IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PUMA BIOTECHNOLOGY, INC. and WYETH LLC,	)	
Plaintiffs,	)	
vs.	)	**Case No. 21 C 1338**
ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB,	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER

MATTHEW F. KENNELLY, District Judge:

Puma Biotechnology, Inc. and Wyeth LLC have 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). The plaintiffs contend that AstraZeneca's drug Tagrisso (osimertinib) infringes claims 1, 3, and 9 of the '314 patent and claim 1 of the '162 patent. AstraZeneca has moved to dismiss the case for lack of Article III standing. In the alternative, AstraZeneca has moved for summary judgment, arguing that the patents are invalid, that Tagrisso does not infringe the patents, and that the plaintiffs are not entitled to pre-issuance damages. The plaintiffs have moved for partial summary judgment on AstraZeneca's advice-of-counsel defense. Both parties have filed motions to exclude certain expert testimony related to damages. For the reasons set forth below, the Court (1) grants AstraZeneca's motion to dismiss with respect to Puma but denies the motion to dismiss with respect Wyeth; (2) grants AstraZeneca's motion for

summary judgment on the issue of pre-issuance damages but otherwise denies AstraZeneca's motions for summary judgment; (3) denies the plaintiffs' motion for summary judgment on AstraZeneca's advice-of-counsel defense; and (4) denies both parties' motions to exclude.

Background

The Court explained the background of this case in its March 29, 2023 claim construction order. The Court will briefly review that background and summarize additional facts relevant to the pending motions.

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 certain 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 the 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 2011, Puma signed an agreement with Pfizer to exclusively license the patents-in-suit with respect to a compound known as neratinib and certain other compounds. It is undisputed that the scope of Puma's license does not cover the use of the patents-in-suit with respect to osimertinib, the compound in AstraZeneca's Tagrisso drug. In 2020, Puma and Pfizer signed an amendment to the license agreement that gave Puma the right to control the enforcement of the patents-in-suit, subject to Pfizer's approval of any settlement agreement. In July 2021, Puma and Wyeth signed a "Confirmatory License" in order to "confirm (i) that the rights controlled by Wyeth in and to [certain intellectual property, including the patents-in-suit] are licensed from Wyeth to Puma in accordance with the Puma License and (ii) that Pfizer had the authority to grant Puma such rights on behalf of Wyeth." Winkler Decl., Ex. 6 at PUMA-TAG00000054 (2021 Confirmatory License).

In September 2021, the plaintiffs sued AstraZeneca, alleging that AstraZeneca's irreversible EGFR inhibitor Tagrisso (osimertinib) infringes both patents-in-suit. The parties disputed the meaning of four claim terms. After briefing and a hearing, the Court issued a March 29, 2023 order construing the disputed terms [dkt. 121]. Now before the Court are AstraZeneca's motions to dismiss and for summary judgment, the plaintiffs' motion for partial summary judgment, and both parties' motions to exclude expert

testimony.

A. Article III standing

AstraZeneca first argues that the case must be dismissed because neither Puma nor Wyeth can satisfy the constitutional requirements for Article III standing. "As the party invoking federal jurisdiction, the plaintiffs bear the burden of demonstrating that they have standing." *TransUnion LLC v. Ramirez*, 594 U.S. 413, 430–31 (2021). "To establish standing, the party invoking federal jurisdiction must demonstrate (1) an 'injury in fact' that is (2) 'fairly traceable' to the defendant's challenged conduct and is (3) 'likely to be redressed by a favorable judicial decision.'" *Apple Inc. v. Qualcomm Inc.*, 17 F.4th 1131, 1135 (Fed. Cir. 2021) (quoting *Spokeo, Inc. v. Robins*, 578 U.S. 330, 338 (2016)). With respect to the injury-in-fact requirement, the Federal Circuit has explained that "the touchstone of constitutional standing in a patent infringement suit is whether a party can establish that it has an exclusionary right in a patent that, if violated by another, would cause the party holding the exclusionary right to suffer legal injury." *Univ. of S. Fla. Rsch. Found., Inc. v. Fujifilm Med. Sys. U.S.A., Inc.*, 19 F.4th 1315, 1323 (Fed. Cir. 2021) (quoting *WiAV Sols. LLC v. Motorola, Inc.*, 631 F.3d 1257, 1266 (Fed. Cir. 2010)).

1. Wyeth

Wyeth is the patentee of the patents-in-suit.[1] Typically, that is all that is needed to satisfy Article III standing in a patent infringement suit. *See Morrow v. Microsoft Corp.*, 499 F.3d 1332, 1340 (Fed. Cir. 2007). But AstraZeneca argues that Wyeth lacks

[1] The patents-in-suit were originally issued to Wyeth and the General Hospital Corporation. The parties do not dispute that General Hospital Corporation assigned all of its rights in the patents-to-suit to Wyeth, leaving Wyeth as the only patentee for purposes of the present litigation.

standing because "it has apparently given away significant and necessary rights" to the patents-in-suit to its parent company Pfizer. Defs.' Mot. to Dismiss at 7. In AstraZeneca's view, "the fact that the original 2011 License Agreement was between Pfizer and Puma, rather than Wyeth and Puma, demonstrates Pfizer holds a substantial, unfettered right to sublicense the patents-in-suit." *Id.* AstraZeneca also points out that the Pfizer-Puma License Agreement states that "as between Pfizer and Wyeth, Pfizer dictates settlement authorization and receives the applicable portion of the recoveries in connection with any T790M Enforcement." *Id.* (quoting 2021 Confirmatory License § 1.5(b)). AstraZeneca argues that these provisions "support[ ] a finding that Wyeth lacks constitutional standing." *Id.*

The Court disagrees. First, the Court disagrees that the agreements between Pfizer and Puma suggest that Wyeth assigned its rights in the patents-in-suit to Pfizer. It is undisputed that Wyeth is a wholly owned subsidiary of Pfizer. The 2011 License Agreement clearly states that it is an agreement between Puma and "Pfizer Inc., . . . on its own behalf *and on behalf of its affiliates*." 2011 License Agreement at 1 (emphasis added). The agreement further states that "PFIZER controls, directly *or through its affiliates*, certain technology relating to a compound known as neratinib . . . ." *Id.* (emphasis added). The agreement further states that the "patent rights" involved in the Pfizer-Puma deal "are controlled by PFIZER *or its Affiliates*." *Id.* at 7 § 1.41 (emphasis added). The fact that Pfizer, as Wyeth's parent company, may conduct deals on behalf of Wyeth does not mean that Wyeth has assigned all of its patent rights to Pfizer. To hold otherwise would imply that no subsidiary has standing to enforce its own patents. In addition, the 2021 Confirmatory License signed by Wyeth, Pfizer, and Puma confirms

that Wyeth *authorized* Pfizer to act on its behalf with respect to certain "rights owned, licensed, or otherwise controlled by Wyeth" for purposes of the Puma deal. If Wyeth had in fact assigned its rights to the patents-in-suit to Pfizer, it would be unnecessary to clarify Pfizer's authority to act on Wyeth's behalf.

Second, the fact that Wyeth must receive approval from Pfizer before entering into a settlement agreement does not mean that Wyeth has not suffered an injury-in-fact for Article III purposes. Even if Wyeth has given Pfizer veto power over settlements in litigation related to the patents-in-suit, the bottom line is that Wyeth, as patentee, maintains the right to grant or refuse a license to AstraZeneca for the alleged infringing conduct. The Federal Circuit has said that these exclusionary rights lie at the heart of the Article III injury-in-fact inquiry. *See Lone Star Silicon Innovations LLC v. Nanya Tech. Corp.*, 925 F.3d 1225, 1234 (Fed. Cir. 2019) ("We have recognized that those who possess 'exclusionary rights' in a patent suffer an injury when their rights are infringed." (quoting *WiAV Sols. LLC*, 631 F.3d at 1264); *Morrow*, 499 F.3d at 1340 (explaining that parties that "hold exclusionary rights and interests created by the patent statutes, but not all substantial rights to the patent" nevertheless have Article III standing). Although Wyeth may have contracted away some sticks in its bundle of patent rights to Puma and Pfizer, this is not a case where the patentee has given up its core exclusionary rights vis-à-vis the alleged infringing conduct. The Court therefore finds that Wyeth has suffered an injury-in-fact for Article III purposes.[2]

[2] The parties do not dispute that the remaining two requirements, traceability and redressability, are satisfied. But because the Court has an independent obligation to evaluate subject-matter jurisdiction, the Court notes for completeness that it finds that the injury is traceable to AstraZeneca's alleged conduct and that it would be redressable

2. Puma

It is undisputed that Puma's exclusive license to the patents-in-suit is "compound-specific"—i.e., Puma holds rights to practice the patents only with respect to certain compounds. Pls.' Opp. to Mot. to Dismiss at 6. Importantly, Puma's exclusive license does *not* permit it to practice the patents-in-suit with respect to osimertinib, the compound in Tagrisso. This means that AstraZeneca's allegedly infringing activity falls outside of the scope of Puma's license. Because Puma has no right to use or exclude others from practicing the patents-in-suit with respect to osimertinib, it has no standing to sue AstraZeneca for infringement. *See WiAV Sols. LLC*, 631 F.3d at 1266 ("Because an exclusive licensee derives its standing from the exclusionary rights it holds, it follows that its standing will ordinarily be coterminous with those rights. Depending on the scope of its exclusionary rights, an exclusive licensee may have standing to sue some parties and not others."); *Flow Devices & Sys., Inc. v. Pivotal Sys. Corp.,* 666 F. Supp. 3d 1024, 1029 (N.D. Cal. 2023) ("[E]xclusionary rights against the defendant are a necessary and sufficient condition for Article III standing" in a patent infringement suit.).

