical claim no matter how obvious to try. Under the proper standard, the factual disputes identified by the Court were not material to the obviousness inquiry and should not have precluded summary judgment.

Second, the USPTO seeks clarification on what genuine issues of material fact remain regarding indefiniteness. In concluding that genuine issues of material fact remained, the court pointed to disputes about the meaning of the intrinsic record. Because the USPTO believes that disputes over the intrinsic record are questions of law, the USPTO seeks clarification and/or affirmance of the district court.

BACKGROUND

1. ImmunoGen seeks a patent on a method of dosing its already patented drug IMGN853. ImmunoGen's own prior publications teach that IMGN853 is effective for treating ovarian cancers, and one reference, Lutz, even teaches dosing IMGN853 at, approximately, 6 mg/kg of the patient's TBW. Specifically, Lutz teaches:

> In one embodiment, the dose of [IMGN853] administered is at least about 4 mg/kg. In another embodiment, the dose is between about 4 mg/kg and about 16 mg/kg. In another embodiment, the dose is between about 4 mg/kg and about 8 mg/kg. In another embodiment, the dose is between about 5 mg/kg and 6 mg/kg. In another embodiment, the dose is between about 6 mg/kg and about 8 mg/kg. In a further embodiment, the dose is between about 6 mg/kg and about 7 mg/kg. In another embodiment, the dose is between about 7 mg/kg and about 8 mg/kg. In yet another embodiment, the dose is between about 4

> mg/kg and 6 mg/kg. In a further embodiment, the dose is between about 4 mg/kg and 5 mg/kg.

Immunogen, 523 F. Supp. 3d 773, 782 (E.D. Va. 2021) (citations omitted).

At the time of the invention, AIBW was a well-known method for dosing drugs to avoid certain negative outcomes that could arise from total body weight dosing. *Id.* at 783 (citing sources). In AIBW dosing, patients' doses are modified based on how far their body weight diverges from their ideal body weight (IBW). There are, however, different formulas for determining both IBW and AIBW. *Id.*

ImmunoGen's purported invention merely uses AIBW with IMGN853: where Lutz dosed IMGN853 at 6 mg/kg based on **TBW**, the claims now dose IMGN853 at 6 mg/kg based on **AIBW**, as recited in representative Claim 1:

> 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,
>
> wherein the immunoconjugate comprises [a set of antibodies and antigen-binding fragments and a maytansinoid—a group of drugs that includes IMGN853], and
>
> wherein the immunoconjugate is administered at a dose of 6 milligrams (mg) per kilogram (kg) of adjusted ideal body weight (AIBW) of the patient.

For patients at their ideal body weight, there is no difference between the AIBW dose claimed in ImmunoGen's application and the TBW dose suggested in the prior art. For patients who are neither clinically obese nor severely underweight, the change in

dose is minor. Both the examiner and the Board rejected ImmunoGen's claims as obvious.

2. ImmunoGen then brought a section 145 action, and the district court granted the USPTO's motion for summary judgment on obviousness and indefiniteness. As to obviousness, the district court found that the prior art taught AIBW dosing and its benefits; it taught that IMGN853 was a promising anti-cancer drug that had already entered clinical trials; it taught that one "can easily determine optimum . . . dosing methodologies" for IMGN853; it taught IMGN853 doses around 6 mg/kg based on total body weight; and it taught that ocular toxicity was often observed with immunoconjugates containing the same payload as IMGN853. *ImmunoGen*, 523 F. Supp. 3d at 780-83 (citations omitted). Based on this, the district court explained that a skilled artisan would discover that IMGN853 could cause ocular toxicity and that the artisan would then experiment with known dosing methodologies, such as AIBW. *Id.* at 793-94. The fact that "the shift from 6 mg/kg of total body weight dosing to 6 mg/kg of AIBW dosing does not significantly change the dose for patients who are not significantly overweight or underweight" underscored its conclusion that the claims would have been obvious. *Id.* at 792-93. The district court found the claims were indefinite because a skilled artisan would not be reasonably certain how to calculate AIBW dosing. In particular, the specification's definitions section says that (i) AIBW can be calculated, "for example," through a specific formula involving ideal body weight (IBW); (ii) IBW itself can "optionally"

account for the patient's body-frame size; and (iii) that IBW can be calculated "for example" through another specific formula that does not account for frame size. *Immunogen*, 523 F. Supp. 3d at 787. Because the specification intentionally uses terms that allow for various methods of calculating AIBW and IBW, the district court concluded that the claims were indefinite. In so doing, it observed that the uncertainty surrounding AIBW was compounded by the specification's incorporation of the Green reference, which provides multiple ways to calculate AIBW. *Id.* The district court recognized that the examples and prosecution history applied the "for example" formula, but it found these to be non-limiting under this Court's precedent. *Id.* at 788-89. ImmunoGen also sought to introduce expert testimony concerning how to interpret the intrinsic record, but the district court found this to be unnecessary. *Id.*

