UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BTG INTERNATIONAL LIMITED, JANSSEN BIOTECH, INC., JANSSEN ONCOLOGY, INC., JANSSEN RESEARCH & DEVELOPMENT, LLC,

Plaintiffs-Appellants

v.

AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., WOCKHARDT BIO AG, WOCKHARDT USA LLC, WOCKHARDT LTD., MYLAN PHARMACEUTICALS INC., MYLAN INC., WEST-WARD PHARMACEUTICALS CORP., nka Hikma Pharmaceuticals USA Inc., HIKMA PHARMACEUTICALS LLC, TEVA PHARMACEUTICALS USA, INC.

Defendants-Appellees

PAR PHARMACEUTICAL, INC., PAR PHARMACEUTICAL COMPANIES, INC., RISING PHARMACEUTICALS, INC.,

Defendants

No. 2019-1147

Appeals from the United States District Court for the District of New Jersey in Nos. 2:15-cv-05909-KM-JBC, 2:16-cv-02449-KM-JBC, and 2:17-cv-06435-KM-JBC, Judge Kevin McNulty.

BTG INTERNATIONAL LIMITED, JANSSEN BIOTECH, INC., JANSSEN ONCOLOGY, INC., AND JANSSEN RESEARCH & DEVELOPMENT, LLC,

Plaintiffs-Appellants

v.

AMERIGEN PHARMACEUTICALS, INC., AMERIGEN PHARMACEUTICALS LIMITED,

Defendants-Appellees

No. 2019-1148

Caption continued on inside cover

Appeal from the United States District Court for the District of New Jersey in No. 2:16-cv-02449-KM-JBC, Judge Kevin McNulty.

JANSSEN ONCOLOGY, INC.,

Appellant

v.

AMERIGEN PHARMACEUTICALS LIMITED, ARGENTUM PHARMACEUTICALS LLC,

Appellees

No. 2019-1323

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2016-00286 and IPR2016-01317.

JANSSEN ONCOLOGY, INC.,

Appellant

v.

MYLAN PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., TEVA PHARMACEUTICALS USA, INC., WEST-WARD PHARMACEUTICAL CORPORATION, HIKMA PHARMACEUTICALS LLC,

Appellees

No. 2019-1324

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2016-01332 and IPR2017-00853.

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JANSSEN ONCOLOGY, INC.,

Appellant

V.

WOCKHARDT BIO AG,

Appellee

No. 2019-1325

Appeal from the United States Patent and Trademark Office,
Patent Trial and Appeal Board in No. IPR2016-01582.

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February 28, 2019

CERTIFICATE OF INTEREST

I, Constantine L. Trela, Jr., counsel for Plaintiffs-Appellants Janssen Biotech, Inc., Janssen Oncology, Inc., and Janssen Research & Development, LLC, certify the following:

1. The full name of every party or *amicus* represented by me is:

Janssen Biotech, Inc., Janssen Oncology, Inc., and Janssen Research & Development, LLC

2. The name of the real party in interest (if the party named in the caption is not the real part in interest) represented by me is:

N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Janssen Biotech, Inc. and Janssen Oncology, Inc. are wholly owned subsidiaries of Johnson & Johnson, which is a publicly held corporation. No other publicly held corporation owns 10% or more of the stock of Janssen Oncology, Inc.

Janssen Research & Development, LLC is a wholly owned subsidiary of Centocor Research & Development, which is a wholly owned subsidiary of Janssen Biotech, Inc., which is a wholly owned subsidiary of Johnson & Johnson, which is a publicly held corporation. No other publicly held corporation owns 10% or more of the stock of Janssen Research & Development.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus* now represented by me in the trial court or agency or are expected to appear in this court (**and who have not or will not enter an appearance in this case**) are:

Sidley Austin LLP: Bindu Donovan, Todd L. Krause, Lisa A. Schneider, S. Isaac Olson, H. Ashley Chi, Andrew T. Langford**,** Amanda A. Potter, Jesselyn C. Pe

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Robinson Miller LLC: Donald A. Robinson, Keith J. Miller, Justin T. Quinn, Michael J. Gesualdo

Desmarais LLP: Bindu Donovan

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

BTG International Limited, et al. v. MSN Pharmaceuticals Inc. & MSN Laboratories Private Ltd., Civil Action No. 18-02372-KM-JBC (D.N.J.); *Janssen Biotech, Inc. et al. v. Mylan Pharms., Inc. et al.*, Civil Action No. 1:15-cv-00130 (N.D. W.Va.); *BTG International Limited, et al. v. Qilu Pharmaceutical Co., Ltd. & Qilu Pharma, Inc.,* Civil Action No. 2:18-cv-16521 (D.N.J.).

Dated: February 28, 2019

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CERTIFICATE OF INTEREST

I, Anthony C. Tridico, counsel for Plaintiffs-Appellants BTG International Ltd., certify the following:

1. The full name of every party or *amicus* represented by me is:

BTG International Limited

2. The name of the real party in interest (if the party named in the caption is not the real part in interest) represented by me is:

N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

BTG International Ltd. is a subsidiary of BTG plc. BTG plc is a publicly held corporation that holds 100% of BTG International (Holdings) Ltd, which in turns owns 100% of BTG International Ltd.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus* now represented by me in the trial court or agency or are expected to appear in this court (**and who have not or will not enter an appearance in this case**) are:

Robinson Miller LLC: Donald A. Robinson, Keith J. Miller, Justin T. Quinn, Michael J. Gesualdo

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page

Cases

Statutes

Other Authorities

INTRODUCTION

Although the inventions claimed in the '438 patent are "methods for the treatment of a prostate cancer," in which two compounds—abiraterone and prednisone—are administered in "therapeutically effective amounts," the Board construed the claims to cover "treatments" that have no effect on cancer at all. That construction led to the Board's conclusion that the claimed inventions would have been obvious. The construction is unreasonable. The obviousness determination therefore cannot stand.