Puma advances various arguments for why it has suffered an injury-in-fact despite its lack of any exclusionary rights with respect to AstraZeneca's conduct. This Court, however, is bound by Federal Circuit precedent on this issue. The Federal Circuit has recognized that it would be "contrary to [its] precedent" to hold that a party with no exclusionary rights has Article III standing. *See In re Cirba Inc.*, No. 2021-154, 2021 WL 4302979, at *3 (Fed. Cir. Sept. 22, 2021) (explaining that to hold that "exclusionary

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by a ruling by this Court. *See Lone Star Silicon Innovations LLC*, 925 F.3d at 1234 ("[I]t is clear that a court could redress an injury caused by [the defendant's infringement].")

rights are not necessary for a concrete injury, and [that a plaintiff] has been sufficiently injured for Article III standing by virtue of [a] competitive injury" would be "contrary to our precedent"). Puma may pursue its arguments on appeal, but its admission that its exclusionary rights to the patents do not overlap with AstraZeneca's alleged infringement ends the inquiry before this Court.

Puma argues that it can proceed as a plaintiff in this case regardless of whether it has Article III standing because its co-plaintiff, Wyeth, has standing. The Supreme Court, however, has emphasized that "Article III does not give federal courts the power to order relief to any uninjured plaintiff." *TransUnion LLC*, 594 U.S. at 430. Puma cannot seek relief in this suit unless it independently satisfies the requirements of Article III. *See id.* ("[S]tanding is not dispensed in gross; rather, plaintiffs must demonstrate standing for each claim that they press and for each form of relief that they seek (for example, injunctive relief and damages).").

Lastly, Puma argues that Federal Rule of Civil Procedure 19 secures its standing in this suit. But procedural rules cannot alter the requirements of Article III standing. *See id.* at 429 ("A regime where Congress could freely authorize *unharmed* plaintiffs to sue defendants who violate federal law [. . .] would violate Article III."). The Court therefore concludes that Puma lacks standing and must be dismissed as a plaintiff in this case.

B. Invalidity

AstraZeneca argues that it is entitled to summary judgment on all of the Wyeth's claims because the patents-in-suit fail to meet the enablement and written description requirements of 35 U.S.C. § 112. At the summary judgment stage, "the court must view

the facts in the light most favorable to the nonmoving party and draw all inferences in that party's favor." *ArcelorMittal Atlantique et Lorraine v. AK Steel Corp.*, 908 F.3d 1267, 1273 (Fed. Cir. 2018) (quoting *Gonzalez v. Sec'y of Dep't of Homeland Sec.*, 678 F.3d 254, 257 (3d Cir. 2012)). "Because patents are presumed valid, 'a moving party seeking to invalidate a patent at summary judgment must submit such clear and convincing evidence of facts underlying invalidity that no reasonable jury could find otherwise.'" *TriMed, Inc. v. Stryker Corp.*, 608 F.3d 1333, 1340 (Fed. Cir. 2010) (quoting *SRAM Corp. v. AD-II Eng'g, Inc.*, 465 F.3d 1351, 1357 (Fed. Cir. 2006)).

A patent must include a specification which contains "a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention." 35 U.S.C. § 112(a). The Federal Circuit has interpreted section 112(a) as containing both a "written description" requirement and an "enablement" requirement. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010). AstraZeneca argues that the patents-in-suit fail both requirements.

1. Enablement

"Enablement is a legal question based on underlying factual determinations." *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 684 (Fed. Cir. 2015). "Because patents are presumed valid, lack of enablement must be proven by clear and convincing evidence." *Baxalta Inc. v. Genentech, Inc.*, 81 F.4th 1362, 1365 (Fed. Cir. 2023). The enablement requirement is satisfied if the specification contains sufficient

information to permit "a person of skill in the art to make and use the claimed invention." *Vasudevan Software, Inc.*, 782 F.3d at 684. "[T]he specification must enable the full scope of the invention as defined by its claims." *Amgen Inc. v. Sanofi*, 598 U.S. 594, 610 (2023). Thus, "[i]f a patent claims an entire class of processes, machines, manufactures, or compositions of matter, the patent's specification must enable a person skilled in the art to make and use the entire class." *Id.* This does not mean, however, that "a specification necessarily [is] inadequate just because it leaves the skilled artist to engage in some measure of adaptation or testing." *Id.* at 611. "[A] specification may call for a reasonable amount of experimentation to make and use a patented invention." *Id*. at 612. "In other words, 'the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.'"[3] *Baxalta Inc.*, 81 F.4th at 1365 (quoting *MagSil Corp. v. Hitachi Glob. Storage Techs.*, Inc., 687 F.3d 1377, 1380 (Fed. Cir. 2012)).

a. Whether the claims enable use of full scope of irreversible EGFR inhibitors

AstraZeneca first argues that the patents-in-suit do not enable a person of ordinary skill in the art (POSA) to practice the claimed method of treatment with the full scope of irreversible EGFR inhibitors described in the specification. Specifically, AstraZeneca argues that the specification fails to enable a POSA to practice the method of treatment using "larger compounds" or with "epoxides or other non-Michael

[3] After the Supreme Court's decision in *Amgen*, the Federal Circuit has used the terms "undue experimentation" and "unreasonable experimentation" interchangeably. *See Baxalta Inc.*, 81 F.4th at 1365–66, 1367 n. 4.

acceptors." Defs.' Mot. for Summ. Judgment on Invalidity at 6. The Court concludes that, drawing all inferences in favor of Wyeth as the non-movant, there are genuine disputes of material fact regarding both issues.

i. "Larger compounds"

At claim construction, the Court interpreted the term "irreversible EGFR inhibitor" in the asserted claims of both patents to mean "[a] compound that irreversibly inhibits EGFR." Claim Constr. Op. at 14. The patent specification, in turn, defines a "compound" as:

> a chemical entity or biological product, or combination of chemical entities or biological products, administered to a person to treat or prevent or control a disease or condition. The chemical entity or biological product is preferably, but not necessarily a low molecular weight compound, but may also be a larger compound, for example, an oligomer of nucleic acids, amino acids, or carbohydrates including without limitation proteins, oligonucleotides, ribozymes, DNA-zymes, glycoproteins, siRNAs, lipoproteins, aptamers, and modifications and combinations thereof.

'314 Patent at 13:3–13; '162 Patent at 13:4–14. AstraZeneca therefore asserts that the specification must enable a POSA to practice the claims with not only a "low molecular weight" irreversible EGFR inhibitor, but also any irreversible EGFR inhibitor that is "a larger compound." Because it is undisputed that the method of treatment claimed in the patents-in-suit cannot be carried out with these so-called "larger compounds," AstraZeneca argues that the claims are invalid for lack of enablement as a matter of law.

The Court disagrees that the mention of "larger compound[s]" in the specification necessarily invalidates the patents. Although it is true that an inventor must enable the full scope of the claim, here, the asserted claims covers only those irreversible EGFR inhibitors that "covalently bind[ ]" to the specified part of EGFR. The relevant question,

therefore, is whether the patent enables a POSA to identify which irreversible EGFR inhibitors will covalently bind to the specified part of EGFR without "undue experimentation." *Baxalta Inc*, 81 F.4th 1362 at 1365.

Certainly, the specification's suggestion that the chosen irreversible EGFR inhibitor "may also be a larger compound"—which both parties agree is incorrect—is evidence that the specification does *not* provide sufficient guidance to a POSA regarding what types of compounds are or are not suitable for practicing the claims. But Wyeth has offered evidence that this arguable red herring in the specification would not impede a POSA from identifying which irreversible EGFR inhibitors are useful for practicing the claims or require a POSA to engage in undue experimentation to do so. Specifically, Wyeth's expert, Dr. Jorgensen, asserts that a POSA would know that "larger compounds" cannot covalently bind to EGFR. *See* Winchester Decl., Ex. 10 at 69:21–70:16 (Jorgensen Dep.) (explaining that "for something to be an inhibitor of a EGFR kinase, because the kinase is in the intracellular area, compounds do have to get into the cell," and that only "small molecules can get into cells," which "precludes other types of molecules as potential EGFR inhibitors, very large molecules, very polar molecules, proteins, nucleic acids, compounds that would have poor or negligible cell permeability"); *id.* at 80:10–19 (Q: And in your opinion, a POSA in 2005 would not consider irreversible EGFR inhibitors that were those larger compounds described [in the specification] as irreversible EGFR inhibitors that could be made to form a covalent bond to a cysteine in the intracellular domain of EGFR, correct? A: A POSA would not be considering molecules like that. He or she would be focusing on small molecules."); *id.* at 89:3–89:5 ("So there is an attempt here to complicate things, and I think in an

unnecessary way, because of the literature at the time on kinase inhibitors is all about small molecules. A POSA knows that.). The Court therefore concludes that there is a genuine dispute regarding whether a POSA would understand that "large molecules cannot bind the EGFR kinase domain and cannot covalently bind to cys773 as the claims require" or whether a POSA would need to experiment in order to rule out such compounds as potential candidates for the claimed method of treatment. Pls.' Stmt. of Material Facts on Invalidity ¶ 9 (emphasis omitted).

ii. Epoxides and other non-Michael acceptors

Next, AstraZeneca argues that the asserted claims of the patents-in-suit "over-reach even with regard to small molecules." Defs.' Mot. for Summ. Judgment on Invalidity at 6. It argues that, although the patents claim a method of treating NSCLC with *any* irreversible EGFR inhibitor that covalently bonds to EGFR, the "examples in the specification are limited to compounds with a specific type of reactive agent (a Michael acceptor) that forms the requisite covalent bond." *Id.* AstraZeneca argues that because "the patents-in-suit fail to describe or enable compounds with other reactive agents, such as epoxides," they are invalid as a matter of law. *Id.*

The Supreme Court's recent decision in *Amgen* makes clear that "the specification must enable the *full* scope of the invention as defined by its claims." *Amgen Inc.*, 598 U.S. at 610 (emphasis added). The Supreme Court clarified, however, that this does not mean that "a specification always must describe with particularity how to make and use every single embodiment within a claimed class." *Id.* at 610–11. "[I]t may suffice to give an example (or a few examples) if the specification also discloses 'some general quality . . . running through' the class that gives it 'a peculiar fitness for

the particular purpose.'" *Id.* at 611 (quoting *The Incandescent Lamp Patent*, 159 U.S. 465, 475 (1895)). Thus, the mere fact that the specification does not expressly describe epoxides or other non-Michael acceptor reactive agents as examples does not necessarily mean that the asserted claims are not enabled. Rather, the key question is whether the specification describes some "general quality" or "rule" that "may reliably enable a person skilled in the art to make and use all of what is claimed, not merely a subset" without having to engage in an "[un]reasonable amount of experimentation." *Id.* at 611–12.

