IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH LLC,	)	
	)	
Plaintiff,	)	
	)	
vs.	)	**Case No. 21 C 1338**
	)	
ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB,	)	
	)	
Defendants.	)	

FINDINGS OF FACT AND CONCLUSIONS OF LAW

MATTHEW F. KENNELLY, District Judge:

Wyeth LLC has sued AstraZeneca Pharmaceuticals LP and AstraZeneca AB (collectively AstraZeneca) for infringement of two patents: United States Patent Nos. 10,603,314 (the '314 patent) and 10,596,162 (the '162 patent).[1] Wyeth contends that AstraZeneca, through the promotion and sale of its drug Tagrisso (osimertinib), induced infringement of claims 1, 3, and 9 of the '314 patent and claim 1 of the '162 patent. After a five-day trial, a jury found AstraZeneca liable for induced infringement and awarded damages. The Court then held a two-day bench trial on AstraZeneca's equitable defenses and its counterclaim that the patents were invalid due to indefiniteness. This decision constitutes the Court's findings of fact and conclusions of law on those issues. For the reasons stated below, the Court finds that (1) the patents are not unenforceable and (2) the asserted claims are not invalid for indefiniteness.

[1] The Court granted the defendants' motion to dismiss Wyeth LLC's co-plaintiff, Puma Biotechnology, Inc., for lack of Article III standing. *See Puma Biotech., Inc. v. AstraZeneca Pharms. LP*, No. 21 C 1338, 2024 WL 1157120 (D. Del. Mar. 18, 2024).

Background

The parties to this suit are pharmaceutical companies that commercialize drugs to treat cancer and other illnesses. The patents-in-suit claim a method of treating a form of non-small cell lung cancer (NSCLC). NSCLC is associated with overactivity of the epidermal growth factor receptor (EGFR), an enzyme that is involved in cell division and growth. Drugs that treat this condition are known as EGFR tyrosine kinase inhibitors (TKIs or inhibitors), and these TKIs bind to certain parts of the EGFR to prevent the enzyme from triggering cancerous cell growth.

Two TKIs, gefitinib and erlotinib (referred to collectively as g/e), showed some promise in treating NSCLC. Gefitinib and erlotinib are classified as "reversible" inhibitors; they form non-covalent bonds with EGFR that dissociate over time. There are two principal limitations to g/e treatment. First, only patients with certain EGFR mutations are sensitive to g/e therapy; the parties refer to these mutations as "sensitizing mutations." In other words, to be a candidate for g/e treatment, a patient needs to have EGFR with the requisite sensitizing mutation(s). Second, "[a] significant limitation in using [reversible inhibitors such as g/e] is that recipients thereof may develop a resistance to their therapeutic effects after they initially respond to therapy, or they may not respond to EGFR-TKIs to any measurable degree at all." '314 Patent at 3:19–23.

The patents-in-suit claim a method for treating "g/e resistant NSCLC." The inventors claim that g/e resistance can be overcome by using "irreversible" EGFR inhibitors that covalently bind to a specific amino acid at a specific location of EGFR. Specifically, the asserted claims of the '314 patent recite:

> 1. A method for treating gefitinib and/or erlotinib resistant non-small cell lung cancer in a patient in need thereof, comprising administering daily to the patient having gefitinib and/or erlotinib resistant non-small cell lung cancer a pharmaceutical composition comprising a unit dosage of an irreversible epidermal growth factor receptor (EGFR) inhibitor that covalently binds to cysteine 773 residue in the ligand-binding pocket of EGFR or cysteine 805 residue in the ligand-binding pocket of erb-B2.
>
> [. . .]
>
> 3. The method of claim 1, wherein the irreversible EGFR inhibitor covalently binds to cysteine 773 residue of EGFR.
>
> [. . .]
>
> 9. The method of claim 1, wherein the route of administration is oral.

'314 Patent at 35:52–36:65.

In addition, the claims of the '162 patent are directed at EGFR with a specific mutation, the "T790M mutation," which is associated with g/e resistance. The asserted claim of '162 patent recites:

> 1. A method of treating gefitinib and/or erlotinib resistant non-small cell lung cancer having a T790M mutation in SEQ ID NO: 1 in a patient, comprising administering daily to the patient having gefitinib and/or erlotinib resistant non-small cell lung cancer having a T790M mutation in SEQ ID NO: 1 a pharmaceutical composition comprising a unit dosage of 2-500 mg of an irreversible EGFR inhibitor that covalently binds to cysteine 773 of the catalytic domain within the SEQ ID NO: 1 having a T790M mutation; wherein the irreversible EGFR inhibitor is not CL-387,785.

'162 Patent at 35:48–36:48.

The patents-in-suit were originally issued to Wyeth and a non-party, General Hospital Corporation. In 2006, General Hospital Corporation assigned its rights in the patents-in-suit to Wyeth. Wyeth was acquired by Pfizer in 2009 and remains a wholly owned subsidiary of Pfizer.

In September 2021, Wyeth sued AstraZeneca, alleging that AstraZeneca's

irreversible EGFR inhibitor Tagrisso (osimertinib) infringes both patents-in-suit. After a claim construction hearing, the Court resolved numerous disputes regarding the meaning of the asserted claims. *See Puma Biotech., Inc. v. AstraZeneca Pharms. LP*, 21 C 1338, 2023 WL 2683559 (D. Del. Mar. 29, 2023). AstraZeneca then moved for summary judgment, arguing in relevant part that (1) the patents were invalid because they failed to meet the enablement and written description requirements of 35 U.S.C. § 112; and (2) use of Tagrisso did not infringe the asserted claims. The Court concluded that there were genuine issues of material fact regarding invalidity and infringement and therefore denied summary judgment on those points. *See Puma Biotech., Inc. v. AstraZeneca Pharms. LP*, No. 21 C 1338, 2024 WL 1157120 (D. Del. Mar. 18, 2024). After a five-day trial, a jury concluded that the patents were not invalid and that AstraZeneca induced infringement of the patents. The Court then held a two-day bench trial on AstraZeneca's equitable defenses and its counterclaim that the patents were invalid due to indefiniteness.

Discussion

A. Equitable defenses

AstraZeneca first argues that the patents are unenforceable because Wyeth engaged in misconduct before the Federal Food and Drug Administration (FDA) with respect to Pfizer's drug Vizimpro (dacomitinib).[2] AstraZeneca asserts that the patents are unenforceable under the doctrines of unclean hands, implied waiver, and patent misuse. Although the legal elements of these defenses vary somewhat, AstraZeneca

[2] The parties do not dispute, for purposes of AstraZeneca's equitable defenses, that Wyeth and Pfizer can be treated as a single actor.

centers its argument on the same core facts, most of which are not disputed. The Court therefore will summarize the relevant facts and then discuss each defense.

The FDA approved AstraZeneca's new drug application for Tagrisso in April 2018. About five months later, in September 2018, the FDA approved Pfizer's new drug application for Vizimpro. Tagrisso and Vizimpro are both irreversible EGFR inhibitors approved for first-line treatment of patients with NSCLC with g/e sensitizing mutations. First-line treatment refers to the first or primary treatment that is given after a patient is diagnosed with a certain condition. The parties do not dispute that Vizimpro's FDA-approved first-line indication is the same as Tagrisso's FDA-approved first-line indication in all relevant respects.