Defendants try to avoid the error, first by asserting waiver, and then by arguing that the erroneous construction made no difference. There was no waiver. The Board's Final Written Decisions address Janssen's proposed construction at length, leaving no doubt that Janssen advanced the same position below and that the Board understood and rejected that position. And the Board's analyses of reasonable expectation of success and objective indicia expressly rest on its erroneous claim construction, leaving no doubt concerning the impact of its error. The Board never found, because its claim construction did not require it to find, that a skilled artisan would have had a reasonable expectation that a combination of two compounds, neither of which had ever demonstrated efficacy against prostate cancer, would result in a therapy in which both drugs have an anti-cancer effect. Likewise, the Board did not assess the nexus between objective indicia and

the claimed invention because it misapprehended the claimed invention. The Board's decisions should be vacated.

As for the district court, its obviousness decision should not exist, for section 315(e)(2) precludes it. The statute is clear and should be applied as written. The legislative history confirms that Congress knew how to impose the scope and finality limitations Defendants want—Congress had done so before—and chose *not* to include them in this statute.

The court's obviousness determination was also deeply flawed on the merits. Using the patent as a roadmap, the court assumed that abiraterone was a known "treatment" for advanced prostate cancer, disregarding the fact that "treatment" requires anti-cancer effects, which had never been demonstrated. Nor did the court explain why a skilled artisan would have looked to a secondary hormonal therapy in the first place when it found elsewhere in its opinion that such therapies had been discredited by the time of invention. Those in the field viewed further pursuit of hormonal therapies as a dead end. That skepticism and the other powerful indicia of non-obviousness might have served as a check on hindsight if the court had applied the correct legal standards. The court failed to do so, and hindsight therefore carried the day.

Finally, Defendants challenge the district court's factual finding that their generic products, administered as directed by their labels, would induce

infringement. Their arguments rest on mischaracterizations of the record and the FDA approval process. The court considered both and correctly found infringement.

ARGUMENT

I. The Board's Decisions Should Be Vacated Because They Rest on an Erroneous Claim Construction.

The Board erred in failing to require that a "therapeutically effective amount" of prednisone be an amount that has an effect on the cancer itself when used in combination with abiraterone. Blue Br. 28-35. Defendants cannot dodge this error by claiming waiver. Janssen submitted its construction to the Board, and the Board addressed it. On the merits, the Board adopted an unreasonably broad construction that requires vacatur.

A. Janssen Presented Its Claim Construction Position Below.

Defendants assert that Janssen waived the claim construction it urges on appeal by failing to press it below. But Janssen consistently argued—starting in the *Amerigen* IPR and continuing through the others—that the specification's express definition means that "treating" requires an effect on the cancer itself. Appx29454; Appx29456-29461; Appx29587-29591; Appx35282-35283; Appx35312-35317; Appx41639-41640; Appx41680-41684. Indeed, the Court need look no further than the Final Written Decisions to see that there was no waiver. The Board devoted several pages to addressing Janssen's construction—

that both components of the claimed invention must have an anti-cancer effect—without so much as mentioning waiver. Appx184-185; Appx204-208; Appx255-256; Appx272-276; Appx310-312; Appx333-334; Appx356-359. Far from presenting "a new question of claim scope" or "new issue on appeal," *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1370-71 (Fed. Cir. 2002), Janssen has advanced the same position all along.

Defendants contend that the Board's rejection of Janssen's request for reconsideration of the *Amerigen* institution decision put Janssen "on notice that the Board's construction did *not* require prednisone to have an anti-cancer effect," and Janssen needed to make its disagreement clear "in its upcoming patent-owner response." Red Br. 21-22. But Janssen did that. Janssen contended that Defendants had to prove that prednisone would have been expected to have an anti-cancer effect, *i.e.*, "that prednisone could be used for 'the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer.'" Appx29588; *see also* Appx29544; Appx29549; Appx29587-29593. Janssen also submitted the district court's *Markman* decision, which the Board explicitly addressed. Appx184-185.

Janssen reiterated its view that "treatment" requires an anti-cancer effect at the hearing, distinguishing administering prednisone for "side effects" from

providing "an anticancer benefit." Appx30087. Although Defendants assert that Janssen never argued that "ameliorating abiraterone's side effects was insufficient to practice the claims" (Red Br. 23), Janssen argued just that: *e.g.*, Petitioners' "focus … has been on the side effects…. They can't go after the invention directly" (Appx30072). And the Board plainly understood Janssen's position. The very first question the Board asked at the *Amerigen* hearing was: "Now, I think one of the patent owner's arguments is about treatment. Is the prednisone … treating the cancer or is it ameliorating the side effects …?" Appx30055-30056. The Board heard Janssen's claim construction position, highlighted it at the hearing, and then rejected it. That is not waiver. *See O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008).