There is a genuine factual dispute regarding whether the specification would enable a POSA to practice the claims with *all* "compound[s] that irreversibly inhibit[ ] EGFR and covalently bind[ ] to [cysteine 773 residue in the ligand-binding pocket of EGFR or cysteine 805 residue in the ligand-binding pocket of erb-B2 / cysteine 773 of the catalytic domain within the SEQ ID NO: 1 having a T790M mutation]" without undue experimentation. For example, AstraZeneca's expert characterizes the three concrete examples provided in the specification as "very similar," while Wyeth's expert characterizes the examples as "quite different" and "showing some variety in the structures." Pls.' Opp. to Mot. for Summ. Judgment at 13 (quoting Pls.' Stmt. of Material Facts on Invalidity ¶ 13). In addition, AstraZeneca's experts state that "potentially . . . many trillions of compounds" fall within the claims, Reider Decl., Ex. A ¶ 337, while Wyeth's expert represents that "the list of . . . likely cores is not big and one could go to the kinase literature and start tabulating the cores. . . . It's not a large list. I don't know how many it would be, but tens, maybe tens of cores. It's not hundreds of different cores." Winchester Decl., Ex. 10 at 167:3–10 (Jorgensen Dep.). Wyeth's experts

further assert that irreversible EGFR inhibitors were already well-studied and that "[a] POSA knew the precise 3-D structure of EGFR and, as a result, the common structural features for an inhibitor to covalently bind to cys773 in the kinase domain of EGFR." Pls.' Opp. to Mot. for Summ. Judgment on Invalidity at 6. The parties also dispute whether epoxides are truly distinct from the basic structures outlined in the specification or whether they are easily derived from those structures. In brief, Wyeth's expert says that a POSA "would readily be able to test" compounds for the relevant qualities identified in the specification and that "the task would be reasonably predictable, unburdensome, and nothing more than a routine process for a medicinal chemist of ordinary skill." Pls.' Stmt. of Material Facts on Invalidity, Ex. A ¶¶ 170–71 (Jorgensen Rep.). Wyeth's evidence is sufficient to carry its burden at the summary judgment stage.

b. Whether the claims enable the treatment of all types of "g/e resistant NSCLC"

AstraZeneca next argues that the patents-in-suit do not enable a POSA to practice the claims for all types of "g/e resistant NSCLC." Defs.' Mot. for Summ. Judgment on Invalidity at 6–7. Specifically, AstraZeneca asserts that the patents-in-suit do not enable a POSA to treat NSCLC that lacks "sensitizing mutations," NSCLC with a "KRAS mutation," or NSCLC with "MET amplification." *Id.* at 7–8.

Wyeth does not dispute that the claimed method does not treat NSCLC that lacks sensitizing mutations, NSCLC with a KRAS mutation, or NSCLC with MET amplification. Instead, it argues that these types of NSCLC are not g/e resistant. Specifically, Wyeth's experts assert that a POSA would not regard these types of NSCLC as g/e resistant.

See Hausheer Decl., Ex. B. ¶ 747 ("[A] POSA would understand that TKI therapy is beneficial for NSCLC patient having EGFR-sensitizing mutations."); Weiss Decl., Ex. B ¶ 9 ("[B]ased on the claim language, and the teachings of the specification, including that EGFR TKIs are beneficial for NSCLC patients having sensitizing mutations, a POSA would understand that the claimed methods of treating are directed to patients with EGFR-sensitizing mutations."); Hausheer Decl., Ex. B ¶¶832–833 (explaining that "A POSA would understand that non-EGFR/ERBB2 dependent pathways [such as MET amplification], would be treatable by other drugs, not EGFR inhibitors."); Winchester Decl., Ex. 34 at 243:13–16 (Hausheer Dep.) (KRAS mutation is "not the type of resistance that the patents – the methods of the patents embody in the claim"); Winchester Decl., Ex. 13 at 75:24–76:8 (Jänne Dep.) ("KRAS mutations . . . are mutually exclusive with EGFR mutations"). The Court concludes that these conflicting expert opinions establish a genuine dispute regarding whether NSCLC that lacks sensitizing mutations, NSCLC with a KRAS mutation, and NSCLC with MET amplification are g/e resistant.

AstraZeneca points out 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 resistance" as evidence that NSCLC without sensitizing mutations is g/e resistant NSCLC. Although this is evidence in AstraZeneca's favor, it is not dispositive. *See Crown Operations Intern., Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1380 (Fed. Cir. 2002) (stating that "inoperative embodiments do not necessarily invalidate the claim" but "support [the party seeking invalidation's] assertion that there is a genuine issue of material fact with respect to

enablement"); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.,* 750 F.2d 1569, 1576 (Fed. Cir. 1984) (holding that, where "patent disclosure list[ed] numerous salts, fuels, and emulsifiers that could form thousands of" claimed combinations, some of which would be inoperable, "the claims [were] not necessarily invalid" for lack of enablement unless a POSA needed to "experiment unduly in order to practice the claimed invention").

2. Written description

AstraZeneca next argues that the patents-in-suit fail to satisfy the written description requirement. A patent specification must contain a written description that "clearly allow[s] persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharms.*, 598 F.3d at 1351 (quoting *Vas–Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)). "The test for the sufficiency of the written description 'is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.'" *Vasudevan Software, Inc.*, 782 F.3d at 682 (quoting Ariad Pharm., Inc., 598 F.3d at 1351). This is a question of fact. *Id.* "A party must prove invalidity for lack of written description by clear and convincing evidence." *Id.* (quoting *Laryngeal Mask Co. Ltd. v. Ambu*, 618 F.3d 1367, 1373–74 (Fed. Cir. 2010)).

Because the asserted claims encompass not just a method of treatment with *specific* irreversible EGFR inhibitors defined by their structure but rather a method of treatment with the entire *class* of irreversible EGFR inhibitors that are capable of performing a specific *function*, the Court agrees with AstraZeneca that the Federal

Circuit's precedent regarding the requirements for the written description of generic and functionally defined claims applies. In particular, the Federal Circuit has explained that "[w]hen a patent claims a genus using functional language to define a desired result, 'the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus.'" *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299 (Fed. Cir. 2014) (quoting *Ariad Pharms.*, 598 F.3d at 1351). "A sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Id.* (quoting *Ariad Pharms.*, 598 F.3d at 1350).

As the Court has explained with respect to AstraZeneca's enablement invalidity argument, there are genuine factual disputes regarding the representativeness of the species disclosed in the specification and regarding whether the specification, combined with the state of the art at the time the patent was filed, would allow a POSA to "visualize or recognize" the compounds that can be used to practice the claims. These same unresolved factual disputes preclude summary judgment in AstraZeneca's favor on the written description defense.

Next, AstraZeneca asserts that the patents-in-suit fail to show possession of the full scope of the claimed methods of treating g/e resistance NSCLC. Again, however, the Court already has concluded that there is a genuine factual dispute regarding whether a POSA would consider the types of NSCLC that AstraZeneca highlights to be

g/e resistant.

Lastly, AstraZeneca argues that the asserted claim of the '162 patent is invalid because there is no written description support for its exclusion of the irreversible EGFR inhibitor CL-387,785. "For negative claim limitations . . . there is adequate written description when, for example, 'the specification describes a reason to exclude the relevant [compound].'" *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, 38 F.4th 1013, 1016 (Fed. Cir. 2022) (quoting *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012)). Here, the specification is not silent regarding the exclusion of Cl-387,785. Rather, it discloses that "[w]hile this work was in progress, another irreversible inhibitor of EGFR [CL-387,785] was shown to inhibit the kinase activity of the T790M EGFR mutant" but "[t]he effectiveness of CL-387,785 in the context of T790M was proposed to result from the absence of a chloride at position 3 of the aniline group" rather than its ability "to bind irreversibly to EGFR." '314 Patent at 18:33–45. This is sufficient to meet the written description requirement for negative claim limitations. AstraZeneca may argue that the exclusion of CL-387,785 casts doubt on whether the specification *enables* a POSA to identify the compounds with which the claimed method of treatment can be practiced without undue experimentation, but as the Court has discussed, genuine disputes of material fact preclude summary judgment on enablement.

C. Non-infringement

AstraZeneca has moved for summary judgment on the ground that Tagrisso does not infringe the asserted claims of the patents-in-suit. "[S]ummary judgment of non-infringement can only be granted if, after viewing the alleged facts in the light most

favorable to the non-movant, there is no genuine issue whether the accused device is encompassed by the claims" as construed by the court. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1304 (Fed. Cir. 1999)).

1. '314 patent

AstraZeneca asserts that there is no genuine dispute that Tagrisso "does not bind in the 'ligand binding pocket' of EGFR (or erbB-2) as required by each of the Asserted Claims of the '314 patent" and therefore it is entitled to judgment as a matter of law. Defs.' Mot. for Summ. Judgment on Non-Infringement at 2. The parties agree that "EGFR is a transmembrane protein that contains three regions, or domains": (1) "the extracellular domain (outside the cell)"; (2) the "transmembrane domain (spans the cell membrane)"; and (3) the "intracellular domain (inside the cell and is also known as the tyrosine kinase domain)." Defs.' Stmt. of Material Facts on Non-infringement ¶ 6. It is further undisputed that "Tagrisso binds to the *intracellular* domain of EGFR, and not the *extracellular* domains of either EGFR or erbB-2." *Id.* ¶ 7 (emphasis added).

The parties dispute whether a POSA would understand the phrase "cysteine 773 residue in the ligand-binding pocket of EGFR or cysteine 805 residue in the ligand-binding pocket of erb-B2" in the asserted claims to refer to the ligand-binding pocket located in the extracellular domain, or whether a POSA would understand the phrase to identify a different ligand-binding pocket located in the intracellular domain.[4]

Because the parties' dispute hinges on the meaning of the claim language rather

[4] For simplicity, the Court will, like the parties, focus its analysis on the portion of the claim that reads "cysteine 773 residue in the ligand-binding pocket of EGFR." The parties do not raise any arguments that are unique to the latter half of the phrase ("cysteine 805 residue in the ligand-binding pocket of erb-B2"), so the Court assumes that part of the claim is not at issue.

than the manner in which Tagrisso functions, the Court agrees with AstraZeneca that this is an issue of claim construction. The question therefore must be resolved by the Court, not the jury. *See O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1362 (Fed. Cir. 2008) ("When the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it.").