FDA drug approval is an extensive process that mandates compliance with a detailed federal regulatory regime. One important piece of this is the Drug Price Competition and Patent Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act was passed to address congressional concerns regarding the balance between "medical innovation and the growing cost of health care." Cong. Rsch. Serv., R44643, *The Hatch-Waxman Act: A Primer*, 1 (2016). "Through amendments to both the patent law and the food and drug law, the Hatch-Waxman Act established several practices intended to facilitate the marketing of generic pharmaceuticals while providing brand-name firms with incentives to innovate." *Id.*

The Hatch-Waxman Act requires, in relevant part, that an innovator (i.e. brand-name) pharmaceutical company applying for FDA approval of a new drug submit "the patent number and the expiration date" of each patent that "claims a method of using such drug for which approval is sought or has been granted" for which "a claim of patent

infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1)(A)(viii)(II). The FDA then lists the patents in a publication entitled *Approved Drug Products With Therapeutic Equivalence Evaluations*, more commonly known as the "Orange Book." *See Janssen Pharmaceutica, N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1355 (Fed. Cir. 2008). In addition, the innovator company must provide a brief, 250-character "use code" that identifies "each pending or approved method of use and related patent claim." 21 C.F.R. § 314.53(b)(1). Use codes are also listed in the Orange Book. The innovator company must submit the relevant patent information within thirty days of FDA approval of the drug or—if the patent is issued after FDA approval of the drug—within thirty days of the issuance of the patent. *See* 21 U.S.C. § 355(c)(2).

Innovator companies have an incentive to timely list relevant patents in the Orange Book. Namely, a generic drug company seeking expedited approval of a generic version of the competing name-brand drug must "certify" that, for each patent listed in the Orange Book, "either (I) no patent information has been filed with the FDA; (II) the patent has expired; (III) the patent will expire on a particular date and approval of the ANDA should be deferred until expiration; or (IV) in the opinion of the ANDA applicant, the patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug." *Janssen Pharmaceutica, N.V.*, 540 F.3d at 1356 (citing 21 U.S.C. § 355(j)(2)(A)(vii)). If an innovator company decides to sue the generic company for patent infringement after receiving notice of the generic's certification to the FDA, the FDA will grant an automatic thirty-month stay of the generic drug's application while the

parties litigate the infringement dispute. 21 U.S.C. § 355(c)(3)(C). The Orange Book listing and certification requirements thus promote the "early resolution of patent disputes between generics and pioneering drug companies." *Id.* Innovator companies who do not comply with the deadlines for Orange Book listings are still permitted to belatedly list the relevant patents, but they are not eligible for the 30-month stay of a competing generic's ANDA application. *See* 21 C.F.R. §§ 314.53(d)(3), 314.94)(a)(vi).

At the time of Vizimpro's approval in 2018, the patents-in-suit had not yet been issued; therefore, Pfizer was under no obligation to list them in the Orange Book. Once the patents issued in 2020, Pfizer was required to list them in the Orange Book within thirty days if it believed that "a claim of patent infringement could reasonably be asserted" against another company that "engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1)(A)(viii)(II); *Id.* § 355(c)(2). Pfizer did not list either of the patents-in-suit for Vizimpro within thirty days of the patents' issuance.

After Wyeth filed its complaint against AstraZeneca for patent infringement with respect to Tagrisso in September 2021, AstraZeneca asserted in its answer that Wyeth's assertion that Tagrisso infringed the patents was inconsistent with Wyeth's failure to list the patents-in-suit in the Orange Book for Vizimpro:

> Pfizer has not submitted patent information for the '314 or '162 Patents to FDA for listing in the Orange Book with the approved Vizimpro NDA. Pfizer has thus recognized, acknowledged, and informed the public that the '314 and '162 Patents do not claim the use of an irreversible EGFR inhibitor for first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Defs.' Answer at ¶ 55. In AstraZeneca's view, because the first-line indications for Vizimpro and Tagrisso are effectively identical, Wyeth's assertion that Tagrisso's first-

line indication infringes the patents necessarily means that Pfizer was required to list the patents for Vizimpro. Thus, AstraZeneca contends, Pfizer's failure to list the patents reveals that "Wyeth/Pfizer did not believe that either patent covered the sole approved indication, which is the first-line treatment of patients with NSCLC." Defs.' Proposed Findings of Fact & Conclusions of L. at 8.

In April 2022, five months after AstraZeneca filed its November 2021 answer, Pfizer submitted the patents-in-suit to the Orange Book. AstraZeneca argues that Wyeth and Pfizer engaged in "bad faith misconduct" by listing the patents-in-suit "only after AstraZeneca's Answer and in an apparent attempt to align their own listings to benefit Wyeth's infringement positions in this case." *Id.* at 11.

AstraZeneca further argues that Wyeth and Pfizer engaged in misconduct by listing the patents because Vizimpro is not approved to treat g/e resistant NSCLC and therefore should never have been listed in the Orange Book at all. Relatedly, AstraZeneca argues that Wyeth and Pfizer submitted "improper use codes" in their Orange Book listing that "do not match the patented claim language nor . . . any approved use of Vizimpro." *Id.* at 16. The use code for the '314 patent reads:

> Administering daily a unit dosage for an irreversible EGFR inhibitor covalently binding as claimed for 1st line treatment of gefitinib [or] erlotinib resistant metastatic NSCLC with EGFR Exon 19 deletion or exon 21 L858R substitution.

DTX-0263. The use code for the '162 patent reads:

> Administering daily a unit dosage for an irreversible EGFR inhibitor covalently binding as claimed for 1st line treatment of gefitinib or erlotinib resistant metastatic NSCLC with EGFR Exon 19 deletion or exon 21 L858R substitution with T790M mutation.

DTX-0263. AstraZeneca asserts that Vizimpro has not been approved to treat g/e

resistant NSCLC and therefore that the use codes are not "supported by the approved labeling for the drug product." Defs.' Proposed Findings of Fact & Conclusions of L. at 18.

1. Unclean hands

AstraZeneca first argues that the patents are unenforceable because Wyeth has "unclean hands" based on Wyeth and Pfizer's untimely and allegedly improper Orange Book listing of the patents-in-suit for Vizimpro. "[A] determination of unclean hands may be reached when 'misconduct' of a party seeking relief 'has immediate and necessary relation to the equity that he seeks in respect of the matter in litigation,' *i.e.*, 'for such violations of conscience as in some measure affect the equitable relations between the parties in respect of something brought before the court.'" *Gilead Scis., Inc. v. Merck & Co.*, 888 F.3d 1231, 1239 (Fed. Cir. 2018) (quoting *Keystone Driller Co. v. Gen. Excavator Co.*, 290 U.S. 240, 245 (1933)). The Federal Circuit has stated that the "immediate and necessary relation" requirement is generally satisfied if there is "objective potential" that the misconduct "would enhance the claimant's position regarding legal rights that are important to the litigation if the impropriety is not discovered and corrected." *Id.* at 1240. The parties agree that "[t]he doctrine of unclean hands applies when (1) a party seeking affirmative relief (2) is guilty of conduct involving fraud, deceit, unconscionability, or bad faith (3) directly related to the matter in issue (4) that injures the other party (5) and affects the balance of equities between the litigants." *Sun Microsystems, Inc. v. Versata Enters., Inc.*, 630 F. Supp. 2d 395, 410 (D. Del. 2009) (internal quotation marks and citation omitted).