3. ImmunoGen appealed, and this Court vacated the grant of summary judgment and remanded for trial. As to obviousness, the Court concluded that the district court had improperly resolved "numerous" factual issues against Immunogen on summary judgment. Op. at 2. The Court specifically identified various facts that it believed created uncertainty as to whether it would have been obvious to use AIBW with IMGN853: (1) ocular toxicity was "not well-understood"; (2) immunoconjugates have "unique pharmacokinetic characteristics" that make it "difficult to generalize pharmacological effects"; (3) it was not known whether IMGN853 would cause ocular toxicity; (4) preliminary testing did not show "serious adverse events or dose-limiting toxicity"; (5) determining the proper dose is "difficult"; and (6) it was unclear

whether "ocular toxicity was a known negative effect of immunoconjugates like IMGN853." Op. 9-10 (citations omitted). In addressing the district court's conclusion that switching from TBW to AIBW dosing did not change the dose for patients at their ideal body weight, the Court observed that there was evidence that switching from 6 mg/kg TBW to 6 mg/kg AIBW reduced adverse ocular events in Phase 1 clinical trials. Op. 10. For indefiniteness, the Court concluded that there were genuine issues of material fact, and it remanded this as well. Op. 7-8.

ARGUMENT

I. The Court's obviousness analysis is flawed

The last time the Supreme Court interpreted the obviousness provision of the Patent Act was in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). There, the Supreme Court explained that obviousness tests that are helpful in some fields may be less helpful in others. *Id.* at 418-19. Thus, the Supreme Court held that it is sometimes appropriate to rely on "common sense" to show that an invention would have been obvious. *Id.* at 420-21. The Supreme Court also explained that the fact that an invention is "obvious to try" can render a claim obvious so long as "there are a finite number of identified, predictable solutions." *Id.* at 421. The expert testimony in *KSR* did not create a genuine issue of material fact because "the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors." *Id.* at 427.

This Court came to a similar conclusion in its 2007 decision in *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir. 2007) (decided while *KSR* was pending before the Supreme Court). Pfizer held a patent to amlodipine besylate tablets. The active ingredient, amlodipine, was taught in the prior art, and the question was whether it would have been obvious to use the besylate salt. The district court ruled that the salt would not have been obvious because "there was no reliable way to predict the influence of a particular salt species on the active part of the compound." *Id.* at 1364. This Court accepted the district court's factual finding as true, but it still reversed because the district court was improperly "equating unpredictability to patentability." *Id.* Likewise, in *Bayer v. Schering Pharma AG v. Barr Labs Inc.*, 575 F.3d 1341 (Fed. Cir. 2009), this Court found that a drug composition would have been obvious because, even though there was uncertainty regarding whether the formulation would work, it would have been considered a "viable option." *Id.* at 1348.

The USPTO recognizes that there is another line of this Court's cases where the Court upholds patent claims seemingly based on a lack of predictability in the pharmaceutical arts. *See Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021) (no "reasonable-expectation-of-success analysis around [the claimed] specific dosage of mifepristone"); *HZNP Medicines LLC v. Actavis Lab'ys UT, Inc.*, 940 F.3d 680, 704 (Fed. Cir. 2019) ("lack of predictability in relation to the changes" from one formulation to another); *Alcon Rsch., Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1370 (Fed. Cir. 2012) ("a person of ordinary skill in the art would not have a

reasonable expectation of success" in using the particular dose"); *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Lit.*, 676 F.3d 1063, 1070 (Fed. Cir. 2012) (obvious to experiment but no reasonable expectation of success); *Novartis Pharms. Corp. v. West-Ward Pharmaceuticals International Ltd.*, 923 F.3d 1051, 1060-62 (Fed. Cir. 2019) (motivation to pursue a treatment but insufficient "expectation of success"). All of these cases involved changes to the formulation, whereas here, the change (where there even is one) is simply the amount of drug given.