A court should construe the words of a claim in accordance with their "ordinary and customary meaning," namely "the meaning that the term would have to 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). Sometimes, the meaning of a term is not immediately apparent, and a court will need to look to other sources to determine "what a person of skill in the art would have understood disputed claim language to mean." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004). These sources include "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* Courts are permitted to consider expert testimony "to ensure that the court's understanding of technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. However, courts must approach expert testimony with caution and ensure that it is "considered in the context of the intrinsic evidence," i.e. "the patent and its prosecution history." *Id.* at 1318–19.

There are two exceptions to the general rule that claim terms are given their ordinary meaning: "1) when a patentee sets out a definition and acts as his own

lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution." *Starhome GmbH v. AT&T Mobility LLC*, 743 F.3d 849, 856 (Fed. Cir. 2014). "To disavow claim scope, the specification must contain expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *See Cont'l Circuits LLC v. Intel Corp.*, 915 F.3d 788, 797 (Fed. Cir. 2019) (internal quotation marks omitted); *see also, Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004) ("Absent a clear disavowal or contrary definition in the specification or the prosecution history, the patentee is entitled to the full scope of its claim language.").

AstraZeneca argues that the intrinsic evidence—namely, the plain meaning, patent specification, and prosecution history—supports its interpretation of the claim language as referring to an extracellular ligand-binding pocket. AstraZeneca points out that the specification states that:

> EGFR is composed of three principal domains, namely, the ***extracellular domain (ECD), which*** is glycosylated and ***contains the ligand-binding pocket*** with two cysteine-rich regions; a short transmembrane domain, and an intracellular domain that has intrinsic tyrosine kinase activity. ***The transmembrane region joins the ligand-binding domain to the intracellular domain***.

Defs.' Mot. for Summ. Judgment on Non-infringement at 3 (quoting '314 Patent at 2:13–19) (emphasis added by AstraZeneca). AstraZeneca also argues that the prosecution history supports its interpretation because "the patent applicants deliberately added the requirement of binding 'in the ligand binding pocket' during prosecution, proposing the following amended claim":

> 29. A method for treating gefitinib and/or erlotinib resistant non-small cell lung cancer in a patient in need thereof, comprising administering to the patient a pharmaceutical composition comprising an irreversible epidermal growth factor

> receptor (EGFR) inhibitor that covalently binds to a cysteine 773 residue in the ligand-binding pocket of EGFR or a cysteine 805 residue in the ligand-binding pocket of erb-B2.

Id. at 4–5 (quoting Defs.' Stmt. of Material Facts on Non-infringement ¶ 14) (underlining reflecting claim amendments). AstraZeneca further asserts that, when the applicants submitted this amendment, they directed the patent officer to "paragraph 0005" of the provisional application, which stated that "the ***extracellular* domain** (ECD) . . . ***contains the ligand-binding pocket*** . . ." *Id.* at 5.

Wyeth does not dispute that EGFR has a "ligand-binding pocket" in the extracellular region or that this extracellular ligand-binding pocket is described in the specification's explanation of EGFR's general structure. It argues, however, that a POSA would understand that the claims refer to a *different* ligand-binding pocket located in the intracellular domain. That is because "EGFR consists of a chain of amino acids bound together, and the 773rd position in the EGFR chain is a cysteine ('cysteine 773')." Pls.' Opp. to Summ. Judgment on Non-Infringement at 2. "Cysteine 773 exists in the intracellular kinase domain, always." *Id.* Wyeth argues that there is an additional ligand, ATP, that "binds inside the cell, where cysteine 773 resides." *Id.* Wyeth asserts that a POSA would "know that the 'ligand-binding pocket' referred to in the claims of the '314 patent is inside the cell where ATP binds and where cysteine 773 resides, not outside the cell where it does not." *Id.* at 5.

The Court construes the term "ligand-binding pocket" to refer to the intracellular ligand-binding pocket of ATP. First, the Court recognizes that the "background" section of the specification includes a reference to "the ligand-binding pocket" in "the extracellular domain." '314 Patent at 2:14–15. But no one disputes that this description

of EGFR's general structure is correct; rather, the question before the court is whether a POSA would understand the "ligand-binding pocket" in the asserted claims to refer to *another* ligand-binding pocket in the intracellular domain. The specification's background reference to the extracellular "ligand-binding pocket" is therefore not dispositive.

Second, the Court disagrees with AstraZeneca that the cited prosecution history sheds light on the issue. The amendment—which added *both* the specific "773" identification and the "ligand-binding pocket" language—came in response to the patent officer's concern that the claims were preempted by prior art (Agus). In response, the applicants explained that the prior art at issue suggested that the "solution to the problem of gefitinib and/or erlotinib resistance in a patient is to simply overwhelm the patient by dosing any TKI at significantly higher doses than the recommended daily dosage or conventional dosage amounts." Winkler Decl., Ex. 30 at 7 ('314 Prosecution Hist., 12/27/2016 Am. and Resp.). In addition, the applicants explained that the prior art failed to "recognize—much less suggest—that the mechanism of action of the selected inhibitor is even a relevant factor in treating gefitinib and/or erlotinib resistant non-small cell lung cancer, nor that the specifically selected inhibitor achieve irreversibility by covalently binding to either the cysteine 773 residue or cysteine 805 residue in the ligand-binding pocket of EGFR or erb-B2, respectively." *Id.* at 8. This reveals only that the applicants sought to provide a more specific identification of how and where the irreversible EGFR inhibitors bind; it does not suggest anything about whether the ligand-binding pocket is extracellular or intracellular.

AstraZeneca is correct that the applicants stated that support for the amendment

could be found in "at least" paragraph 0005, which contains a general description of the structure of EGFR that refers to "the ligand-binding pocket" in the extracellular domain. But that paragraph also contains an explanation that EGFR is made up of "1186 amino acid residues" and a citation to an Ulrich 1984 study, which discloses the complete amino acid sequence of EGFR, including cysteine 773, and explains that the intracellular "cytoplasmic" domain contains "the stretch of the amino acid sequence (approximately residues 690–940)." Winchester Decl., Ex. 18 at PUMA-TAG00000547 (Ulrich 1984). This could just as plausibly be the "support" for the amendment's identification of cysteine 773's location that the applicants were referring to in their response and amendment. The Court therefore does not see how the prosecution history reduces any ambiguity in the claim language.

Finally, both parties have proffered expert testimony on whether a POSA would understand the claim language to refer to an extracellular or intracellular binding site. *Compare, e.g.*, Hausheer Decl., Ex. C ¶¶ 27, 51 ("Within the catalytic domain, EGFR has a binding site for ATP, also known as the ATP-binding pocket. The ATP binding pocket is also sometimes referred to as the ligand-binding pocket because ATP is a ligand that binds to the ATP-binding pocket in the catalytic domain" and "a POSA with a basic understanding of pharmacology, chemistry, and/or biochemistry readily knows that a ligand (Latin; *ligare* meaning 'to bind') means the binding action of the pharmacophore to its intended biologic target, and in this case the irreversible EGFR kinase inhibitor forms a ligand in the kinase domain in EGFR (not somewhere else on EGFR) and covalently binds to the cysteine 773 sulfur atom in the kinase domain of EGFR, thereby inhibiting the aberrant EGFR kinase activity.") *and* Weiss Decl., Ex. C

¶¶ 149, 151 ("[A] POSA would understand that the claim term is *not* referring to the ligand-binding pocket in the extracellular domain. The identification, by number, of the specific cysteine residue in the claim language, would leave no doubt in the POSA's mind that the claim term is referring to a cysteine that is present in the intracellular domain of EGFR" and "would also know that 'ligand binding pocket' in the context of these claims refers to the well-known ATP-binding pocket of EGFR. A 'ligand' for EGFR, in this context is ATP, *i.e.*, ATP, when bound to the ATP-binding pocket, is referred to as a ligand of EGFR.") *with* Reider Decl., Ex. B ¶¶ 136–37 ("The POSA would understand that the 'ligand-binding pocket' referred to in claim 1 of the '314 patent is in the extracellular domain of EGFR . . . . The specification cites to publications that further confirm that EGF is the 'ligand' for EGFR and the 'ligand-binding pocket' is in the extracellular domain of the EGR and is distinct from the intracellular kinase domain.") *and* Jänne Decl., Ex. A ¶¶ 46, 49 ("[T]he '314 Patent itself is clear that the ligand-binding pocket of EGFR is different from the tyrosine kinase domain (which contains the ATP-binding pocket) . . . . A [POSA] reading the patent would understand that the ligand-binding pocket referenced in the [claims] is part of the EGFR enzyme located outside the cell where the EGFR ligand . . . binds, and is not the tyrosine kinase domain inside the cell to which ATP binds.").

The Court notes that there is a key fact that appears to be undisputed by the parties: the asserted claims identify a specific amino acid—cysteine 773—that is *always* found in the intracellular region. Despite the centrality of this fact to Wyeth's arguments, AstraZeneca does not dispute in its brief that cysteine 773 is always located in the intracellular domain or that this is readily known by a POSA. AstraZeneca's

proposed construction would therefore require binding to cysteine 773 outside of the cell, which "is impossible" and would mean that "no compound could practice the invention." Pls.' Opp. to Mot. for Summ. Judgment on Non-Infringement at 4. The Federal Circuit has instructed that, with respect to ambiguous claim language, "where claim language permits an operable construction, the inoperable construction is wrong." *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 904 F.3d 965, 972 (Fed. Cir. 2018) (citing *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1345 (Fed. Cir. 2009)). In *Power Integrations*, for example, the Federal Circuit found that where the claim term was ambiguous but expert testimony demonstrated that one construction would be inoperable, the construction that rendered the claims operable was correct. *Id.* Here, where the location of cysteine 773 was apparently well-established before the patent application was filed and where experts have explained that an additional, intracellular ligand-binding pocket exists (the ATP-binding pocket), the Court is disinclined to adopt a construction that would require a POSA to ignore this existing knowledge and would render the invention inoperable.