The parties dispute whether the Court may hold the patents unenforceable as a

result of an Orange Book violation when the Hatch-Waxman Act does not expressly authorize that remedy for untimely or improper listings. The parties also dispute whether Pfizer's Orange Book listing for Vizimpro is improper (aside from its untimeliness, which Wyeth concedes). The Court need not reach either of these issues because it concludes that AstraZeneca has not shown that the alleged misconduct at issue here "has immediate and necessary relation" to "the matter in litigation." *Gilead Scis., Inc.*, 888 F.3d at 1239.

AstraZeneca has not shown how Wyeth and Pfizer's alleged misconduct with respect to Vizimpro in any way enhanced or had the potential to enhance Wyeth's position in this litigation or to harm AstraZeneca's position. At the bench trial and in its proposed findings of fact and conclusions of law, AstraZeneca offered only two theories regarding how Vizimpro's Orange Book listing could have harmed AstraZeneca. First, AstraZeneca's expert witness, Prescott Lassman, testified that Wyeth's late listing "remove[d] an issue from the case" by eliminating the "inconsistency between the listing behavior and the arguments that [Wyeth] made in the complaint." Bench Trial Tr. at 192:5–17. The Court disagrees. Wyeth and Pfizer's belated listing did not erase the past; no one disputes that they did not list the patents as covering Vizimpro until AstraZeneca pointed out the issue. Nothing about Wyeth's subsequent decision to list the patents negates the "inconsistency" that Pfizer and Wyeth did not list the patents-in-suit when they issued. Nor did Pfizer and Wyeth's conduct "remove" this issue from the case. If AstraZeneca wished to present this inconsistency to the jury to argue in support of its position on non-infringement and/or inducement, the Court does not see (and AstraZeneca has not identified) any reason why Wyeth's late listing prevented it from

doing so. But AstraZeneca never raised this issue before the jury and never sought to do so. Nor did Wyeth ever introduce or rely on Vizimpro's Orange Book patent listings to bolster its case. The Court therefore does not see how this theory establishes any relation, much less an "immediate and necessary" one, between Wyeth's alleged Orange Book misconduct and "the matter in litigation." *Keystone Driller Co.*, 290 U.S. at 245.

Second, AstraZeneca briefly hypothesized in its closing arguments that if Wyeth had timely listed the patents-in-suit, AstraZeneca "could have gotten an outside opinion of noninfringement for" Tagrisso's first-line indication. AstraZeneca argued that "under the Supreme Court's inducement case law," if AstraZeneca "believe[s] it doesn't infringe, that can be a defense to inducement." Bench Trial Tr. at 304:19–305:1. The Court is not persuaded by this theory of harm. To start, AstraZeneca's contention that it might be in a better position in this suit if Pfizer had timely listed the patents-in-suit in the Orange Book is highly speculative. AstraZeneca has introduced no evidence to support this proposition, nor has it developed this argument in its proposed findings of fact and conclusions of law. In addition, AstraZeneca conceded that "there's no evidence that AstraZeneca relied on the non-listing" to make any relevant decisions with respect to Tagrisso and the patents-in-suit. *See* Bench Trial Tr. at 311:10–13. That is consistent with the testimony of Wyeth's expert, Daniel Troy, which the Court found credible and persuasive, that pharmaceutical companies conduct their own research regarding patents and do not rely exclusively on Orange Book listings. *See id.* at 252:1–253:22. Finally, as the Court has explained, nothing prevented AstraZeneca from arguing (or seeking to argue) to the jury that Pfizer's failure to list the patents-in-

suit was evidence that AstraZeneca's belief that Tagrisso's first-line indication does not infringe was reasonable.

In sum, AstraZeneca has not provided evidence sufficient to support a finding that Wyeth and Pfizer's alleged misconduct with respect to Vizimpro's Orange Book listings had any actual or potential effect on the outcome of Wyeth's infringement suit against AstraZeneca for Tagrisso. The Court therefore concludes that AstraZeneca has failed to meet the requirements for unclean hands and is not entitled to relief on this basis.

2. Implied waiver

AstraZeneca next argues that Wyeth and Pfizer's failure to list the patents-in-suit in the Orange Book for Vizimpro constitutes an implied waiver of Wyeth's right to enforce the patents against first-line use of Tagrisso. "Implied waiver occurs when the patentee's 'conduct was so inconsistent with an intent to enforce its rights as to induce a reasonable belief that such right has been relinquished.'" *Core Wireless Licensing S.A.R.L. v. Apple Inc.*, 899 F.3d 1356, 1365 (Fed. Cir. 2018) (quoting *Hynix Semiconductor Inc. v. Rambus Inc.*, 645 F.3d 1336, 1347–48 (Fed. Cir. 2011)). The "reasonable belief" requirement is an objective standard. *See id.* at 1367 ("[T]here is no requirement under the implied waiver doctrine that a third party must interpret the patentee's conduct as constituting a waiver of its rights to enforce the patent."). AstraZeneca has the burden of proving implied waiver by clear and convincing evidence. *See Hynix Semiconductor Inc.*, 645 F.3d at 1348.

The Court concludes that AstraZeneca has not shown by clear and convincing evidence that Wyeth's conduct amounted to implied waiver. First, the Orange Book

expressly warns on Vizimpro's listing page that "Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner." *See* DTX-0263. This disclaimer strongly suggests that it would *not* be reasonable for an Orange Book user to assume that an unlisted patent will not be enforced.

Second, Wyeth's conduct with respect to its Orange Book listings must be viewed in the context of the Hatch-Waxman regulatory regime. As previously discussed, the FDA expressly permits pharmaceutical companies to late list patents. Although there are consequences for late listing, these consequences do not include losing the ability to enforce the patents. This clearly suggests that the FDA does not view Orange Book requirements as "list it or lose it" obligations. In other words, "[t]he FDA's regulatory scheme presupposes that late-listed patents are enforceable." Pl.'s Proposed Findings of Fact & Conclusions of L. at 54. AstraZeneca has not proffered any persuasive evidence that pharmaceutical companies view the Hatch-Waxman Act as imposing even stricter requirements than those recognized by the FDA.

Third, Wyeth's expert, Daniel Troy, former Chief Counsel of the FDA, testified persuasively that no prudent pharmaceutical company would assume that a company's failure to list patents in the Orange Book would mean that they would not enforce those patents. Although AstraZeneca's FDA expert, Prescott Lassman, testified that Orange Book listings serve an important "notice" function by providing "relevant information" that companies "rely on when they're assessing their exposure to patent litigation," he agreed that a prudent company would not rely solely on the Orange Book. *See* Bench Trial Tr. at 212:23–213:15.

Finally, there is no evidence that AstraZeneca in fact relied on the Vizimpro Orange Book listings when making any decisions regarding Tagrisso or whether to license the patents-in-suit. Although the doctrine of implied waiver does not require evidence that AstraZeneca subjectively believed that Wyeth had relinquished its rights, the Court may still weigh this fact to determine whether Wyeth's conduct would induce an objectively reasonable belief that it had relinquished the right to enforce its patents.

For all of these reasons, the Court is not persuaded that Wyeth's failure to timely list the patents-in-suit "induce[d] a reasonable belief that [the right to enforce the patents] has been relinquished." *Core Wireless Licensing S.A.R.L.*, 899 F.3d at 1365. The Court therefore overrules AstraZeneca's request to hold the patents unenforceable due to implied waiver.