B. The Board's Claim Construction Was Unreasonably Broad.

The Board adopted an unbounded construction under which a "treatment" for cancer need not have any effect on cancer, or any specific effect whatsoever. As Janssen explained (Br. 28-35) and the district court held (Appx4061-4082), that construction cannot be reconciled with the claims or specification, which make clear that a "therapeutically effective amount"—whether of abiraterone or prednisone—is "an amount sufficient to treat the cancer" when used together, and that the claimed "method[s] for the treatment of a prostate cancer" are therapies in which both drugs have an anti-cancer effect. The '438 patent addresses only one

condition requiring treatment: cancer. It never mentions pain relief, palliation, or any other effect. Blue Br. 30-31, 33. The Board's construction thus "expand[s] the scope of the claims far beyond anything described in the specification." *Kinetic Concepts, Inc. v. Blue Sky Med. Grp., Inc.*, 554 F.3d 1010, 1019 (Fed. Cir. 2009).

To be sure, "the claims refer to 'treatment of a prostate cancer *in a human*'" (Red Br. 27), but italicizing the phrase "in a human" does not change the object or nature of the "treatment." The invention is a method for the "treatment of a prostate cancer," not the treatment of a human's reaction to cancer therapy. Defendants further try to expand "treatment" by rewriting the definition, asserting that it "refers to 'management' and 'control' of cancer, which are not limited to attacking cancer cells." Red Br. 25. However, the definition refers not to "management" and "control" of cancer generally, but to "management or control of a tumor or … metastatic cancer cells or tissue" in particular. Appx759(3:46-50).

Defendants attempt to avoid the absurdity of construing claims to methods of treating cancer to cover therapies that have no anti-cancer effect by contending that the claims require abiraterone, which has an anti-cancer effect. Red Br. 28. But under the Board's construction, neither abiraterone nor prednisone is required to provide an anti-cancer effect—even though both must be administered in a "therapeutically effective amount." If one can practice the claimed method by

administering prednisone without an anti-cancer effect, then neither component needs to have such an effect—a plainly unreasonable construction.

The construction is also unreasonable in its boundlessness, because it sweeps in any possible effect, whether or not it has anything to do with cancer cells or tumors. Blue Br. 28, 32-33. Defendants assert that the construction is limited "only to effects of prednisone related to prostate-cancer treatment as described in the prior art." Red Br. 29. The Board's decisions reflect no such limitation, nor would it find support in the specification, which says nothing about "effects of prednisone … described in the prior art." *Id.*

Defendants also point to the specification's listing of prednisone as a steroid, which they say suggests "that prednisone may 'treat' cancer by producing familiar steroid effects." Red Br. 26. But the specification nowhere mentions "familiar steroid effects." To the contrary, it states that the "amount of the steroid administered to a mammal having cancer is an amount that is sufficient to treat *the cancer*." Appx762(10:21-24) (emphasis added). The specification identifies the same effect—*i.e.*, on the cancer itself—for anti-cancer agents and antibiotics, which include prednisone. Appx761(7:51-54) ("amount of the additional anti-cancer agent … is an amount that is sufficient to treat the cancer"); Appx762(9:47-50) (same for "antibiotic agent"); Blue Br. 30-31. The patentees thus did not "separately highlight[] steroids" (Red Br. 26)—they simply identified steroids as a

class of compounds that can include agents with anti-cancer effects when administered in sufficient amounts. Appx761-762.[1] And "to treat the cancer" means the eradication, removal, *etc*. of a tumor or cancer cells or tissue (Appx759(3:46-50)), not palliation or dealing with side effects.

Defendants, like the Board, ultimately seize on the term "include" in the specification's definition of "treatment," viewing it as making the definition open-ended, so that "treatment" can occur without *any* anti-cancer effects. That conclusion is wrong as a matter of law. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1344-45 (Fed. Cir. 2003) (*Amgen I*). Even ignoring the claims and the rest of the specification, and giving "include" its broadest possible meaning, the Board's construction cannot be justified. Blue Br. 31-35.

Defendants try to avoid the case law, arguing, for example, that *Amgen I* dealt with "comprising" rather than "including," and that it did not consider use of the term in a specification. Red Br. 29. *Amgen I* concerned "a misconstruction of the term 'including,'" 314 F.3d at 1344, and the Court addressed whether the *specification's* reference to a particular structure "*as including* 166 specified amino acid residues" required 166 amino acids or permitted fewer. *Id.* at 1343, 1344

[1] Defendants also rely (Br. 27) on arguments the patentees did *not* make during prosecution. That is wrong as a matter of law. *DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314, 1326-27 (Fed. Cir. 2001) ("[J]ust as we can draw no inference from what the examiner did not say, we can draw no inference from what [patentee] did not argue.").

n.14. The Court held that "including" as used in that specification meant "that the named elements are essential, but other elements may be added." *Id.* at 1345. Accordingly, it would be "simply illogical" to construe the claims to mean anything other than the sequence "must have—at minimum—all 166 amino acids shown in Figure 6." *Id.* Likewise, in *Lucent Technologies, Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1214 (Fed. Cir. 2008), the Court reiterated that it "has consistently interpreted 'including'" to mean "that the listed elements … are essential but other elements may be added." *Id.* *Lucent* dealt with claim language (Red Br. 30), but the Court relied principally on *Amgen I*, confirming that "include" does not have a broader meaning when used in a specification rather than a claim. *Id*.

Of course, when "include" or "including" is not used to identify a minimum set of requirements, it may have a different effect. Thus, in the case Defendants cite (Br. 30), "included" was used to identify examples within a broader "class." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1302 (Fed. Cir. 2006) ("Included within the class of humans treatable with products of the invention…."). If the '438 patent had similarly specified that certain effects are "included within the class" that qualify as treatment, that might support the Board's construction. But the patent does not do that. The patent makes clear that the claimed method of cancer "treatment" must "treat" the cancer. Because the

Board's construction encompasses methods of treatment that have no effect on cancer at all, it is unreasonable.

