IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ALEXION PHARMACEUTICALS, INC. and ALEXION PHARMA INTERNATIONAL OPERATIONS LTD.,	)	
Plaintiffs,	)	C.A. No. 24-5-GBW
v.	)	[redacted]
SAMSUNG BIOEPIS CO. LTD.,	)	
Defendant.	)	

PLAINTIFFS' REPLY BRIEF IN SUPPORT OF THEIR EMERGENCY MOTION FOR INJUNCTION PENDING APPEAL AND TEMPORARY RESTRAINING ORDER PENDING RESOLUTION OF THIS MOTION

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I. INTRODUCTION

Samsung's opposition brief (D.I. 68, "Op. Br.") misconstrues facts and law to diminish the importance, validity, and enforceability of Alexion's PI Patents. Namely, Samsung contradicts its own argument regarding Alexion's alleged delay, ignores binding statutory and Federal Circuit law, incorrectly accuses Alexion of an improper reply regarding validity of the '176 patent, and incorrectly characterizes Dr. Blasco's testimony.

Additionally, Samsung continues to incorrectly suggest that Alexion's settlement with another challenger is somehow indicative of a lack of harm to Alexion upon biosimilar entry. If Samsung were allowed to launch, Alexion cannot be put back into the place that it would have been had its patent rights been respected. That harm to Alexion cannot be fully calculated or fully compensated. The injunctive relief Alexion seeks is thus required to maintain the status quo pending the outcome of Alexion's appeal, which will not prejudice or harm Samsung.

II. SAMSUNG'S DELAY ARGUMENT IS BELIED BY THE FACTS

Alexion did not delay. Samsung's July 7, 2023 Notice of Commercial Marketed stated [redacted] Samsung's argument about Alexion's alleged "[u]nexplained delay," Op. Br. at 15, is thus belied by its contradictory statement that "there is no emergency," *id*. at 2. Accordingly, this argument should be rejected.

The case law cited by Samsung also supports Alexion's position that there was no delay. Pfizer waited until after Ranbaxy launched to file suit and move for a preliminary injunction, which the district court granted and the Federal Circuit affirmed. *Pfizer, Inc.* v. *Teva Pharms., USA, Inc.*, 429 F.3d 1364, 1381 (Fed. Cir. 2005) (finding no abuse of discretion in finding that Pfizer did not delay.). Genentech did not file a motion for preliminary injunction until "fourteen months after receiving the Notice of Commercial Marketing, three months after receiving a fairly specific launch date, and almost one month after Amgen had FDA approval." *Genentech, Inc.* v. *Amgen Inc.*, No. CV 18-924-CFC, 2019 WL 3290167, at *2 (D. Del. July 18, 2019), *aff'd*, 796 F. App'x 726 (Fed. Cir. 2020).

III. SAMSUNG FAILS TO REBUT ALEXION'S LIKELIHOOD OF SUCCESS

Samsung has not addressed Alexion's infringement allegations. *See, e.g.*, D.I. 38 at 7, n.3. For purposes of these proceedings, then, infringement by Samsung is undisputed.

Nor did Samsung succeed at raising a substantial question regarding the validity of either of the PI Claims. The Court's May 6, 2024 decision (D.I. 57 ("Opinion")) denied Alexion's motion for a preliminary injunction for a single reason—a failure to show a likelihood of success on the merits—and did not address the three other elements for issuing an injunction. The Court's reasoning for why Alexion failed to show a likelihood of success rested on two findings: (1) the PTAB's Institution Decision regarding the '189 patent; and (2) the combination of Noris (2005) and the Soliris® Label (2007) regarding the '176 patent. Alexion is likely to succeed on appeal because, among other reasons, statutory law will estop Samsung from raising its obviousness arguments at trial, and the combination of Noris (2005) and the Soliris® Label (2007) fails to provide a reasonable expectation of success and is tainted by impermissible hindsight.