The Court concludes that a POSA would understand the ligand-binding pocket referred to in the claims to be the ligand-binding pocket in the intracellular domain (namely, the ATP-binding pocket), where cysteine 773 is located, and not the ligand-binding pocket in the extracellular domain. The Court therefore construes the phrase "cysteine 773 residue in the ligand-binding pocket of EGFR" in the asserted claims as follows: cysteine 773 residue in the ATP-binding pocket of EGFR.

Because AstraZeneca's motion for summary judgment on non-infringement of the '314 patent is premised on a claim construction which the Court has declined to adopt,

the Court denies the motion. Any remaining questions regarding whether Tagrisso infringes the asserted claims of the '314 patent as constructed by the Court must be resolved by the jury.

2. '162 patent

AstraZeneca next asserts that there is no genuine dispute of fact that Tagrisso does not infringe the asserted claim of the '162 patent because Tagrisso does not bind "within the SEQ ID NO: 1 having a T790M mutation." The term "SEQ ID NO:1" refers to "the sequence of 1,210 amino acids making up EGFR ***without any mutations***," which is also known as "wild type" EGFR. Defs.' Mot. for Summ. Judgment on Non-Infringement at 8. AstraZeneca argues that the asserted claim only covers treatment with compounds that bind to wild type EGFR with a single mutation (the T790M mutation) and *with no other mutations*. It is undisputed, however, that "each of Tagrisso's approved indications requires that the patient's cancer have mutations in EGFR different from—or in the case of the second line indication, in addition to—the T790M mutation." *Id.* at 8. Specifically, Tagrisso requires that patients have sensitizing mutations. Because "[t]he Asserted Claim of the '162 patent, by contrast, plainly requires EGFR to have *only* a T790M mutation," AstraZeneca argues that it does not infringe the patent. *Id.*

In response, Wyeth argues that the claim's reference to "SEQ ID NO: 1 having a T790M mutation" "provides information about the *location* of particular mutation (T790M) in the chain; it does not preclude the existence of any other mutation." Pls.' Opp. to Mot. for Summ. Judgment on Non-infringement at 8. In brief, Wyeth argues that a POSA would understand that the entire method of treatment described in the patents

is aimed at patients with sensitizing mutations, and therefore would not read the claim in a manner which would exclude EGFR with sensitizing mutations.

Like AstraZeneca's previous non-infringement argument, the Court concludes that the parties' dispute on this issue hinges on the scope of the claim language (does it cover additional mutations?) and therefore necessitates further claim construction by the Court.

AstraZeneca argues that one of the embodiments in the specification is consistent with its interpretation of the claim. 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, e.g., ***the T790M mutation*** in EGFR, e.g., increased EGFR internalization." Defs.' Mot. for Summ. Judgment on Non-infringement at 9 (quoting '162 Patent at 8:42–47) (emphasis by AstraZeneca). In addition, AstraZeneca argues that the prosecution history supports its construction of the claim because "[t]he applicants intentionally narrowed the claim of the '162 patent during prosecution to require the specific wild-type + T790M sequence." *Id*. at 9. Specifically, AstraZeneca asserts that the claim originally recited the phrase "having a T790M mutation in EGFR (SEQ ID NO: 1)" which the examiner rejected for indefiniteness noting that it suggests that "the ***broad recitation*** *is EGFR* and the claim also recites ***SEQ ID NO: 1 which is the narrower*** statement of the range/limitation." *Id.* (quoting Winkler Decl., Ex. 36 at 7 ('162 Pros. Hist., 06/27/2019 Non-Final Rejection)) (emphasis by AstraZeneca). The applicants then amended the claim "to clarify that the T790M mutation is with respect to SEQ ID NO: 1." Winkler Decl., Ex. 37 ('162 Pros. Hist., 10/28/2019 Am. & Resp.). AstraZeneca

thus argues that "the applicants fully considered whether to elect the broader term, 'EGFR' having a T790M mutation . . . but deliberately declined to do so." Defs.' Mot. for Summ. Judgment on Non-infringement at 10.

In response, Wyeth argues that the plain language of the claim "does not expressly exclude patients with sensitizing mutations, nor does it use the 'closed' language that a patentee might employ to signal that T790M must exist to the exclusion of all other mutations." Pls.' Opp. to Mot. for Summ. Judgment on Non-infringement at 8. Rather, "[a] POSA would understand that the reference sequence provides information about the location of a particular mutation (T790M) in the chain; it does not preclude the existence of any other mutation." *Id.*

Wyeth argues that the plain language of the claim would be reinforced by a POSA's knowledge of the art at the relevant time. Wyeth explains that prior scientific research cited in the patent and familiar to a POSA established that g/e should only be given to patients with at least one sensitizing mutation. Therefore, "a POSA would understand that the '162 patent claims a method of treating patients who are or have become resistant to treatment with gefitinib or erlotinib—two drugs only given to patients with at least one sensitizing mutation." *Id.* at 9. Therefore, a POSA would not understand the phrase "within the SEQ ID NO: 1 having a T790M mutation" as referring exclusively to wild-type EGFR with a single T790M mutation (and no other mutations).

Wyeth also emphasizes that the patent specification "includes numerous examples describing the use of irreversible EGFR inhibitors with NSCLC samples containing sensitizing mutations, including the H1975 cell line, which had both sensitizing mutations and the T790M resistance mutation." *Id.* In addition, Wyeth

points out that AstraZeneca focuses on a single embodiment in the claim, while ignoring two additional embodiments *with* sensitizing mutations.

Finally, Wyeth argues that AstraZeneca misstates the prosecution history of the amendment changing EGFR (SEQ ID NO: 1) to SEQ ID NO: 1. At the time of the examiner's rejection and the subsequent amendment, the specification incorrectly identified SEQ ID NO: 1 as the *nucleic acid* sequence, rather than the *amino acid sequence*. Wyeth's expert explains that a protein, such as EGFR, "can be encoded for by different nucleic acid sequences." Weiss Decl., Ex. C ¶ 37. Therefore, at the time of the examiner's objection, the claim recited "both EGFR generally (the broader limitation) and *a specific nucleic acid sequence* (the misidentified SEQ ID NO: 1)." Weiss Decl., Ex. C ¶ 38. The examiner further noted that it was unclear where the T790M mutation was located in the nucleic acid sequence. The applicants amended the specification to clarify the SEQ ID NO: 1 refers to the amino acid sequence of EGFR and to identify where the mutation occurs by referring to SEQ ID NO: 1 (the amino acid sequence) in the claim. Thus, Wyeth argues that, when read in context, the prosecution history reflects an attempt to identify the location of the T790M mutation and does *not* reflect any intention to limit the claims to *only* wild-type EGFR having a T790M mutation and no other mutations.

The Court declines to adopt AstraZeneca's construction of the claim. First, AstraZeneca's construction would require the Court to add an additional limitation that the compound covalently bind "within the SEQ ID NO: 1 having *only* a T790M mutation *and no other mutations*." But courts cannot "redraft claims." *Process Control Corp. v. HydReclaim Corp*., 190 F.3d 1350, 1357 (Fed. Cir. 1999)

Second, the Court agrees with Wyeth that "[a] POSA would understand that the reference sequence provides information about the location of a particular mutation (T790M) in the chain; it does not preclude the existence of any other mutation." Pls. Opp. to Mot. for Summ. Judgment on Non-infringement at 8. The patent specification highlights that "[t]he inventors of the present invention have surprisingly discovered that irreversible EGFR inhibitors are effective in the treatment of cancer in subjects who are no longer responding to gefitinib and/or erlotinib therapies." '162 Patent at 3:48–51. At the time the patent application was filed, the scientific literature taught that "only those NSCLC patients who had at least one EGFR sensitizing mutation would respond to gefitinib or erlitinib"; therefore those drugs were "given only to patients with at least one sensitizing mutation." Pls.' Opp. to Mot. for Summ. Judgment on Non-infringement at 9. The Court must consider how a POSA would "read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313. AstraZeneca's construction would mean that, despite the specification's indication, the patented method of treatment could not be used on a key patient population—those who had initiated treatment with g/e but developed resistance to those drugs.

Finally, the Court disagrees with AstraZeneca that the prosecution history clearly evidences the applicants' intent to narrow the scope of the claim to include only wild-type EGFR with a single T790M mutation to the exclusion of all other mutations. At best, given the competing explanations of the prosecution history, the evidence is ambiguous. AstraZeneca points to no reason, for example, *why* the applicants would be inclined to specifically disclaim critical embodiments and contradict the purpose of

the invention described in the specification. The examiner's objection (as AstraZeneca frames it) could have been resolved just as easily by amending the claim to include "EGFR having a T790M mutation" and excluding the parenthetical "SEQ ID NO: 1." That would leave unresolved, however, the examiner's concern about the failure to identify the location of T790M. Thus, AstraZeneca's reading of the prosecution history seems to raise more questions than it answers. In sum, the Court does not believe that the prosecution history evidences any intentional choice to limit the plain meaning of the claim in the manner that AstraZeneca now asserts. *See Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004) ("Absent a clear disavowal or contrary definition in the specification or the prosecution history, the patentee is entitled to the full scope of its claim language.").

Because AstraZeneca's motion for summary judgment on non-infringement of the '162 patent is premised on a claim construction which the Court has declined to adopt, the Court denies the motion. Any remaining questions regarding whether Tagrisso infringes the asserted claim of the '162 patent as constructed by the Court must be resolved by the jury.