C. The Board's Erroneous Construction Requires Vacatur.

The Board did not assess the patentability of the inventions actually claimed, so its decision must be vacated. Blue Br. 44; *see also Vivint, Inc. v. Alarm.com Inc.*, No. 2017-2218, 2018 WL 6720031, at *5 n.6 (Fed. Cir. Dec. 20, 2018) (claim construction error precluded review of "the Board's application of that construction to the prior art"). When, as here, the Board's reasoning is based on a false premise, this Court cannot supply alternate grounds on appeal. *See SEC v. Chenery Corp.*, 332 U.S. 194, 196 (1947). The "Board's judgment must be reviewed on the grounds upon which the Board actually relied." *In re Applied Materials, Inc.*, 692 F.3d 1289, 1294 (Fed. Cir. 2012).

Defendants' attempt to salvage the Board's decisions runs headlong into *Chenery*, so Defendants invoke findings the Board never made. For example, Defendants say "[t]he Board specifically found that Wockhardt established a reasonable expectation 'that prednisone would "treat" prostate cancer' even under a narrower definition of 'treat.'" Red Br. 31 (citing Appx359). But the Board did not find, much less provide a basis for finding, that prednisone would have been expected to have an anti-cancer effect when combined with abiraterone as in the claimed methods. Indeed, given the concessions of Defendants' own experts,

noted by Janssen (Br. 15-16, 57-58) and largely ignored by Defendants, the Board could not have made such a finding on this record.

Defendants also point to evidence that, in their view, shows that the Board was "entitled" to make certain necessary findings, or that the Board was not "compelled" to make findings that would support non-obviousness. *E.g.*, Red Br. 32, 33, 35. Whether the Board *could* have made findings sufficient to support its decisions is irrelevant. The Board did *not* make such findings, because it was focused on the wrong invention. Similarly, the fact that the Board did not make certain findings that might support non-obviousness—that, for example, it did not find that abiraterone and prednisone were "incompatible" (Red Br. 31)—is no substitute for findings that support obviousness. Obviousness requires a finding that a person of ordinary skill would have reasonably expected abiraterone and prednisone to both produce an anti-cancer effect in combination. The lack of any such finding warrants vacatur.

Defendants' attempt to rehabilitate the Board's treatment of objective indicia fares no better. Defendants do not dispute that the Board's assessment of the objective evidence rested entirely on its erroneous understanding of the claimed invention—findings concerning the nexus between objective indicia and the invention the Board *thought* was claimed are no substitute for findings concerning the invention actually claimed. Blue Br. 39-45.

Long-Felt Need. — The Board discounted evidence of long-felt need because it concluded that abiraterone had been "available and underutilized" for a decade. Appx366. That actually underscores that there was an unmet need for the invention, properly understood. Abiraterone may have been available, but it had not met the need for an effective treatment, hence its "underutilization." On a proper understanding of the claims, the fact that the claimed combination therapy—in which *both* elements provide anti-cancer benefits—succeeded in extending lives while compounds that had long been available did not strongly supports non-obviousness.

Defendants do not dispute that the claimed combination therapy met an urgent, previously unmet need by improving survival of mCRPC patients as no therapy had before. Instead, Defendants say the claims do not *require* "improved survival" or "treating mCRPC patients." Red Br. 33. But the specific need does not have to be identified in the claims. If it did, claims to novel compounds—which do not identify the problem they solve—would never satisfy a long-felt need. *Millennium Pharmaceuticals, Inc. v. Sandoz Inc.*, 862 F.3d 1356 (Fed. Cir. 2017), is instructive. There, this Court reversed as clearly erroneous a decision discounting evidence that the invention met needs such as improved "remission" and "survival rates," even though the claims did not mention those needs. *See id.* at 1369.

Commercial Success. — Defendants suggest that commercial success comes down to a series of factual disputes the Board resolved in Defendants' favor. But any such findings related to the nexus between ZYTIGA's unquestioned commercial success and an invention the patentees never claimed. Because the Board addressed the wrong questions, its answers cannot justify its decision.

On a proper reading of the claims, abiraterone's "availability (and underutilization) for approximately a decade" (Appx366) only underscores the powerful evidence of commercial success. Whereas abiraterone alone was a failure, abiraterone administered "in combination with prednisone for the treatment of patients with [mCRPC]" according to its FDA-approved label (Appx38907) was an undisputed success. Defendants point to a supposed blocking patent, but it is undisputed that BTG, a licensing company—not "Janssen" (*contra* Red Br. 35)—made that patent "available for licensing" and "actively shopped [it] around to other companies" between 2000 and 2004. Appx368-369. And Boehringer had rights to abiraterone in the 1990s but abandoned them. Appx42683. It was not until Dr. de Bono's counterintuitive insight that abiraterone could be used in a combination therapy with prednisone to treat cancer that the molecule took off.

Skepticism. — Janssen identified skepticism regarding secondary hormonal therapies, which would include *both* abiraterone *and* prednisone. Blue Br. 43. The Board's construction prevented it from considering the weight of such skepticism

against an invention that claims a combination of two secondary hormonal therapies, both having an anti-cancer effect. Defendants cannot justify the Board's failure to consider this evidence in light of the invention claimed and so simply skip over it.

With the Board's claim construction error laid bare, its obviousness analysis falls apart. The Board's decisions should be vacated.