3. Patent misuse

AstraZeneca's third and final equitable defense is that the patents-in-suit are unenforceable based on the doctrine of patent misuse. "Patent misuse is an affirmative defense to an accusation of patent infringement, the successful assertion of which 'requires that the alleged infringer show that the patentee has impermissibly broadened the "physical or temporal scope" of the patent grant with anticompetitive effect.'" *Virginia Panel Corp. v. MAC Panel Co.*, 133 F.3d 860, 868 (Fed. Cir. 1997) (quoting *Windsurfing Int'l, Inc. v. AMF, Inc.*, F.2d 995, 1001 (Fed. Cir. 1986)). The Federal Circuit has emphasized "the narrow scope of the [patent misuse] doctrine" and has been reluctant to expand the doctrine beyond "the specific [restrictions] that have been held to be outside the otherwise broad scope of the patent grant." *Princo Corp. v. Int'l Trade Comm'n*, 616 F.3d 1318, 1329 (Fed. Cir. 2010). AstraZeneca argues that "[t]he

'314 and '162 patents are unenforceable due to patent misuse because Wyeth has impermissibly broadened their scope by mislisting them in the Orange Book as covering first-line use of Vizimpro." Defs.' Proposed Findings of Fact & Conclusions of L. at 25.

To start, the Court is doubtful that the doctrine of patent misuse is applicable. Patent misuse typically involves scenarios where the patentee conditions the sale or grant of a license for a patented device upon the purchase of some non-patented item or otherwise "has used restrictive conditions on licenses or sales to broaden the scope of the patent grant." *Princo Corp.*, 616 F.3d at 1328. AstraZeneca's patent misuse claim is not based on any allegedly anticompetitive terms of any licenses to the patents-in-suit. Rather, the alleged misuse is Wyeth and Pfizer's representation to the FDA that the patents-in-suit cover an approved use of Vizimpro. Although this practice may in some sense be anticompetitive in that improper Orange Book listings present an obstacle that a generic company must overcome to gain FDA approval, the Federal Circuit has "emphasized that the defense of patent misuse is not available to a presumptive infringer simply because a patentee engages in some kind of wrongful commercial conduct, even conduct that may have anticompetitive effects." *Id.* at 1329. The Court is skeptical that the "narrow scope" of the patent misuse doctrine extends to what appears to be a run-of-the-mill dispute between a patentee and its competitor over the scope of a patent's claims. *Id.* This is particularly so given that the Hatch-Waxman Act and the accompanying FDA regulations presuppose that there will be disagreements between innovator companies and generic companies regarding the scope and validity of listed patents and use codes. *See, e.g.*, 21 C.F.R. § 314.53(f) (establishing a procedure for "disputes [over] the accuracy or relevance of patent

information submitted to the Agency" for publication in the Orange Book).

At any rate, the Court finds that AstraZeneca has not provided sufficient evidence to sustain a finding that Wyeth's conduct "impermissibly broadened" the scope of its patent grant with anticompetitive effect. Vizimpro is not an accused product in this suit. The Court therefore has no basis for drawing any independent conclusions about whether Vizimpro practices the asserted claims other than the parties' and their experts' representations that Vizimpro's first-line indication is identical to Tagrisso's for all relevant purposes. The parties have vigorously disputed throughout this litigation whether Tagrisso's first-line indication practices the asserted claims. AstraZeneca argues that it does not; Wyeth argues that it does. Both parties presented evidence in favor of their positions, and the jury ultimately found that Tagrisso's first-line indication infringes the patents-in-suit. AstraZeneca now essentially requests that the Court not only find that the jury verdict was unreasonable as a matter of law, but also that Wyeth acted "impermissibly" or "wrongful[ly]" by taking the position that the first-line indication infringes the patents in the first place. *Princo Corp.*, 616 F.3d at 1329. The Court declines to do so because it finds that AstraZeneca has not provided persuasive or sufficient evidence that Wyeth's position regarding first-line infringement is unreasonable, frivolous, in bad faith, or otherwise impermissible or wrongful.

Finally, to the extent that AstraZeneca argues that the root of Wyeth and Pfizer's "misuse" is because Vizimpro allegedly is not FDA-approved to practice the claims, that is not a proper basis for a patent misuse claim. As the Court has explained, the Federal Circuit has emphasized that not all anticompetitive conduct that involves a patent or patented product constitutes patent misuse. *See Princo Corp.,* 616 F.3d at 1329 ("An

antitrust offense does not necessarily amount to misuse merely because it involves patented products or products which are the subject of a patented process." (quoting *Kolene Corp. v. Motor City Metal Treating, Inc.*, 440 F.2d 77, 84–85 (6th Cir. 1971))). Rather, the misconduct at issue must involve some attempt to expand the scope of the *patent* monopoly. It is well-established that a method of treatment need not be FDA-approved to be patentable. *See, e.g.*, *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1369 (Fed. Cir. 2023) ("Questions of safety and efficacy in patent law have long fallen under the purview of the FDA."); *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995) ("[T]he requirements under the law for obtaining a patent" are different from "the requirements for obtaining government approval to market a particular drug for human consumption."). Thus, any argument that Wyeth and Pfizer misrepresented whether the FDA has approved the use of Vizimpro to practice the asserted claims cannot support a defense of patent misuse.

4. Conclusion

In sum, the Court concludes that AstraZeneca has not established its defenses of unclean hands, implied waiver, or patent misuse. The Court notes that, even if AstraZeneca had satisfied the elements of one of these equitable defenses, that would not automatically entitle it to a ruling that the patents-in-suit cannot be enforced against it. The Federal Circuit has made clear that district courts have discretion over what kind of equitable sanction to impose on a party who is found to have engaged in misconduct, including the option of imposing no sanction at all. *See Core Wireless Licensing S.A.R.L. v. Apple Inc.*, 899 F.3d at 1368. The sanction of unenforceability is strong medicine, and the Federal Circuit has stated that courts must "require either a showing

of prejudice or egregious misconduct sufficient to justify the sanction of unenforceability of the patent at issue." *Id.* As discussed, AstraZeneca has not shown how it was prejudiced by Wyeth and Pfizer's failure to list the patents-in-suit in the Orange Book. Nor has AstraZeneca shown that Wyeth's alleged misconduct was "egregious" enough to merit the sanction of unenforceability. At most, AstraZeneca has shown that Wyeth deprived potential competitors of earlier notice of its position that the patents cover first-line use of Vizimpro. Although this conduct violated a statutory requirement, that violation has since been remedied. Moreover, AstraZeneca has provided no evidence that Wyeth failed to list the patents-in-suit for Vizimpro to mislead competitors, to gain an unfair advantage over them, or for some other inappropriate reason. The Court therefore does not find that the alleged misconduct at issue is sufficiently egregious to warrant a declaration that the patents-in-suit are unenforceable.

B. Indefiniteness

AstraZeneca argues that the asserted claims are invalid because the term "gefitinib and/or erlotinib resistant" NSCLC as construed is indefinite. Under 35 U.S.C. § 112(b), a patent specification must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention." The Supreme Court has interpreted section 112(b) "to require that a patent's claims, viewed in light of the specification and prosecution history, inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014). A patent that fails to meet this "definiteness requirement" is "invalid for indefiniteness." *Id.*; *id.* at 901.