Although ImmunoGen has already received several patents on its IMGN853 drug and on its various uses,[3] this Court's ruling suggests that ImmunoGen may be able to obtain additional patents, with additional term, based on the unpredictability in the art. As the USPTO explained in its brief (pp. 40-46), that should not matter because a skilled artisan in ImmunoGen's shoes—having a promising anti-cancer drug—would continue experimenting to find a workable dose so that it could bring its drug to market. Resp. Br. 46. ImmunoGen's claimed AIBW dose for most patients amounts to nothing more than an optimized dose within the prior art range of around 6 mg/kg TBW. That would have been obvious. *See, e.g.*, *Almirall, LLC v. Amneal Pharms. LLC*, 28 F.4th 265, 272 (Fed. Cir. 2022) ("A prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." (citations omitted)).

[3] *See* U.S. Patent Nos. 8,557,966; 8,709,432; 9,133,275; 9,598,490; 9,670,280.

The Court's decision, remanding for trial, is inconsistent with *Pfizer* and *Bayer*. It is inconsistent with *Pfizer* because the fact that the precise results of changing the dose would have been unpredictable should not be equated to patentability. *Pfizer*, 480 F.3d at 1364. And it is inconsistent with *Bayer* because, even if the results of using AIBW dosing would have been uncertain, there should be no dispute that AIBW dosing would have been considered a viable option, given that the lower doses under AIBW would necessarily reduce side effects. *See Bayer*, 575 F.3d at 1348. At bottom, ImmunoGen should not receive a patent for running those basic experiments. This Court's decision fails to address this basic motivation.

The Court points to certain purported factual disputes, but, upon close scrutiny, none of them are material. The Court quotes the district court's conclusion that "'ocular toxicity was a known negative effect of [immunoconjugates] like IMGN853,'" but it goes on to fault the district court because, purportedly, the expert testimony did "not directly support that statement." Op. 9 (citing *Immunogen*, 523 F. Supp. 3d at 794 n.40). Respectfully, as the USPTO explained in its brief (p. 40), the expert testimony does directly support the statement. The district court quoted ImmunoGen's expert's report that "Off-target ocular toxicity – especially for DM4 and MMAF payloads – has always been a challenge in designing and manufacturing ADCs [immunoconjugates]." *ImmunoGen*, 523 F. Supp. 3d at 794 n.40. ImmunoGen's claimed immunoconjugate uses a DM4 payload. *See id.* at 778-79. Thus, the district court properly concluded that there was no dispute that ocular toxicity was a known

negative effect of immunoconjugates *like* IMGN853—even if the prior art did not conclusively teach that IMGN853 would necessarily have that toxicity. As the USPTO explained in its brief (p. 52), it should be beyond dispute that a skilled artisan would at least test for ocular toxicity. The Court failed to address this issue.

Next, the Court cites evidence to the effect that there was a degree of uncertainty regarding potential side-effects: "(1) ocular toxicity is not well-understood; (2) immunoconjugates have unique pharmacokinetic characteristics, making it difficult to generalize pharmacological effects; (3) it was not known that [IMGN853] would cause ocular toxicity; and (4) published results for Phase 1 testing of [IMGN853] reported no study drug-related serious adverse events or dose-limiting toxicity." Op. 9. To be clear, as discussed above, there was no dispute that immunoconjugates with the same payload as IMGN853 are associated with ocular toxicity; knowing this, a skilled artisan would have would have been concerned about the potential for ocular toxicity with IMGN853 (a specific immunoconjugate) and would have been motivated to look for ways to reduce those potential effects. As the USPTO explained in its brief (pp. 52-53), these kinds of uncertainties (which exist at some level for every pharmaceutical patent) are immaterial, because they would not have stopped a skilled artisan from trying to figure out how to optimize the dose and dosing methodology for administering IMGN853. It is worth noting that similar uncertainties may well exist if a subsequent patent applicant files an application for using AIBW dosing on another relatively untested drug. It should not be the case that every attempt to use a

dosing method known to yield good results for some drugs will require a full-blown district court trial before applying it to the next drug would be considered obvious.

In addressing the prior art's repeated teachings that one could "easily determine" the optimum dosing methodology, the Court states that these statements are "in the context of treating patients" as opposed to "determining a safe and effective dose." Op. 9. However, since the patent covers treating patients, this should not matter. Moreover, the basic dose here had already been determined in the prior art; the only question was whether AIBW dosing would be better than TBW dosing. There was nothing difficult about making that determination.