II. The District Court's Interpretation of Section 315(e)(2) Ignores the Statute's Text and Clear Legislative History.

The starting point when construing a statute is the statute's text, and where the text is clear, that is also the ending. *Puerto Rico v. Franklin Cal. Tax-Free Tr.*, 136 S. Ct. 1938, 1946 (2016). Neither Defendants nor the district court identify any ambiguity in the text of section 315(e)(2). The statute is unambiguous and should be construed to mean exactly what it says.

A. Section 315(e)(2) Applies to All Petitioners, Not Only Unsuccessful Petitioners.

Defendants largely ignore the actual text of section 315(e)(2), which provides that the petitioner in an IPR "that results in a final written decision … may not assert in … a civil action … that the claim is invalid on any grounds that the petitioner raised or reasonably could have raised during" the IPR. The statute draws no distinction between successful and unsuccessful petitioners, and does not

require final agency action or an appealable order. Blue Br. 46-52. When an IPR "results in a final written decision," the petitioner is estopped.

The analysis can and should stop there. *United States v. Woods*, 571 U.S. 31, 46 n.5 (2013) (legislative history relevant, if at all, only when text is ambiguous). But the legislative history only confirms what the statute's text makes clear. Section 315(e)(2)'s *inter partes* reexamination predecessor, section 315(c), applied only to unsuccessful petitioners (*see* Blue Br. 47-48), and only after all appeals had run their course.[2] The legislative history of the AIA describes the estoppel of section 315(e)(2) as "enhanced" and "strengthened." Blue Br. 47. And those descriptions do not refer, as Defendants and their *amicus* assert, to the fact that estoppel under the new statute applied both to grounds that were raised and those that could have been raised. Red Br. 52; AAM Br. 19-20. As Defendants concede, the predecessor statute had the same scope, so section 315(e)(2) was not "enhanced" or "strengthened" in that regard. Their alternative speculation that perhaps legislators were referring to legislation proposed years earlier and never

[2] Section 315(c) provided for estoppel where a patent had been "finally determined to be valid and patentable," language this Court held required exhaustion of all appeals. *See Bettcher Indus. Inc. v. Bunzl U.S.A., Inc.*, 661 F.3d 629, 642-48 (Fed. Cir. 2011).

adopted is equally illogical and unfounded.[3] Nor can the change be dismissed as merely "substitut[ing] the new term of art 'final written decision'" for the prior statute's phrasing (AAM Br. 21), because "final written decision," unlike a final determination that a patent is "valid and patentable," is outcome-neutral, and encompasses IPRs in which petitioners succeed as well as those in which they fail. When Congress changes statutory language, the change is presumed to signify a change in meaning. *See Stone v. INS*, 514 U.S. 386, 397 (1995). Congress changed the relevant language here, and that change should be given effect.

B. Defendants' Contrary Arguments Are Untethered from the Statute and Legally Unfounded.

With nothing in the statute's text or history to support their position, Defendants are forced into arguments that defy logic.

They begin by categorizing parts of section 315—subsections (a) and (b)—as forum-choice provisions and subsection (e) as somehow different. Br. 48-49. Defendants ignore that section 315 as a whole, through its subsections, ensures that prior art validity challenges are decided in only one forum. Subsections (a) and (b) identify when validity can be determined only in district court, and subsection (e) identifies when it can be determined only in an IPR. Read as a whole, the statute

[3] *See* J. Matal, *A Guide to the Legislative History of the America Invents Act: Part II of II*, 21 Fed. Cir. B. J. 539, 617-19 (2012).

makes clear that a single forum will decide the relevant validity challenges. That disposes as well of Defendants' assertions regarding "inconsistent results." Br. 50-51. Where only one result is reached on invalidity, as the statute provides, inconsistent results are impossible.

Defendants point to section 315(e)'s heading as dictating a meaning contrary to its text, but ignore that a heading is relevant *only* where the statute's text is ambiguous, *see Bhd. of R.R. Trainmen v. B&O R.R.*, 331 U.S. 519, 528-29 (1947), and Defendants do not even attempt to identify ambiguity in this statute's text. Even more telling, although the heading Defendants invoke is "Estoppel," they quickly discard that broad term (*see* Blue Br. 47 n.3) and assert, without support, that it is really *collateral* estoppel that is "relevant here" (Red Br. 50). After that leap in logic, they take another, asserting that since Congress borrowed a "term[] of art," it is presumed to have incorporated into the statute "the cluster of ideas" that have accumulated around that term, unless the statute "otherwise instruct[s]." Br. 51 (citations omitted). Congress did not borrow a term of art—at least not the one, "collateral estoppel," Defendants wish—and the statute *does* "otherwise instruct," by providing that its estoppel applies to "petitioner[s]," without limitation, and also includes other features not found in the "cluster of ideas" Defendants say Congress must have meant to adopt. *E.g.*, PTO Br. 6 n.1.

Defendants also argue that to apply section 315(e)(2) as written would threaten due process (Br. 49) and produce absurd results (Br. 53-54). As to the first, they fail to explain how due process is imperiled when Congress provides alternative routes for presenting invalidity defenses and gives the defendant a choice. Indeed, a generic manufacturer can choose to file an IPR petition challenging Orange Book-listed patents long before any ANDA or infringement suit is filed. *Cf. Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2143-44 (2016) (petitioner "need not have a concrete stake in the outcome"). This option, among others, eliminates any "Catch-22" (AAM Br. 2) or possible conflict between the Hatch-Waxman Act and AIA. As to the second, there is nothing absurd about enjoining a drug maker whose product is found to infringe unless and until the patent is ultimately held invalid by an Article III court—whether in an infringement suit absent an IPR or on appeal after a PTAB decision—as shown by, for example, decisions enjoining generic launches pending appeal of invalidity determinations. *See, e.g.*, *Eli Lilly & Co. v. Actavis Elizabeth LLC*, No. 2010-1500, 2010 WL 3374123 (Fed. Cir. Aug. 26, 2010) (per curiam).[4] The fact that

[4] Defendants likewise err in asserting (Br. 37) that the Court need not address section 315(e)(2) if it affirms the PTAB. Even if the patent were ultimately held invalid, Janssen had a right to exclusivity under the Hatch-Waxman Act until invalidity was decided in accordance with the statute. Whether Defendants were unjustly enriched by procuring an erroneous ruling that allowed them to launch prematurely, and whether Janssen is entitled to a remedy, should be addressed on remand.