"[D]efiniteness is measured from the viewpoint of a person skilled in [the] art at the time the patent was filed." *Id.* at 908 (emphasis omitted). Although the definiteness requirement "mandates clarity," it does not demand "absolute precision." *Id.* at 910. The standard is "not greater than is reasonable, having regard to their subject-matter." *Id.* at 910–11 (quoting *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261, 270 (1916)). Moreover, "the legal test for definiteness 'does not require that a potential infringer be able to determine *ex ante* if a particular act infringes the claims." *Niazi Licensing Corp. v. St. Jude Med. S.C., Inc.*, 30 F.4th 1339, 1346 (Fed. Cir. 2022) (quoting *Nevro Corp. v. Bos. Sci. Corp.*, 955 F.3d 35, 40 (Fed. Cir. 2020)). Definiteness is a question of law. *Id.*

The parties dispute the definition of a POSA in this case, but at a baseline level they agree that a POSA would have at least one advanced degree in a discipline such as organic or medicinal chemistry, medicine, pharmacology, biochemistry, or pharmaceutical sciences; approximately three to five years of work experience in the development of cancer treatments; and work on a multidisciplinary team that includes at least one physician.[3] Both parties assert that the analysis remains the same regardless

[3] Wyeth asserts that "[a] POSA at the time of the inventions would: (a) have a doctoral degree in a discipline such as organic or medicinal chemistry, medicine, pharmacology, biochemistry, or pharmaceutical sciences, and at least three years of practical experience in drug discovery and development, including for cancers that may benefit from kinase inhibition; or a B.S. or M.S. degree in at least one of the disciplines above and at least five years of practical experience in drug discovery and development, including for cancers that may benefit from kinase inhibition; and (b) work together with one or more team members with experience developing cancer treatments, including biologists, molecular biologists, geneticists, medicinal chemists, preclinical researchers, cancer treating clinicians, and/or oncologists in a multidisciplinary team to solve a given problem." AstraZeneca asserts that a POSA would have "(1) a medical degree with three to five years of experience consulting with a team including a chemist with a masters or post-graduate degree in chemistry, including medicinal chemistry, organic

of which party's definition of a POSA is applied. *See* Pl.'s Proposed Findings of Fact & Conclusions of L. at 66 n.31; Defs.' Proposed Findings of Fact & Conclusions of L. at 32 n.8. The parties also dispute the "time the patent was filed." *Nautilus, Inc.*, 572 U.S. at 908. AstraZeneca asserts that the relevant date is February 2, 2006, which is the filing date of "the earliest non-provisional patent application to which the asserted claims of the '314 and '162 patents could be entitled priority." Defs.' Proposed Findings of Fact & Conclusions of L. at 33. Wyeth argues that the relevant dates are February 3, 2005 for the '314 Patent and April 15, 2005 for the '162 Patent, which correspond to the dates the provisional patent applications were filed. Neither party supports its proposed dates with citation to relevant legal authority regarding the standard for determining the "time the patent was filed." Because both parties assert that the analysis remains the same regardless of which parties' timeframe applies, the Court will consider the relevant timeframe as between February 3, 2005 to February 2, 2006 for the '314 Patent and between April 15, 2005 and February 2, 2006 for the '162 Patent.

1. Objective boundaries

AstraZeneca first argues that the term "g/e resistant" is indefinite because the patents-in-suit establish no objective boundaries regarding whether a patient's NSCLC is g/e resistant. AstraZeneca argues that, because the Court concluded at claim construction that the term "g/e resistant" is not limited to patients who actually received

---

chemistry, biochemistry, pharmaceutical science, or a related discipline and experience designing and evaluating pharmaceutical compounds; or (2) a masters or postgraduate degree in chemistry, including medicinal chemistry, organic chemistry, biochemistry, pharmaceutical science, or a related discipline, with about three to five years' work experience in this area designing and evaluating medicinal pharmaceutical compounds consulting with a team including a physician."

g/e treatment and whose cancer nevertheless progressed, the term is indefinite because a POSA would not know with reasonable certainty which patients would be considered to be "g/e resistant." (Progressed, in this context, means that the cancer got worse.) AstraZeneca argues that "a wide variety of patients, for example, those who lack EGFR sensitizing mutations, those with KRAS mutations, and those with MET amplifications, have NSCLC that will not be expected to respond to treatment with gefitinib and/or erlotinib, beyond merely patients who have resistance attributable to T790M." Defs.' Proposed Findings of Fact & Conclusions of L. at 34.

Wyeth responds that a POSA would not consider these forms of NSCLC to be g/e resistant because a POSA would not consider patients with these conditions to be candidates for g/e treatment to begin with. That is because, Wyeth argues, a POSA would understand that g/e would only be effective in patients with sensitizing mutations and would not be effective (at least not as a sole treatment method) if patients' NSCLC had certain other conditions such as KRAS mutation or MET amplification that were not dependent on EGFR pathways. Wyeth also argues that AstraZeneca's indefiniteness argument cannot be squared with the jury's verdict because the jury found that the patents were not invalid despite AstraZeneca raising arguments based on essentially identical evidence with respect to the enablement and written description requirements. In other words, Wyeth argues that the jury credited its position regarding what types of NSCLC a POSA would consider to be g/e resistant and not AstraZeneca's position.

The Court finds that AstraZeneca has not shown by clear and convincing evidence that the term g/e resistant is indefinite due to a lack of objective boundaries. As the Court discussed at the summary judgment stage in response to AstraZeneca's

substantially similar argument regarding the enablement and written description requirements, Wyeth presented extensive evidence that a POSA in 2005–2006 would have understood the scope of the term "g/e resistant NSCLC," as that term is used in the patents-in-suit, as describing NSCLC that a POSA would consider a candidate for g/e treatment but that nevertheless would not respond well to that treatment, whether immediately or after a period of time. AstraZeneca's contrary evidence does not clearly and convincingly show that a POSA would not be reasonably certain of this meaning.

As an initial matter, the Court disagrees with AstraZeneca that the plain meaning of "g/e resistant" NSCLC is simply any NSCLC that does not improve when a patient is given g/e, regardless of the reason for the lack of improvement. By that logic, a broken bone or a case of the chicken pox would also be "g/e resistant." Claim terms must be viewed through the eyes of "a person of ordinary skill in the art in question at the time of the invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005). In the context of a complex disease such as NSCLC that was experiencing fast-paced scientific breakthroughs at the time of the invention, the Court is persuaded by Wyeth's evidence that a POSA would have understood that the patents were directed at addressing a specific issue: a subpopulation of NSCLC patients who, although they met what were then considered the basic criteria for treatment with reversible EGFR inhibitors like g/e, were not responding well to that treatment. Indeed, this is precisely how one of the named inventors, Dr. Haber, described the progression of his research in his testimony. *See* Jury Trial Tr. at 298:3–13 (Haber testimony) (explaining that, after his team made their discoveries regarding the role of sensitizing mutations in predicting a patient's response to g/e, "understanding [the mechanisms underlying acquired

resistance to g/e] and making drugs that can circumvent that is certainly the direction that this would take").