D. Pre-issuance damages

AstraZeneca argues that it is entitled to summary judgment on Wyeth's request for pre-issuance damages because these damages are unavailable for induced infringement (the only type of infringing conduct of which AstraZeneca is accused). The Court agrees. As a general rule, "patent owners may only collect damages for patent infringement that takes place during the term of the patent." *Rosebud LMS Inc. v. Adobe Sys. Inc.*, 812 F.3d 1070, 1073 (Fed. Cir. 2016). There is "a narrow exception to

that rule," codified at 35 U.S.C. § 154(d), that provides some "provisional rights" to patent owners while the patent application is pending. These provisional rights include "the right to obtain a reasonable royalty from any person who, during the period beginning on the date of publication of the application for such patent . . . and ending on the date the patent is issued":

> (A)(i) makes, uses, offers for sale, or sells in the United States the invention as claimed in the published patent application or imports such an invention into the United States; or
>
> (ii) if the invention as claimed in the published patent application is a process, uses, offers for sale, or sells in the United States or imports into the United States products made by that process as claimed in the published patent application[.]
>
> [. . .]

35 U.S.C. § 154(d)(1). Notably, the language of subsections (A)(i) and (A)(ii) parallels the language of 35 U.S.C. §§ 271(a) and 271(g), which define certain acts constituting infringement during the term of the patent. But section 154(d) includes *no* provision incorporating the language of section 271(b), which defines induced infringement during the term of a patent. The clear takeaway is that the statute does not authorize pre-issuance damages for induced infringement.

Wyeth does not dispute that AstraZeneca's alleged conduct falls outside the scope of sections 154(d)(1)(A)(i) and (ii). Rather, it argues that because section 271(b) states that "[w]hoever actively induces infringement of a patent shall be liable as an infringer," there is no need for section 154(d) to "expressly mention *induced* infringement." Pls.' Opp. to Mot. for Summ. Judgment on Non-infringement at 11. The Court disagrees, for two reasons. First, Wyeth's interpretation is contrary to the plain

text of section 271(b), which covers induced infringement "*of a patent.*" (emphasis added). By definition, pre-issuance damages occur before any patent exists. Therefore, section 271(b) does not permit recovery. Second, Wyeth's interpretation is contrary to section 154(d). Section 154(d) does not extend *all* post-issuance patent rights to the pre-issuance period; rather, it is a "narrow exception" that permits recovery only for certain conduct that is specifically enumerated in the statute. *Rosebud LMS Inc.*, 812 F.3d at 1073. Because AstraZeneca is only accused of induced infringement, it cannot be liable for pre-issuance damages as a matter of law.

E. Advice-of-counsel defense

Wyeth has moved for partial summary judgment on AstraZeneca's advice-of-counsel defense to Wyeth's willful infringement claim. Wyeth asserts that AstraZeneca cannot argue that it relied on advice of its counsel regarding whether Tagrisso infringed the patents-in-suit because there is no evidence that such advice was communicated to "business decisionmakers with the authority to decide whether to go forward with potentially infringing acts." Pls.' Mot. for Summ. Judgment on Advice-of-Counsel Defense at 1. AstraZeneca argues that the Court is not authorized to resolve this issue at the summary judgment stage because "[a]n accused infringer's reliance on advice of counsel is not a standalone issue . . . [but] instead one consideration among the 'totality of circumstances' bearing on alleged 'culpability' and the ultimate question of willfulness." Defs.' Opp. to Mot. for Summ. Judgment on Advice-of-Counsel Defense at 1 (quoting *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 811 (Fed. Cir. 2007)). AstraZeneca argues in the alternative that the evidence supports its advice-of-counsel defense.

In *Halo Electronics, Inc. v. Pulse Electronics, Inc.*, 579 U.S. 93 (2016), the Supreme Court clarified that the standard for "willful" infringement is a subjective standard that depends on the infringer's state of mind at the time it infringed. *Id.* at 105. "[A]n accused infringer's reliance on an opinion of counsel regarding noninfringement or invalidity of the asserted patent" is "relevant to the infringer's state of mind." *Sunoco Partners Mktg. & Terminals L.P. v. U.S. Venture, Inc.*, 32 F.4th 1161, 1178 (Fed. Cir. 2022) (quoting *Omega Pats., LLC v. CalAmp Corp.*, 920 F.3d 1337, 1353 (Fed. Cir. 2019)). By presenting an advice-of-counsel defense, "an accused willful infringer aims to establish that due to reasonable reliance on advice from counsel, its continued accused activities were done in good faith." *In re Seagate Tech., LLC*, 497 F.3d 1360, 1369 (Fed. Cir. 2007), *abrogated on other grounds by Halo Elecs., Inc.*, 579 U.S. 93. "Typically, counsel's opinion concludes that the patent is invalid, unenforceable, and/or not infringed." *Id.* "Although an infringer's reliance on favorable advice of counsel, or conversely his failure to proffer any favorable advice, is not dispositive of the willfulness inquiry, it is crucial to the analysis." *Id.*

As an initial matter, the Court concludes that this issue is appropriate for summary judgment. Rule 56(a) permits parties to seek summary judgment on "part" of a "claim or defense." *See* Fed. R. Civ. P. 56(a) ("A party may move for summary judgment, identifying each claim or defense—*or the part of each claim or defense*—on which summary judgment is sought.") (emphasis added). If no reasonable jury could conclude based on the record that AstraZeneca relied on the advice of counsel with respect to its alleged infringement of the patents-in-suit, then the Court has the authority to grant summary judgment on that issue in favor of Wyeth. Although this would not

resolve whether AstraZeneca's infringement was willful, it would resolve "part" of AstraZeneca's defense to that claim. The Court concludes that Wyeth's motion is proper and thus will address its merits.

AstraZeneca asserts that it relied on opinions from outside counsel, Robert Armitage, concerning the validity of the patents-in-suit. The parties refer to these opinions as the Armitage Opinions. It is undisputed that "the only persons at AstraZeneca with whom [Armitage] discussed the Armitage Opinions were in-house attorneys," specifically, Dr. Scott Alban (Senior Vice President for Global Intellectual Property), Dr. Shannon Carroll (Assistant General Counsel, IP Oncology), and Christin Sullivan-Miller (Senior Counsel, Oncology). Pls.' Stmt. of Material Facts on Advice-of-Counsel Defense ¶ 12.[5]

AstraZeneca designated Dr. Alban as its Rule 30(b)(6) witness and "confirmed that Dr. Alban was prepared to testify about how any opinion of counsel . . . made its way to a decisionmaker at AstraZeneca." Pls.' Stmt. of Material Facts on Advice-of-Counsel Defense ¶ 32. During the deposition, the following exchange took place between the plaintiffs' counsel and Alban:

> Q: So with respect to the continued marketing of Tagrisso by AstraZeneca, who has the authority to – at AstraZeneca to say, you need to stop marketing Tagrisso, or will you just continue marketing Tagrisso?
>
> A: That would probably be a board level decision.

Winchester Decl., Ex. 12 at 76:22–77:4 (Alban Dep.). Dr. Alban also testified during the deposition that he discussed the Armitage Opinions with only two other people (besides

[5] There appears to be some confusion between the parties over the exact job titles of Dr. Alban, Dr. Carroll, and Sullivan-Miller, but any dispute is immaterial to the present motion.

Dr. Carroll and Sullivan-Miller): Jeffrey Pott, General Counsel at AstraZeneca, and Benjamin McDonald, in-house counsel at AstraZeneca. Dr. Alban stated that neither Pott nor McDonald were on AstraZeneca's Board of Directors.

After Dr. Alban's deposition, Wyeth served subpoenas for the depositions of Sir Pascal Soriot (the CEO of AstraZeneca), Dr. Alban, McDonald, Pott, and Sullivan-Miller. AstraZeneca filed a motion for a protective order to prevent the depositions. In granting the motion, the Court stated that AstraZeneca would not be able to rely on the testimony of the employees whose depositions it declined. *See* Pls.' Stmt. of Material Facts on Advice-of-Counsel Defense ¶ 37 ("That's the price you pay by preventing their depositions. They won't be able to be witnesses. That means an affidavit on a summary judgment motion, an affidavit in response to a summary judgment motion, a witness at a trial or other hearing, full stop.") (internal citation omitted).

Wyeth now argues that, because Dr. Alban stated that only the Board could decide whether to continue selling Tagrisso, and because there is no evidence that the Armitage Opinions or in-house counsel's conclusions from those opinions were communicated to members of the Board of Directors, AstraZeneca's advice-of-counsel defense fails as a matter of law. AstraZeneca responds that Alban, Pott, and McDonald—not the Board—were the relevant decisionmakers, and that there is evidence from Dr. Alban's 30(b)(6) deposition and from e-mail communications that Dr. Alban, Pott, and McDonald relied on the advice from the Armitage Opinions in deciding not to license the patents-in-suit. Wyeth counters that in-house lawyers categorically cannot be considered "business decisionmakers" for purposes of the advice-of-counsel defense, and that, at any rate, it is undisputed that Alban, Pott, and McDonald lacked

the authority to pull Tagrisso from the market.

Neither the law nor the evidence supports Wyeth's contention that only AstraZeneca's Board of Directors can be considered the relevant "decisionmaker" that must rely directly on the Armitage Opinions for purposes of the advice-of-counsel defense. First, Wyeth cites no support for its categorical rule that "[a]dvice of counsel cannot provide a defense to a charge of willful infringement if it starts and ends in the legal group." Pls.' Mot. for Summ. Judgment on Advice-of-Counsel Defense at 2. Although the Court agrees with the straightforward proposition that the legal advice at issue must have been "communicated to the defendant's decisionmakers," *Omega Pats., LLC*, 920 F.3d at 1353, there is nothing that prevents a business from delegating some decision-making authority to employees who happen to be lawyers (as AstraZeneca asserts that it does). Courts examining this issue have focused on the authority of the employees relying on (or ignoring) the advice of counsel, not on their job titles. *See, e.g.*, *Harris Corp. v. Ericsson Inc.*, 417 F.3d 1241, 1259 (Fed. Cir. 2005) (upholding a jury's finding of willfulness because the defendant "could not confirm that any executive with decision-making authority in [the defendant's] marketing or engineering departments had ever relied on the opinion" *or* "whether the known recipients of the opinion, *two in-house attorneys, had any product or marketing responsibility*" (emphasis added)); (overturning jury's finding of willfulness in part because the defendant presented evidence that it had commissioned an opinion from outside counsel and the defendant's "head of U.S. Patent Litigation" testified that "he relied on the opinion letter to conclude that [the defendant] had a legitimate invalidity defense"); *Chiron Corp. v. Genentech, Inc.*, 268 F. Supp. 2d 1117, 1121 (E.D. Cal.