Congress gave infringement defendants the option of challenging validity via an alternate process with a relaxed standard of proof, but otherwise left in place the carefully crafted and balanced requirements of the Hatch-Waxman Act (Blue Br. 49-50), is not only not absurd, but reflects a legislative determination on an important policy question that the courts should respect.[5]

Finally, Defendants' attempt to import into the "final written decision" that triggers section 315(e)(2) a requirement of appealability is misguided. As noted above (p. 15-16), estoppel under the predecessor statute was tied to exhaustion of all appeals, and Congress's decision to change that is presumed to have meaning. And, as the PTO explains (PTO Br. 14-15), nothing about the fact that a final written decision *can* be appealed per section 319 means that a final written decision must be appealable to trigger section 315(e). A court's final judgment can generally be appealed, *see* 28 U.S.C. § 1291, but the fact that post-judgment motions may make a final judgment temporarily non-appealable does not mean it

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[5] Defendants also fail to recognize that section 315(e)(2), and the AIA in general, are far broader in scope than litigation under the Hatch-Waxman Act. Even if the statute's plain language produced a "puzzling result[]" in this context—and it does not—"if that effect was unintended, it is a problem for Congress, not one that federal courts can fix." *Lewis v. City of Chi.*, 560 U.S. 205, 216-17 (2010). Courts cannot act as super-legislatures to "harmonize" (AAM Br. 23) unambiguous statutes. Moreover, estoppel without regard to outcome perfectly fits Congress's objective of providing an "alternative" and "complete[] substitute" for district court litigation of invalidity defenses. Blue Br. 48.

is not still a final judgment (or that it is not entitled to preclusive effect, *see* PTO Br. 11; Blue Br. 51).[6] As this Court has explained, it is important "to distinguish between different concepts of finality," for "[d]efinitions of finality cannot automatically be carried from appeals cases to preclusion problems." *Fresenius USA*, 721 F.3d at 1340-41. Defendants ignore that important distinction.

III. On the Merits, Defendants Cannot Defend the District Court's Erroneous Obviousness Determination.

Apart from its error in addressing obviousness at all, the court further erred in assessing the merits.

[6] Defendants brush aside the denial of Janssen's rehearing requests by asserting that an infringement case ceases to be "a civil action" once appealed and that an appellee defending a judgment of invalidity is not making an "'assertion' of invalidity." Red Br. 60. An appeal does not change "a civil action" into something else. *See, e.g.*, *M.R. v. Ridley Sch. Dist.*, 744 F.3d 112, 125-26 (3d Cir. 2014) ("an appeal is part of a 'civil action … in a district court'"). An infringement suit appealed after a final judgment is an action that "remains pending before this court," which is why post-judgment determinations that claims are unpatentable apply even on appeal. *Fresenius USA, Inc. v. Baxter Int'l, Inc.*, 721 F.3d 1330, 1332 (Fed. Cir. 2013). And Defendants' notion that appellees do not make "assertions of invalidity" when defending judgments on appeal is inconsistent with this Court's understanding. *See, e.g.*, *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 716 (Fed. Cir. 1991) ("appellee asserts that the patent is invalid" due to obviousness).

A. The District Court Failed to Identify a Reason to Select Abiraterone.

The district court's obviousness determination rests on a threshold legal error: failure to identify any reason a skilled artisan would have selected abiraterone in 2006. Blue Br. 53-55.

Defendants do not dispute that the law required the court to identify a reason for plucking abiraterone out of the sea of prior art—instead, they repeat the court's error by focusing on references involving abiraterone as their starting point. Red Br. 38-39. But the issue is not whether abiraterone had been considered a possible prostate cancer treatment; it is whether there was a reason a skilled artisan would have selected abiraterone over the hundreds of other more promising alternatives available at the time. Blue Br. 55; *see In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000) ("findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components"); *In re Rouffet*, 149 F.3d 1350, 1359 (Fed. Cir. 1998) (same). Neither Defendants nor the court specifically address that issue. If anything, the court's findings point the other way, including the finding that the "prevailing belief" was that the cancer became androgen-independent after ADT, making potential second-line hormonal therapies—including abiraterone and prednisone, separately or together—futile and not worth pursuing. Appx87.

B. The District Court Applied the Wrong Legal Standard for Reasonable Expectation of Success.

The court committed a further legal error in assessing the requirement of a reasonable expectation of success by failing to consider the appropriate scope of the claimed invention—namely, whether a skilled artisan would have expected *both* abiraterone and prednisone to have an anti-cancer effect in a combination therapy. Blue Br. 56-59. Defendants respond by asserting that "only a *reasonable expectation* of success, not certainty" is required. Red Br. 41. True enough, but the court's error was not that its expectation standard was too lax; it was that it failed to assess the reasonable expectation of success in achieving the "*claimed invention*." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016). The court correctly construed the claims (Appx3599),[7] but failed to consider whether, or find that, a skilled artisan would have expected each component in the combination to meet its definition of "treatment," which required both to have an anti-cancer effect. Blue Br. 56, 58-59.