First, the Court is persuaded that a POSA would understand with reasonable certainty that the patents-in-suit were directed to NSCLC with g/e sensitizing mutations. The patent specification states that "[c]ancers may *initially* be diagnosed as gefitinib/erlotinib sensitive or predicted to be gefitinib/erlotinib sensitive by means of the methods described in Lynch et al., 2004." '314 Patent at 7:47–49 (internal citation omitted) (emphasis added). The specification then goes on to state that "[c]ancers may be diagnosed as gefitinib and/or erlotinib resistant after treatment with gefitinib and/or erlotinib has commenced. Alternatively, cancers may be diagnosed as gefinitib and/or erlotinib resistant prior to initiation with such compounds." *Id.* at 7:57–61. The specification thus differentiates between "g/e sensitive" and "g/e resistant," which supports Wyeth's argument that the two concepts are distinct in this context. In other words, the patent does not teach that g/e resistance can be determined by testing for whether the patient's NSCLC lacks sensitizing mutations.

The testimony of Wyeth's experts, which the Court found persuasive, reinforces this understanding of the patents-in-suit. *See, e.g.*, Jury Trial Tr. at 181:15–22 (Weiss testimony) ("Q: Does the definition [of g/e resistant NSCLC] that you applied include people who do not have sensitizing mutations? A: No. It requires that all of these patients would have a sensitizing mutation. Q: And how do you know that? A: Because in order to have received or to be eligible for gefitinib and/or erlotinib, one needs to have a sensitizing mutation."); Jury Trial Tr. at 815:11–20 (Hausheer testimony) ("Q: You mentioned sensitizing mutations. And what's your opinion

whether—as to whether gefitinib/erlotinib resistance means the patient has to have sensitizing mutations or not? A: They have to have sensitizing mutations. Q: Why is that? A: Because this is the basis for the gefitinib/erlotinib to be administered to such a patient. These are called sensitizing mutations. So reversible inhibitors will be used, and they're much more effective."); *id.* at 818:7–10. ("Non-small cell lung cancer patients that do not have sensitizing mutations are out of the scope of the claims, and the specification does not need to describe or enable patients lacking, or any example, lacking sensitizing mutations."). This interpretation is also consistent with the testimony of the named inventors of the patents-in-suit. *See, e.g.*, Settleman Dep. Tr. at 196:02 (Q: So among the gefitinib or erlotinib resistance, that you are describing for which an irreversible EGFR inhibitor would be a treatment is gefitinib or erlotinib resistant non-small cell lung cancer with wild-type EGFR, correct? A: I generally don't think about gefitinib or erlotinib resistance in the context of wild-type EGFR because that's not the patients who are treated.); *id.* at 197:25 ("Q: So would a patient who had wild-type EGFR therefore, be identified as having gefitinib and/or erlotinib resistant non-small cell lung cancer? A: That's not how we would describe them."); Jury Trial Tr. at 296:18–22 (Haber testimony) (explaining that sensitizing mutations "predict[ ] who's going to respond, who's not going to respond. So that's very important because you're not giving drugs to people who won't benefit from them. You can actually be smart about that.").

AstraZeneca emphasizes the fact that the specification states that "[i]n one embodiment, the subject's tumor does not harbor mutations indicative of gefitinib and/or erlotinib sensitivity and does harbor mutations indicative of gefitinib and/or erlotinib resistance." *See* Defs.' Proposed Findings of Fact & Conclusions of L. at 35–36

(quoting '314 Patent at 8:39–43). The Court disagrees, however, that this one sentence must control despite the contrary evidence that the Court has just discussed. AstraZeneca argues that "excluding an embodiment explicitly described in the specification is 'in contravention of controlling Federal Circuit precedent.'" *Id.* at 36–37 (quoting *Wyeth I*, 2023 WL 2683559, at *5). That, however, is only true if the claims "can reasonably [be] interpreted to include a specific embodiment." *See Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1277 (Fed. Cir. 2008) ("[W]here claims can reasonably to interpreted to include a specific embodiment, it is incorrect to construe the claims to exclude that embodiment, absent probative evidence on the contrary."). In this case, the Court disagrees with AstraZeneca that the claims can reasonably be read to include NSCLC that lacks sensitizing mutations.

Second, the Court is not persuaded by AstraZeneca's argument that a POSA would not know whether the term "g/e resistant" covered NSCLC with KRAS mutations or MET amplification. To begin, it is undisputed that MET amplification would not yet be known to a POSA at the time of the invention. The Court therefore disagrees with AstraZeneca's premise that the term "g/e resistant" is ambiguous because it could theoretically cover a condition that had not yet been discovered. The Supreme Court has emphasized that courts should not take this type of hindsight-oriented approach to indefiniteness. *See Nautilus, Inc.*, 572 U.S. at 908 ("Third, definiteness is measured from the viewpoint of a person skilled in [the] art *at the time the patent was filed*." (internal quotations and citation omitted)). Moreover, the Court again relies on the Supreme Court's instruction that a POSA must understand the scope of a claim with certainty that "is not greater than is reasonable, having regard to their subject-matter."

Nautilus, Inc., 572 U.S. at 910 (quoting *Minerals Separation Ltd.*, 242 U.S. at 270). No inventor can predict the future with certainty; inventors therefore cannot reasonably be expected to draft claims in a way that ensures no subsequent discoveries in their field will ever cast doubt on the scope of a claim term. *See United Therapeutics Corp.*, 74 F.4th at 1371 ("[E]very claim to a method of treatment of an ailment has refinements. That is, for any given method of treatment claim, there may be a subset of patients who would not benefit from or should not take the claimed treatment."). This is sufficient grounds for overruling AstraZeneca's argument with respect to MET amplification.

Regardless, even setting aside the hindsight issue, the Court is persuaded by the evidence that a POSA would not consider NSCLC with a KRAS mutation or MET amplification (if they had been aware of it) to be "g/e resistant" in the context of the patent and the state of the art in 2005–2006. *See, e.g.*, Jury Trial Tr. at 181:23–182:1 (Weiss testimony) ("Q: Does the plain and ordinary meaning of gefitinib or erlotinib resistance depend on a specific kind of signaling pathway? A: It depends on the EGFR signaling pathway."); Jury Trial Tr. at 818:16–819:25 (Hausheer testimony) ("KRAS is a separate protein system. The mutations in KRAS are well known. It is independent of the EGFR pathway. And it's just not—it's not part of this. [. . .] KRAS is not a EGFR-mediated pathway. It's bypassing EGFR. It's a different protein system. You know, this is all well-known."); Haber Dep. at 58:05–13 (Q: [P]atients with gefitinib or erlotinib-resistant non-small cell lung cancer that exhibit MET amplification will not obtain a therapeutic benefit from an EGFR inhibitor; correct? A: [. . .] Based on lab experiments, you would predict not, because MET bypasses the entire pathway."). As the Court previously explained, it is persuaded that a POSA would be sufficiently

sophisticated and familiar with the seminal research cited in the patents-in-suit to understand that "g/e resistant" NSCLC does not refer to all types of NSCLC that do not exhibit a strong response to g/e regardless of the reason. Rather, the Court agrees that the evidence shows that a POSA would understand "g/e resistant" NSCLC to refer to NSCLC that a POSA would generally consider to be a candidate for treatment with reversible EGFR inhibitors like g/e in the first instance. A claim term need only inform a POSA with "reasonable certainty" of the scope of the claim; it need not eliminate every possible ambiguity in order to satisfy the definiteness requirement. *See Nautilus, Inc.*, 572 U.S. at 910 ("The definiteness requirement . . . mandates clarity, while recognizing that absolute precision is unattainable.").