2002) (noting that the actor "ultimately responsible for deciding not to license [the plaintiff's] patent" was the defendant's "Executive Committee," which included the defendant's "general counsel").

Second, Dr. Alban's testimony that only the Board of Directors held the power to decide whether to pull Tagrisso from the market does not establish that the Board is the only relevant decisionmaker for purposes of the willfulness inquiry. As AstraZeneca explains, pulling Tagrisso—a highly successful drug—from the market was likely not a plausible option. There is evidence that AstraZeneca considered but declined to license the patents-in-suit, which likely would have been a more realistic option for responding to the alleged infringement. Although Dr. Alban's 30(b)(6) testimony establishes that only the Board had the authority to pull Tagrisso from the market, it does not establish that only the Board had authority to make the kind of IP licensing decision at issue here.

The Court notes that, given AstraZeneca's refusal to permit Wyeth to depose Pott, McDonald, and Alban in his personal capacity, there may be lingering evidentiary and sufficiency issues with AstraZeneca's apparent intention to argue now that those actors were, in fact, the decisionmakers whose subjective reliance on the Armitage Opinions is the crux of its defense. But because Wyeth has not pressed this issue in its summary judgment motion, the Court will not consider whether summary judgment is warranted on these grounds.

F. Motions to exclude expert testimony

"Pursuant to *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L.Ed.2d 469 (1993), district courts perform a gatekeeping function to ensure that expert testimony meets the requirements of Federal Rule of Evidence 702."

Karlo v. Pittsburgh Glass Works, LLC, 849 F.3d 61, 80 (3d Cir. 2017). "Rule 702 embodies three distinct substantive restrictions on the admission of expert testimony: qualifications, reliability, and fit." *Id.* (quoting *Elcock v. Kmart Corp.*, 233 F.3d 734, 741 (3d Cir. 2000)).

First, to satisfy the "qualifications" requirement, the witness must "possess specialized expertise." *Pineda v. Ford Motor Co.*, 520 F.3d 237, 244 (3d Cir. 2008) (quoting *Scheider ex rel. Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003)). The Third Circuit "interpret[s] Rule 702's qualification requirement liberally." *Id.* Accordingly, a "broad range of knowledge, skills, and training qualify an expert"; the expert need not be the "best qualified" or "have the specialization that the court considers most appropriate" to satisfy Rule 702. *Id.* (quoting *Holybrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d Cir. 1996)).

Second, to satisfy the "reliability" requirement, the expert testimony "be based on the methods and procedures of science, not on subjective belief and unsupported speculation." *In re TMI Litig.*, 193 F.3d 613, 663 (3d Cir. 1999). "The standard for reliability is 'not that high' [and] is 'lower that the merits standard of correctness.'" *Karlo*, 849 F.3d at 81 (quoting *In re TMI Litig.*, 193 F.3d at 665). The question is whether "the expert's testimony is supported by 'good grounds.'" *Id.* (quoting *In re TMI Litig.*, 193 F.3d at 665). "Where there is a logical basis for an expert's opinion testimony, the credibility and weight of that testimony is to be determined by the jury, not the trial judge." *Leonard v. Stemtech Int'l Inc.*, 834 F.3d 376, 391 (3d Cir. 2016) (quoting *Breidor v. Sears, Roebuck & Co.*, 772 F.2d 1134, 1138–39 (3d Cir. 1983)).

Finally, the "fit" requirement "goes primarily to relevance" and "ensures that the

evidence or testimony '[helps] the trier of fact to understand the evidence or to determine a fact in issue.'" *Karlo*, 849 F.3d at 81 (quoting *In re TMI Litig.*, 193 F.3d at 663).

1. Mulhern and Dr. Bivona

Wyeth first argues that the Court should exclude the opinions of AstraZeneca's damages expert, Carla Mulhern. Mulhern's damages opinion relies on her statistical analysis of patient health data compiled from Flatiron, a health technology company that "maintains a database of information abstracted from electronic medical records," including records from oncology patients. Defs.' Opp. to Mot. to Exclude Test. of Mulhern & Bivona at 2. Mulhern used this data to calculate the percentage of certain NSCLC patients with a T790M mutation. (Wyeth asserts that the prevalence of this mutation is relevant to distinguishing infringing from non-infringing uses of Tagrisso.) Mulhern calculated that the rate of pretreatment T790M recorded in the Flatiron data was approximately 3.8%. This is significantly lower than the 35% estimate offered by Wyeth's expert, Dr. Alice Berger.

Wyeth first argues that Mulhern's opinion must be excluded because she is "an economist with no scientific or medical training" and therefore is not qualified to opine about the prevalence of T790M. Pls.' Mot. to Exclude Test. of Mulhern & Bivona at 1. The Court disagrees. The scope of Mulhern's report and testimony with respect to T790M prevalence is clear: she conducted a statistical analysis of the Flatiron patient data. That is squarely in her wheelhouse as an experienced economist. Contrary to Wyeth's argument, Mulhern need not be a "clinician, genomics researcher, or an epidemiologist" merely because the data she is analyzing relates to genetic cancer

testing. *Id.* at 6. Mulhern is not personally testing patients for T790M, opining on the sensitivity or accuracy of such testing, or otherwise offering medical or scientific opinions about the substance of the data. The fact that Wyeth believes that Dr. Berger's expertise as a cancer researcher makes her opinion on T790M prevalence based on scientific studies more *persuasive* than Mulhern's statistical analysis of real-world patient data does not mean that Mulhern is not qualified to conduct such an analysis or that her opinion is unreliable. There is no requirement that an expert be the "best qualified," *Pineda*, 520 F.3d at 244, or that an expert's opinion be based on the "best foundation" or the "best methodology" to be admissible. *Karlo*, 849 F.3d at 81. Apart from questioning the reliability of the Flatiron data (which the Court addresses next), AstraZeneca offers no reason to doubt Mulhern's ability to reliably calculate the prevalence of T790M mutation in that data.

Wyeth next argues that Mulhern's testimony should be excluded because the Flatiron data is unreliable. Wyeth asserts that Mulhern does not know, for example, if AstraZeneca "processed or otherwise manipulated the data before it was given to Ms. Mulhern," "whether the Flatiron data is representative of the population of Tagrisso patients," or "whether the T790M mutation status was recorded in all of the underlying electronic health records that she used," among other potential flaws with the raw data. Pls.' Mot. to Exclude Test. of Mulhern & Bivona at 11. Along the same lines, Wyeth argues that Mulhern makes too many "unwarranted assumptions" regarding the Flatiron data because she assumes that the Flatiron data is representative of the relevant patient population, that all patients in the dataset were tested for T790M, and that the test results were reliably recorded in the dataset. *Id.* at 14.

The Court disagrees that these potential flaws with the Flatiron data justify the exclusion of Mulhern's opinion as unreliable. Generally, when the data supporting an expert's opinion is called into question, courts need only "assess whether there are good grounds to rely on this data to draw the conclusion reached by the expert." *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 749 (3d Cir. 1994); *see also In re Zoloft Prod. Liab. Litig.*, 858 F.3d 787, 792–93 (3d Cir. 2017) ("A court should not, however, usurp the role of the fact-finder; instead, an expert should only be excluded if the flaw is large enough that the expert lacks the good grounds for his or her conclusions." (internal quotations and citations omitted)). Here, there is evidence that the Flatiron data contains a large sample size from a demographically and geographically diverse population and that this data is used by pharmaceutical companies and researchers. In addition, there is evidence that the Flatiron data was "specifically designed to permit analysis of the biologic makeup—including the T790M status—of Tagrisso patients in a comprehensive way." Defs.' Opp. to Mot. to Exclude Test. of Mulhern & Bivona at 11. The Court concludes that this is sufficient to establish that Mulhern had "good grounds" to rely on the Flatiron data to estimate the prevalence of T790M mutations in Tagrisso patients. Wyeth's critiques of the limitations of the Flatiron data are more appropriately explored on cross-examination. *See Daubert*, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.").

Wyeth also suggests that AstraZeneca failed to timely produce the Flatiron data during discovery. According to Wyeth, "[a]t no point during the fact discovery period did

AstraZeneca produce Flatiron data or suggest that historical Flatiron data was appropriate for determining the prevalence of de novo T790M" and "[t]he first time Flatiron data was used in this case was in Ms. Mulhern's rebuttal report." *Id.* at 14. To the extent that Wyeth is requesting that the Court exclude Mulhern's testimony as a sanction under Rule 37(c) for a discovery violation, the Court declines to do so because Wyeth has not explained whether and how it was prejudiced by the late disclosure. As AstraZeneca points out, there is no dispute that Wyeth eventually received the raw Flatiron data and that Wyeth's expert examined that data following Mulhern's report and arrived at "nearly identical calculations" regarding the T790M rate in the patient records. Defs.' Opp. to Mot. to Exclude Test. of Mulhern & Bivona at 17. The Court therefore concludes that any violation of Rule was harmless. *See* Fed. R. Civ. P. 37(c)(1) ("If a party fails to provide information . . . as required by Rule 26(a) or (e), the party is not allowed to use that information . . . unless that failure was substantially justified or is harmless.").

Finally, Wyeth argues that Dr. Bivona's opinion should be excluded because he relies on Mulhern's data analysis. Because the Court has concluded that Mulhern's testimony is admissible and Wyeth offers no independent rationale for exclusion, the Court declines to exclude Dr. Bivona's testimony.

2. Dr. Jänne and Mulhern

Wyeth argues that the Court should exclude Dr. Jänne's testimony because he "has no experience or specialized knowledge regarding economics, marketing, or licensing and thus lacks the relevant expertise" to offer opinions regarding Tagrisso's commercial success, commercial acquiescence to the patents-in-suit, and market

competition between Pfizer's Vizimpro product and Tagrisso. Pls.' Mot. to Exclude Test. of Jänne & Mulhern at 1. Specifically, Wyeth takes issue with three of Dr. Jänne's conclusions: (1) Tagrisso's sales are not driven by the patented features, (2) the industry did not acquiesce that the patents-in-suit have value, and (3) Vizimpro does not compete with Tagrisso.