Lastly, in response to the district court's observation that switching "'from 6 mg/kg of [TBW] dosing to 6 mg/kg AIBW dosing does not significantly change the dose for patients who are not significantly overweight or underweight,'" Op. 10 (citing 523 F. Supp. 3d at 792-93), the Court states that "the '809 Application and other evidence show that this switch to AIBW dosing reduced adverse ocular events in Phase 1 clinical trials." *Id.* The Court's response misses the district court's point, which was that, as a matter of arithmetic, someone at their ideal body weight would receive the same 6 mg/kg dose that they would have received in the prior art. *See* USPTO Resp. Br. at 34; Appx8179. The Court's failure to address the district court's point about how a person at their ideal body weight would receive the same dose as in the prior art is a stand-alone reason for revisiting the Court's decision. As the USPTO explained (Resp. Br. at 36), ImmunoGen's claims are "broad enough to read on

obvious subject matter," so they "are unpatentable." *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1281 (Fed. Cir. 2015), *aff'd on other grounds sub nom. Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261 (2016).

Beyond that, the fact that AIBW dosing reduced adverse ocular events in clinical trials is wholly unsurprising, since, for anyone above their ideal body weight, AIBW dosing will result in lower doses, and thus fewer and less severe side effects, than TBW dosing. This expected result should not allow ImmunoGen to receive a claim that covers even patients for whom there is no change in dose.

Ultimately, as in *KSR*, there is no genuine issue of material fact because "the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors." *Id.* at 427.

II. The USPTO requests guidance on the indefiniteness remand or, alternatively, an affirmance

The Court concluded that there were genuine issues of material fact precluding a finding of indefiniteness. Op. 7-8. Should the Court remand, the USPTO seeks clarification on what factual issues are still open.

This Court's decision reviewed the intrinsic record—the definitions section (where the specification expressly allows multiple AIBW formulas), the examples (where the specification applies a specific AIBW formula), and the prosecution history (where the USPTO did not make an indefiniteness rejection and applied the "for

example" formula). Op. 7-8. The interpretation of the intrinsic record is a pure question of law, so that should not be the basis for a genuine issue of material fact. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1342 (Fed. Cir. 2015); Resp. Br. 27-29. This Court also noted that, as to extrinsic evidence, "both parties' experts testified that AIBW dosing involves drug-specific formulas and correction factors." Op. 8. As the Court recognized and the USPTO explained in its brief (p. 28), that is an undisputed fact.

The Court concluded that, "When we view this evidence in the light most favorable to ImmunoGen—as we must in our review—we conclude that there are still disputed questions of material fact and summary judgment is therefore inappropriate." Op. 8. Given that the meaning of the intrinsic record is a pure question of law and given that it is an undisputed fact that, as a general proposition, AIBW dosing involves drug-specific formulas and correction factors, the USPTO is uncertain as to what disputed questions of material fact remain. The USPTO respectfully seeks clarification on what issues remain for the remand. In the alternative, this Court should simply affirm the district court's indefiniteness ruling.

CONCLUSION

Because the remand order in this case is incorrect as to obviousness and unclear as to indefiniteness, the panel should rehear this case and affirm the district court.

Respectfully,

/s/ Daniel Kazhdan

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CERTIFICATE OF COMPLIANCE WITH
FEDERAL RULES OF APPELLATE PROCEDURE 32 AND 35

I hereby certify that this petition complies with the requirements of Federal Rule of Appellate Procedure 32(a)(5) and (6) because it has been prepared in 14-point Garamond, a proportionally spaced font. I further certify that this petition complies with the word limitation of Federal Rule of Appellate Procedure 35(b)(2)(A) because it is 3,626 words, excluding the parts exempted under Circuit Rule 35(c)(2).

/s/ Daniel Kazhdan
DANIEL KAZHDAN

CERTIFICATE OF SERVICE

I hereby certify that on July 8, 2022, I electronically filed this petition with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the appellate CM/ECF system. I further certify that I will cause 18 paper copies to be filed with the Court within two days unless another time is specified by the Court, in accordance with Circuit Rule 35(c)(4) and this Court's Administrative Order Regarding Electronic Case Filing, ECF-10(D).

The participants in the case are represented by registered CM/ECF users and service will be accomplished by the appellate CM/ECF system.

/s/ Daniel Kazhdan
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