AstraZeneca cites to a single statement by the patent examiner that "MET amplification" was a "mechanism[ ] for the development of EGFR resistance." DTX-0036 at 11 ('314 Patent Prosecution History, June 14, 2018 Non-Final Rejection). AstraZeneca provides no indication, however, of the response, if any, of the applicants to this statement. The application process involved extensive back-and-forth between the examiner and the applicants; therefore, the examiner's statement does not necessarily reflect the understanding of the inventors or of a POSA. Further, as discussed, MET amplification was not known at the time of the invention, and thus the Court does not see the materiality of any alleged confusion regarding whether "g/e resistant" would include the future discovery of MET amplification. Finally, it is well established that, although a court may consider the prosecution history of a patent to determine indefiniteness, *see Nautilus, Inc.*, 572 U.S. at 901, a court need not defer to the examiner's claim interpretation. *See SRAM Corp. v. AD-II Eng'g, Inc.*, 465 F.3d

1351, 1359 (Fed. Cir. 2006). For these reasons, the Court does not find the examiner's single statement within an extensive, years-long prosecution history to be clear and convincing evidence of indefiniteness, even when considered with the remainder of AstraZeneca's arguments.

AstraZeneca also points to various references in the specification that suggest that mechanisms of g/e resistance may not be limited to the T790M mutation. The Court does not agree that these statements indicate that the term "g/e resistant" is indefinite. Although the specification teaches that identifying the T790M mutation is one method of identifying g/e resistant NSCLC, the specification also states that g/e resistant NSCLC can be identified by monitoring cancer growth after the patient has initiated treatment with g/e. The specification need not identify every mechanism underlying g/e resistance for a POSA to understand the meaning of that term with reasonable certainty.

AstraZeneca further argues that the testimony of the inventors of the patents-in-suit, namely Dr. Sordella and Dr. Haber, clearly shows that a POSA would not be reasonably certain regarding the scope of the term "g/e resistant." Wyeth responds that "'inventor testimony, obtained in the context of litigation, should not be used to invalidate issued claims' for indefiniteness." Pl.'s Proposed Findings of Fact & Conclusions of L. at 33–34 (quoting *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1380 (Fed. Cir. 2000)). Wyeth is correct that the Federal Circuit has stated that courts should not base their understanding of a patents' terms based on an inventor's subjective belief about the scope of the invention. That is because claim terms are "evaluated from the perspective of someone skilled in the relevant art." *Nautilus, Inc.*, 572 U.S. at 908. This

does not necessarily mean, however, that inventor testimony cannot be relevant to determining a *POSA*'s understanding of the claim terms, i.e. "the claim's objective meaning and scope." *Solomon*, 216 F.3d at 1380.

Regardless, the Court does not find the named inventors' testimony to be persuasive evidence in AstraZeneca's favor. To the contrary, a significant portion of the named inventors' testimony is *consistent* with Wyeth's position regarding the scope of that term. For example, AstraZeneca argues that Dr. Sordella "testified that the term 'can indicate multiple' scenarios, such as when a 'patient has not responded to either 'gefitinib or erlotinib,' but also testified that NSCLC ***responding*** to gefitinib treatment could nevertheless be considered 'gefitinib and/or erlotinib resistant' 'from a molecular point of view.'" Defs.' Findings of Fact & Conclusions of L. at 42 (quoting Sordella Dep. 98:11–100:1). But this is entirely consistent with Wyeth's position that the T790M mutation is an early indicator of resistance. Because the T790M mutation may be present in some NSCLC cells but not others in the same patient, the fact that the patient has some response to g/e therapy due to its non-T790M harboring cells does not alter the bottom line that the T790M-harboring NSCLC cells are g/e resistant and the patient will ultimately stop responding to g/e therapy. *See, e.g.*, Haber Dep. 191:03–15 ("[C]linical resistance is defined when the X-ray shows that the tumor is growing. Resistance can be seen in other ways before that. So if you're looking—if you're counting tumor cells in the blood and the number of cells in the blood goes up, you clearly have a sense that the tumor is growing back and not responsive to the drug as much as it was. And in this case, we could find T790M mutation in some cases in the blood before the x-ray changed. And that's—again, the idea is to treat in real time and

to treat effectively."); *see also* Jury Trial Tr. 652:15–20 (Jänne testimony) ("Q: And you agree that if the T790M is present even in a small number of cells, the response to gefitinib may not last as long, correct? A: Patients can still respond, but, correct, the response may be of shorter duration than in somebody that—in the absence of a small amount of T790M.").

AstraZeneca attempts to seize on the inventors' distinction between what might be seen and determined *clinically* and what can be seen and determined in a lab to argue that a POSA would not understand the scope of the term "g/e resistant." For example, AstraZeneca asserts that Dr. Haber testified that "you can't make rules" on whether a patient's NSCLC was g/e resistant. Defs.' Proposed Findings of Fact & Conclusions of L. at 42. But Dr. Haber was in fact testifying that it was difficult to make rules for "*clinical hypotheticals*" and that he was "not the one to comment on those." *See* Haber Dep. 193:10–193:18 (emphasis added). Read in context, the inventors' testimony is consistent with Wyeth's basic premise—recited in the patent specification—that a POSA would understand that resistance can be predicted before the patient experiences the clinical results of that resistance (i.e., tumor growth). *See, e.g.*, Haber Dep. at 191:16–192:13 ("Q: And so would you view a patient whose—who had a non-small cell lung cancer and whose disease was—tumors were not growing while on gefitinib but where the T790M was detected at lower allylic fraction in CTCs, would that patient have gefitinib- and/or erlotinib-resistant non-small cell lung cancer? A: That's not really answerable in an easy way. [. . .] [W]e've had patients early on in these studies where we could pick up T790M and the patient responded to [g/e] and we said, oh, my God, maybe they still respond. But then it grew back. So it's a complicated

question because if 1—percent of your cells have this resistant mechanism, you will kill 99—percent of the cells. You will get a response. But ultimately the cancer is likely to grow back. So to answer your question, clinically, there are clinical parameters for response table disease progression. Scientifically, in the lab, you see the tumor cells get killed or not get killed. And then the sequencing data really point to mechanism."); Sordella Dep. 99:12–100:01 ("Q: So when the non-small cell lung cancer is responding to gefitinib, at that point the cancer is not gefitinib or erlotinib resistant, correct? A: It is, again, like—it depends on the definition. If we are considering just from a clinical point of view, that would be a fair statement because, again, like, you give a particular treatment, in this case gefitinib, and then you measure clinical response to the treatment. If we would have analyzed the same patient from a molecular point of view, that again, like, in what context we want to examine it, then it could be interpreted differently.").

In the Court's view, much of the inventors' testimony tends to underscore that cancer treatment is a field in which there is a high baseline level of uncertainty. The Supreme Court has made clear that "the certainty which the law requires in patents is not greater than is reasonable, having regard to their subject-matter." *Nautilus, Inc.*, 572 U.S. at 910 (quoting *Minerals Separation Ltd.*, 242 U.S. AT 270). Thus, although the Court has weighed the experts' various references to uncertainty surrounding g/e resistance, the Court does not find that this testimony shows that a POSA in 2005–06 would not understand the scope of the term g/e resistant with reasonable certainty. Rather, the Court views such remarks as evidence that cancer treatment is a field in which significant uncertainty is par for the course due to the vast possibility for

individualized differences in medical conditions and genetic makeup, the limitations on testing on real-life patients, and numerous other factors.