First, Wyeth asserts that Dr. Jänne is not qualified to opine that Tagrisso's sales are not driven by patented features because he is not an economics or marketing expert. Wyeth also argues that Dr. Jänne impermissibly relies on "his own personal prescribing practices" that are not generalizable to other physicians. *Id.* at 4–5.

The Court disagrees with this characterization of Dr. Jänne's opinion. Dr. Jänne's testimony is largely focused on explaining the differences between the method of treatment claimed by the patents-in-suit and the uses, effects, and advantages of Tagrisso. For example, he explains that Tagrisso is prescribed to "multiple patient populations (not just T790M+ patients)" because patients tend to tolerate it far better than other drugs. Defs.' Opp. to Mot. to Exclude Test. of Jänne & Mulhern at 8. As an expert in the clinical treatment of NSCLC and the development of drugs to treat NSCLC, Dr. Jänne clearly is qualified to explain the clinical attributes of Tagrisso that lead oncologists to prescribe the drug. This type of testimony requires precisely Dr. Jänne's expertise—not knowledge of economic or marketing strategies.

Second, Wyeth argues that Dr. Jänne should not be permitted to offer a rebuttal opinion that licensing activity demonstrates disregard for the patents-in-suit "because he is not an expert in patent licensing and he has never been involved in negotiation of a patent license." Pls.' Mot. to Exclude Test. of Jänne & Mulhern at 6. Again, however,

Dr. Jänne's rebuttal opinion is based on his extensive experience in the field of NSCLC treatment research and drug development. Wyeth's expert, Dr. Rao, asserts that there is evidence of commercial acquiescence to the non-obviousness of the patents-in-suit; Dr. Jänne counters that "the groups and companies developing [ ] irreversible inhibitors did not seek access to the technology within the patents-in-suit through a license," which "contradicts Dr. Rao's opinions that the licensing activity amongst the Plaintiffs demonstrates that the patents-in-suit are valuable or non-obvious." Defs.' Opp. to Mot. to Exclude Test. of Jänne & Mulhern at 13. Dr. Jänne's specialized knowledge regarding the research groups, companies, and institutions operating in this specific area qualifies him to opine on whether and how these groups' lack of licensing activity reflects on the industry's view of the value of the patents-in-suit. This is underscored by his identification and evaluation of specific entities and clinical trials that have undertaken relevant work in the area of irreversible EGFR inhibitors.

Wyeth emphasizes that Dr. Jänne fails to explain whether the entities and clinical trials that he identifies "needed" licenses to the patents-in-suit. But this argument begs the question. The Court understands the thrust of Dr. Jänne's testimony to be that, if the patents were as valuable as Wyeth claims, these are precisely the groups that one would expect to license them. In other words, whether the groups "needed" licenses would depend at least in part on whether the groups viewed the patents-in-suit as valuable. At any rate, the fact that Wyeth may be able to advance an alternative explanation for these actors' behavior for reasons unrelated to the value of (or the commercial acquiescence to) the patents-in-suit does not render inadmissible Dr. Jänne's testimony to the contrary.

Third, Wyeth argues that Dr. Jänne lacks the necessary economic/marketing expertise to opine whether Vizimpro is a "competitor" to Tagrisso. In addition, Wyeth argues that Dr. Jänne based his opinion only on his personal prescribing preferences. Pls.' Mot. to Exclude Test. of Jänne & Mulhern at 7. Again, however, the Court disagrees with Wyeth's characterization of Dr. Jänne's testimony. Dr. Jänne does not purport to offer an *economic* opinion on the issue. Nor does he rely solely on his personal prescribing preferences as a physician. Rather, his opinion compares Vizimpro and Tagrisso from a medical and scientific perspective. For example, Dr. Jänne compares the approved indications of each drug, the presence/absence of each drug in clinical practice guidelines, and the published research regarding the effectiveness, resistance, and other aspects of the drugs. Thus, Dr. Jänne properly relies on his technical expertise as an oncologist-researcher specializing in the treatment of NSCLC to rebut Wyeth's experts' testimony regarding the similarity of the drugs. In sum, the Court concludes that Dr. Jänne is qualified to offer his technical opinion on the nexus between the commercial success of Tagrisso and the patents-in-suit, commercial acquiescence to the patents-in-suit, and market competition between Tagrisso and Vizimpro.

With respect to Mulhern, Wyeth mainly argues that her opinions should be excluded because she relies on Dr. Jänne's opinions. Because the Court has concluded that Dr. Jänne's opinions are admissible, the Court will not exclude Mulhern's opinions for that reason. In addition, Wyeth argues that Mulhern (like Dr. Jänne) "opines that third-party development of irreversible EGFR inhibitors by others without a license undermines [Wyeth's] expert's opinions on commercial acquiescence," but "fails

to consider whether those third-parties even needed a license." Pls.' Mot. to Exclude Test. of Jänne & Mulhern at 2. The Court declines to exclude Mulhern's opinion on that basis for the same reasons already discussed.

3. Dr. Rao

AstraZeneca argues that the Court should exclude the opinion of Wyeth's damages expert, Dr. Mohan Rao, regarding a reasonable royalty rate because he relies on six licenses of patents that he has not shown are comparable to the patents-in-suit. In AstraZeneca's view, Dr. Rao "failed to offer any analysis . . . showing that the patents exchanged in any of those licenses are technically comparable to the patents at issue" in this case. Defs.' Mot. to Exclude Test. of Rao at 2. Wyeth responds that Dr. Rao has adequately established the comparability of the licenses and accounted for technological and economic differences between the comparator licenses and the hypothetical license of the patents-in-suit.

"The party proffering a license bears the burden of establishing it is sufficiently comparable to support a proposed damages award." *Adasa Inc. v. Avery Dennison Corp.*, 55 F.4th 900, 915 (Fed. Cir. 2022). This means that "the proponent 'must account for differences in the technologies and economic circumstances of the contracting parties.'" *Id.* (quoting *Finjan, Inc. v. Secure Computing Corp.*, 626 F.3d 1197, 1211 (Fed. Cir. 2010)). But the Federal Circuit has held "that the issue of comparability is often one of sufficiency of the evidence, not admissibility." *Bio-Rad Lab'ys, Inc. v. 10X Genomics Inc.*, 967 F.3d 1353, 1373 (Fed. Cir. 2020). "[T]he fact that a license is not perfectly analogous generally goes to the weight of the evidence, not its admissibility." *Id.* (quoting *Ericsson, Inc. v. D-Link Sys., Inc.*, 773 F.3d 1201,

1227 (Fed. Cir. 2014)). As a result, "the 'degree of comparability' of the license agreements is a 'factual issue[ ] best addressed by cross examination and not by exclusion.'" *Id.* (quoting *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1333 (Fed. Cir. 2012)). Expert testimony on reasonable royalty rates based on allegedly comparable licenses generally is admissible so long as the expert has made "a showing of 'baseline comparability.'" *Id.* at 1374.

The Court concludes that Dr. Rao has established the "baseline comparability" of the six licenses at issue and the patents-in-suit. To identify comparable licenses, Dr. Rao relied on BioSciDB, "a comprehensive, peer-reviewed reference database on biopharma alliances consisting of more than 11,000 contracts." Pls.' Opp. to Mot. to Exclude Test. of Rao at 2. The licenses Dr. Rao analyzed (1) "all involved running royalties to sell products to treat lung cancer patients," (2) were entered into within ten years of the hypothetical negotiation between the parties, and (3) involved technology "at the same or similar stage of development as Tagrisso." Pls.' Opp. to Mot. to Exclude Test. of Rao at 2. Moreover, Dr. Rao explained in his report and deposition the various adjustments he made to account for the different circumstances of each license, such as whether the licenses were exclusive, entered into under threat of litigation, contained redacted terms, or included potentially more valuable patents such as compound patents. This is sufficient to establish "baseline comparability" between the licenses for purposes of the admissibility of Dr. Rao's testimony. Accordingly, AstraZeneca's critiques regarding the alleged differences between the BioSciDB licenses and patents-in-suit are more appropriate for cross-examination or to argue that the evidence is insufficient to support Wyeth's reasonable royalty calculation.

AstraZeneca also argues that the Court should exclude Dr. Rao's testimony because the BioSciDB licenses appeared for the first time in his opening expert report and were not disclosed during fact discovery. But the Court does not see, and AstraZeneca does not explain, how it has been prejudiced by the late disclosure (which, at any rate, was eight months before trial). AstraZeneca briefly states in its reply that the late disclosure "prevent[ed] discovery into those licenses." Defs.' Reply to Mot. to Exclude Test. of Rao at 1. It is unclear, however, and AstraZeneca does not explain, what additional discovery it needed given that the licenses were obtainable from a publicly available database. The Court therefore concludes that any late disclosure was harmless. *See* Fed. R. Civ. P. 37(c)(1) ("If a party fails to provide information . . . as required by Rule 26(a) or (e), the party is not allowed to use that information . . . unless that failure was substantially justified or is harmless.").

Conclusion

The Court grants AstraZeneca's motion to dismiss [dkt. 268] with respect to Puma Biotechnology but denies the motion to dismiss with respect to Wyeth. The Court denies AstraZeneca's motion for summary judgment on invalidity [dkt. 270]. The Court denies AstraZeneca's motion for summary judgment on non-infringement [dkt. 273], except with respect to the issue of pre-issuance damages, on which the Court rules in favor of AstraZeneca. The Court denies Wyeth's motion for summary judgment on AstraZeneca's advice-of-counsel defense [dkt. 288]. Finally, the Court denies Wyeth's motions to exclude the testimony of Mulhern, Dr. Bivona, and Dr. Jänne, [dkt. 277 & dkt. 280] and denies AstraZeneca's motion to exclude the testimony of Dr. Rao [dkt. 276]. The case is set for a telephonic status hearing on March 22, 2024 at 8:30

a.m. The following call-in number will be used: 888-684-8852, access code 746-1053. Trial counsel should participate in the hearing. Prior to that date, the parties are to confer regarding the motion to limit prior art defenses to attempt to agree upon appropriate limitations.

MATTHEW F. KENNELLY
United States District Judge

Date: March 18, 2024