Defendants' unsupported assertion that "many references had taught to use CYP17 inhibitors with corticosteroids, and no studies had proven that abiraterone and prednisone worked at cross-purposes" (Red Br. 43-44) merely repeats the

[7] Defendants failed (Red Br. 42) to preserve any challenge to the court's construction. *United States v. Great Am. Ins. Co. of N.Y.*, 738 F.3d 1320, 1328 (Fed. Cir. 2013) ("arguments that are not appropriately developed in a party's briefing may be deemed waived"); *see* Fed. Cir. R. 30(a)(2)(E).

court's error. It provides nothing to suggest an expectation that abiraterone and prednisone in combination would each have anti-cancer effects; it merely conflates motivation to combine with reasonable expectation of success. That is error. *Intelligent Bio-Sys.*, 821 F.3d at 1367 (inquiry requires "a reasonable expectation of achieving what is claimed").

C. The District Court Legally Erred in Evaluating Objective Indicia.

The court also committed legal errors in assessing objective indicia.

Among other errors, the court reached a determination of obviousness and then shifted the burden to Janssen to disprove obviousness through objective indicia. Blue Br. 59-64. Defendants dismiss this as mere quibbling over phrasing. Red Br. 44-45. The court's error, however, was not its choice of words, but its failure to integrate objective indicia into its analysis of the prior art. For instance, the court read references such as O'Donnell without considering the contemporaneous, real-world reaction to it—namely, that one of the world's largest pharmaceutical companies, with every incentive to develop abiraterone, abandoned it after the study addressed in O'Donnell, and that other major companies, given the study results and an opportunity to license abiraterone, passed. Blue Br. 57.

The court compounded this error by shifting the burden to Janssen. Blue Br. 61-64. For example, Janssen established that ZYTIGA with prednisone, as

labeled, has been an enormous commercial success. The FDA-approved label for ZYTIGA specifically tracks the claimed invention—administration of abiraterone in combination with prednisone for the treatment of prostate cancer. Appx132. The commercial embodiment of the '438 patent is thus precisely what is marketed. Rather than presuming nexus, however, the court put the burden on Janssen and accepted Defendants' argument, without evidence, that any success was due to abiraterone alone. Blue Br. 60-61. This is no mere factual dispute. *See* Red Br. 46. As this Court has explained, "if the marketed product embodies the claimed features, … then a nexus is presumed and the burden shifts to the party asserting obviousness." *Brown & Williamson Tobacco Corp. v. Phillip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000). The burden was on Defendants, and the court failed to hold them to it. Blue Br. 61.

The court's burden-shifting is also evident in how the court dealt with the supposed "blocking patent." Blue Br. 61-62. The effect of any so-called blocking patent, especially when there are licensing efforts, is context-specific, *Acorda Therapeutics, Inc. v. Roxane Labs., Inc.*, 903 F.3d 1310, 1338 (Fed. Cir. 2018), and it was *Defendants'* burden to show that the context here indicated that the patent actually blocked others. Rather than hold Defendants to their burden, the court *presumed* (without evidence) a deterrent effect and then turned to Janssen to demonstrate that BTG's licensing efforts were not "desultory" or "lackluster."

That was error. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359-60 (Fed. Cir. 2007) (burden "never shifts to the patentee.").

The court committed the same error in assessing skepticism—although the court acknowledged skepticism toward second-line hormonal treatments, which would include the claimed combination of abiraterone and prednisone, it nonetheless said that any skepticism was attributable to abiraterone alone, and required Janssen to disprove that. Blue Br. 62-63. Defendants assert that skepticism of abiraterone may have come from expected side effects (Red Br. 46-47), but offer nothing in support. None of the evidence credited by the court (Appx121) relied on abiraterone side effects; it rested on the "prevailing belief" that second-line hormonal treatments in general were not worth pursuing. Blue Br. 62. Defendants say that "[s]ome researchers were pessimistic about second line therapies; others were not" (Red Br. 46), but if the evidence is mixed, the tie does *not* go to the patent challenger, who always has the burden to establish invalidity by clear and convincing evidence. The court erred by shifting the burden to Janssen.

Finally, the court committed additional legal errors in assessing long-felt need: the court erred in concluding a 60 percent improvement in survival was a mere difference in degree, and it further failed to consider the unique benefits offered by ZYTIGA plus prednisone over other therapies. Blue Br. 63-64.

Defendants ignore these problems, simply asserting without support that "the court was entitled to consider [any benefit] 'a real improvement' and not a quantum leap." Br. 47. And Defendants dismiss the multiple FDA priority reviews given to ZYTIGA and other therapies as "simply show[ing] that prostate cancer was an important problem." Br. 47. The priority reviews, however, illustrate the continuing long-felt need for the kind of dramatic improvement provided by ZYTIGA and, in fact, underscore it. *Cf. Millennium*, 862 F.3d at 1362 (reversing obviousness findings, noting that the "FDA approved [a cancer drug] in record time"). Better treatment for advanced prostate cancer was needed, and FDA's priority review for ZYTIGA and other drugs confirms that. ZYTIGA filled that need by improving survival rates by 60 percent, while also improving quality of life. Blue Br. 64. Had achieving that sort of improvement been obvious, others would have done so.

IV. The District Court Correctly Found Infringement.

In a final effort to preserve the judgment, Defendants challenge the court's infringement findings. Infringement "is a question of fact which [this Court] review[s] for clear error on appeal from a bench trial." *Glaxo, Inc. v. Novopharm*,

Ltd., 110 F.3d 1562, 1565 (Fed. Cir. 1997).[8] The district court committed no clear error.