2. Standard testing

Finally, AstraZeneca argues that the claims are indefinite for the additional reason that "testing for the T790M mutation would not provide reasonable certainty regarding whether a patient falls within or outside the claims." AstraZeneca's Proposed Findings of Fact & Conclusions of L. at 43. That is because, AstraZeneca asserts, "the detection of T790M varies depending on the testing method used, and thus a patient could test ***negative*** for T790M on one test but ***positive*** **on another**, leading to conflicting results as to whether treating the patient would infringe the claims under Wyeth's view." *Id.*

The Court is not persuaded that the fact that different tests have different sensitivities to T790M means that a POSA would not understand that scope of the term "g/e resistant," which is the only question before the Court regarding indefiniteness. The Court has repeatedly declined to adopt AstraZeneca's view that the asserted claims require a physician to diagnose a patient with g/e resistant NSCLC and/or with the T790M mutation. As the Court stated when ruling on the parties' motions in limine before the jury trial:

> [W]hether a patient has been diagnosed with T790M—and thus whether or not doctors have knowledge of a specific pre-treatment diagnosis—is not a required element to practice the asserted claims. No prior knowledge of whether a patient is g/e resistant is required to practice the asserted claims. One administering the treatment can intend to target g/e resistant NSCLC without knowing that's the patient's condition. Thus there doesn't have to be a pre-existing diagnosis, test, or other indication of g/e resistance for infringement to take place.

May 7, 2024 Ruling on Remaining Motions in Limine at 7 (internal quotations and

citations omitted).

The relevant question with respect to the definiteness inquiry thus is not whether a given test could be reasonably certain to detect the presence of the T790M mutation, but rather whether a POSA could be reasonably certain that the T790M mutation, *if detected*, means that the NSCLC is "g/e resistant." The Court is persuaded that a POSA in 2005–2006 would have considered NSCLC with the T790M mutation to be "g/e resistant." The fact that some tests are better able to detect the T790M mutation than others does not change the fact that a POSA would associate T790M with resistance.

AstraZeneca cites to various cases in which courts have held that claims are indefinite due to lack of a standard method for testing or measuring a certain claim term. But in those cases, the claim term *itself* necessitated some form of measurement or test in order to hold meaning. For example, in *Ball Metal Beverage Container Corp. v. Crown Packaging Technology, Inc.*, the patent-in-suit claimed a metal can end that had certain angle measurements between two specific points on the can end; however, there was no single way to locate the required second point. 838 F. App'x 538, 542 (Fed. Cir. 2020). Similarly, in *Dow Chemical Co. v. Nova Chemicals Corp.*, the patent-in-suit claimed certain "ethylene polymer compositions (a type of plastic)" that had "a slope of strain hardening coefficient greater than or equal to 1.3"; however, there were different methods of calculating the slope coefficient. 803 F.3d 620, 624–25 (Fed. Cir. 2015). Here, the Court is persuaded that a POSA would understand the scope of the term "g/e resistant." The question of which tests best or most accurately pick up on the presence of T790M does nothing to cast doubt on whether a POSA would understand

that T790M is associated with g/e resistance. To draw an analogy, AstraZeneca essentially is arguing that the term "COVID-19" would be indefinite simply because an at-home rapid test might produce less reliable results than a state-of-the-art lab test. A POSA in this case, with the necessary experience in looking at the chemical and biological composition of NSCLC, would understand that certain genetic indicators such as the T790M mutation can indicate that cancer will behave in a certain manner regardless of whether those genetic indicators are discernable by, for example, clinically available tests.

AstraZeneca also argues that the term "g/e resistant" is indefinite because the patent also describes, for example, monitoring tumor growth as a manner of assessing g/e resistance. AstraZeneca posits that a POSA would not understand whether a patient's cancer was g/e resistant in a scenario in which, for example, the patient's tumor was observed as shrinking but the patient tested positive for the presence of the T790M mutation. The Court disagrees that this scenario renders the claims indefinite. It is undisputed that a patient may harbor some NSCLC cells with the T790M mutation and others without the mutation. As a result, experts on both sides testified that a patient with the T790M mutation may still show some response to g/e therapy. *See, e.g.*, Bench Trial Tr. at 47:02–12 (Levy testimony); *id.* at 125:19–20 (Weiss testimony). That does not mean that the presence of T790M mutation is not indicative of resistance. Eventually, patients with NSCLC that has the T790M mutation will fail on g/e therapy. Bench Trial. Tr. at 125:06–23 (Weiss testimony). Thus, the Court agrees with Wyeth that "[t]he existence of multiple tests to measure resistance does not render the asserted claims indefinite because a POSA would understand that a 'positive' value on

any of these tests meant the claim term was met." Pl.'s Proposed Findings of Fact & Conclusions of L. at 33. Again, as the Court has discussed, the fact that some methods of testing will result in earlier *detection* of g/e resistance than other methods does not mean that a POSA does not understand the scope of the term g/e resistant with reasonable certainty.

The core issue for AstraZeneca, as the Court sees it, is that there is evidence that physicians *proactively* prescribe Tagrisso for the purpose of treating g/e resistance even if they are not certain that a patient has that condition. *See, e.g.*, Jury Trial Tr. at 189:6–15 (Weiss testimony) ("[G]iving a patient a reversible inhibitor which does not overcome T790M resistance can be a problem for these patients . . . . [S]ome of these patients may not live long enough if you tried something else first before giving Tagrisso because their cancer may continue to spread or cause them significant problems where they're not eligible for additional treatment."). That is because there is little drawback to starting the patient immediately on Tagrisso, even if the doctor has not confirmed, via as-sensitive-as-possible T790M testing or via starting a patient on g/e therapy, that the patient has g/e resistant NSCLC. *See id.* at 189:17–190:2. But the fact that doctors treating real-life patients have limited incentive to confirm whether a patient has g/e resistant NSCLC as that term is defined in the patents-in-suit does not mean that a POSA cannot be reasonably certain of the scope of the term in the asserted claims. Stated differently, there is no requirement that a POSA's certainty about the scope of the invention correspond with the manner in which physicians diagnose and treat patients in the real world. The Court finds it unremarkable that physicians tasked with treating cancer patients are not concerned with seeking to ascertain with legal precision

whether those patients have "g/e resistant NSCLC" as that term is used in the patents-in-suit.

Wyeth also argues that AstraZeneca's indefiniteness argument is fundamentally inconsistent with the jury's verdict and therefore that the Court would be precluded under the Seventh Amendment from finding in AstraZeneca's favor. Because the Court has determined based on its independent findings of fact and conclusions of law that the asserted claims are not indefinite, it need not address whether a contrary conclusion would violate the Seventh Amendment.

Conclusion

For the reasons stated above, the Court finds that (1) the patents are not unenforceable based on the equitable doctrines of unclean hands, implied waiver, or patent misuse; and (2) that the asserted claims are not invalid for indefiniteness.

MATTHEW F. KENNELLY
United States District Judge

Date: August 6, 2024