Induced infringement traditionally requires "'first that there [be] direct infringement', and 'second, that the alleged infringer knowingly induce[] infringement and possess[] specific intent to encourage another's infringement.'" *MEMC Elec. Materials, Inc. v. Mitsubishi Materials Silicon Corp.*, 420 F.3d 1369, 1378 (Fed. Cir. 2005). This analysis applies in Hatch-Waxman cases with an exception: because the proposed generic products have not yet been approved, proof of actual direct infringement is not required. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003); *see Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1331 (Fed. Cir. 2003) (per curiam).

Rather, the "pertinent question" in a Hatch-Waxman case "is whether the proposed label instructs users to perform the patented method," *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010), such that "if a particular drug *were* put on the market, it *would* infringe the relevant patent," *Vanda Pharm. Inc. v. W.-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018). If so, this

[8] Defendants argue that the infringement findings are subject to *de novo* review (Br. 61), citing *Bayer Schering Pharma AG v. Lupin Ltd.*, 676 F.3d 1316 (Fed. Cir. 2012). The Court's opinion in *Bayer* does not address the standard of review, and to the extent the Court applied *de novo* review, that is because it was reviewing a dismissal under FRCP 12(c), which is always reviewed *de novo*. Neither *Bayer* nor any other decision suggests that *de novo* review applies where, as here, the district court enters infringement findings following trial.

"establishes the requisite intent for inducement," *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1369 (Fed. Cir. 2017), and the "active steps taken to encourage direct infringement," *Takeda Pharm. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 630 (Fed. Cir. 2015).

Here, the court found "[t]he *only* way to follow [Defendants'] labels is to administer abiraterone, together with prednisone, in specific doses, to a mCRPC patient." Appx66. "The defendants' proposed labels," the court concluded, "would infringe each element of the asserted claim. They teach the reader to perform every element of the patented method." Appx67; Appx60 ("the combination therapy embodied in the label meets the claim limitations of the patent."); *see* Appx51-52. In reaching this conclusion, the court found that abiraterone and prednisone "are FDA-approved in combination to treat cancer." Appx56 (citing Appx21316). The court further found that FDA's approval indicates that prednisone is approved for its anti-cancer effect in the combination. Appx56-57 (citing Appx21317-21318, Appx21321, Appx21777-21778). According to the court, the labels also "embody an intent to induce a physician to" infringe (Appx61)—they "clearly express an intent that physicians be authorized to prescribe abiraterone plus prednisone for the treatment of mCRPC" (Appx63 (citing Appx21324)). In short, "the content of the ANDA labels virtually compels an inference of specific intent to encourage the infringing use" (Appx65), and the

court found the evidence and studies underlying FDA's approval of ZYTIGA supported this (Appx53-67).

Defendants principally challenge the finding that their labels sufficiently disclose the effects of prednisone. They note FDA has not approved prednisone as a monotherapy to treat cancer and argue that Janssen's reading of the labels conflicts with regulations requiring "'adequate and well-controlled' clinical trials" for new uses. Red Br. 62. If Defendants were marketing prednisone, the label and indications for prednisone might be relevant. But here Defendants sought approval for generic abiraterone products, so what matters is what their abiraterone labels instruct. Those labels specifically teach that abiraterone should be co-administered with prednisone, and the court found that these labels "signif[y] that these agents are FDA-approved in combination to treat cancer." Appx56; *see* Appx10-16, Appx56-58, Appx60.

Moreover, the court found that the labels are based on sufficient studies. *See* Appx58 ("[t]he fact remains that the FDA did approve the combination-based treatment of mCRPC based on a combination study."). The court found that the information submitted to FDA demonstrated prednisone has an anti-cancer effect in combination with abiraterone. *See, e.g.*, Appx12 ("this suggested that a glucocorticoid such as prednisone, at least when administered in combination with abiraterone, has an anti-cancer effect."); Appx12-13 & n.11.

Ignoring this, Defendants assert that "Zytiga's label teaches only the non-infringing use of prednisone for safety, not anti-cancer efficacy." Red Br. 63. However, in rejecting that argument, the court credited expert testimony on how those in the relevant field would understand the labeling. Appx56. Defendants come nowhere close to showing any clear error.

Finally, Defendants argue that the court erred because it failed to find direct infringement. Red Br. 64. As this Court has explained, the relevant issue is whether "if a particular drug *were* put on the market, it *would* infringe the relevant patent." *Vanda Pharm.*, 887 F.3d at 1129. And this is precisely what the district court found: the "*only* way to follow these labels is to administer abiraterone, together with prednisone, in specified doses, to a mCRPC patient." Appx66. Thus, the "defendants' proposed labels here would infringe each element of the asserted claim. They teach the reader to perform every element of the patented method." Appx67.

CONCLUSION

The Court should vacate the Board decisions and remand for further proceedings. The Court should also reverse the district court's judgments and direct entry of judgment for Janssen, or, alternatively, vacate the judgments of invalidity and remand for further proceedings.

Dated: February 28, 2019

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on February 28, 2019, I electronically filed the foregoing using the Court's CM/ECF system, which will send notifications to all counsel registered to receive electronic notices.

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Circuit Rule 32(a), because it contains 6,952 words (as determined by the Microsoft Word 2016 word-processing system used to prepare the brief), excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

This brief also complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type-style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared in a proportionally spaced typeface using the Microsoft Word 2016 word-processing system in 14-point Times New Roman font.

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