A. The '189 Patent

1. Estoppel Prevents Samsung from Relying on its IPR Challenge

As this Court and Samsung both acknowledge, "at the preliminary injunction stage it is the patentee 'who must persuade the court that, despite the challenge presented to validity, the patentee nevertheless is ***likely to succeed at trial on the validity issue***." Opinion at 3 (citing *Titan Tire Corp.* v. *Case New Holland, Inc.*, 566 F.3d 1372, 1377 (Fed. Cir. 2009)) (emphasis added). Samsung presented two theories regarding the '189 patent in response to Alexion's motion—the obviousness grounds it raised in its IPR, and inequitable conduct. Op. Br. at 5-7. Samsung did not sufficiently plead the latter, which requires a high threshold of proof, including proving that Alexion "specific[ally] intend[ed] to deceive the PTO." *Therasense, Inc.* v. *Becton, Dickinson & Co.*, 649 F.3d 1276, 1287 (Fed. Cir. 2011). No such proof exists here. *See* D.I. 36 at 6-18. Nor did this Court address Samsung's inequitable conduct argument in the decision now on appeal.

As for the former, by operation of law and act of Congress, Samsung will be estopped from asserting its obviousness theories at trial. 35 U.S.C. § 315(e)(2). This statutory mandate is undisputed. Nor is it disputed that Section 315(e)(2) applies regardless of the outcome at the PTAB. Win or lose, Samsung will be estopped from raising all the grounds of invalidity it raised in its IPR and those it "reasonably could have raised." *Id*. Accordingly, here, there is no scenario in which Samsung will succeed ***at trial*** on its obviousness theories because Samsung will be statutorily estopped from raising them ***at trial***. *Titan Tire*, 566 F.3d at 1379 ("the trial court . . . must determine whether it is more likely than not that the challenger will be able to prove ***at trial***, by clear and convincing evidence, that the patent is invalid.") (emphasis added).

Samsung argues that this outcome is unfair. Op. Br. at 6-7. Namely, it argues that "Alexion's audacious position" "improperly dismisses the equitable nature of the injunction

remedy." *Id*. at 6. But it was Samsung's decision to challenge the '189 patent using a proceeding that it knew, or should have known, would result in estoppel in the follow-on district court litigation that it knew, or should have known, was forthcoming. This is the straightforward, logical conclusion that flows from the governing IPR estoppel statute and Federal Circuit case law. It is thus unfair that the statutory remedy available to Alexion has been tossed aside.

Even so, Samsung's confidence in the PTAB to cancel claim 1 of the '189 patent based on its institution decision alone is misplaced. This same PTAB Panel, faced with nearly identical grounds in the 2019 Amgen IPRs, then delivered a series of strikingly different institution decisions, crediting many of the same arguments Alexion makes now. For example, in its analysis of Evans and Mueller, which form the basis of Samsung's Ground 2 in the '189 IPR, this Panel previously found there to be "no express link between the teachings of Mueller and Evans," Cochran Decl., Ex. B at 52, and found that "Patent Owner's arguments" regarding the "improper hindsight" combination of Mueller and Evans, "ma[de] some sense." *Id*. at 54. Likewise, in its analysis of both Hillmen and Hill, which are cumulative of Bell (the basis of Samsung's Ground 3), the same Panel previously found that Amgen did "not carr[y] its burden to show a reasonable likelihood of anticipation of the claim of the '189 patent." *Id.* at 28, 44.

Nor is the invalidation of the '189 patent by the PTAB a statistical certainty. *See* Op. Br. at 6. As noted in Alexion's April 11, 2024 Reply (D.I. 49), Samsung's alleged 77% statistic is artificially inflated, and very heavily skewed towards the "Mechanical & Business Method" and "Electrical/Computer" art units. D.I. 49 at 3-4; D.I. 40, Ex.10. Samsung ignores the fact that in FY2023 only 7% of all IPR petitions related to the "Bio/Pharma" art unit. D.I. 49 at 4; D.I. 40, Ex.10. Accordingly, Samsung's statistical argument is speculation, at best.

B. The '176 Patent

Samsung also fails to raise a substantial question concerning the validity of claim 1 of the '176 patent, because: (1) its asserted obviousness combination of Noris (2005) and the SOLIRIS® Label (2007) relies on improper hindsight and fails to provide a POSA with a reasonable expectation of success, and (2) Chatelet (2008) does not qualify as prior art.

1. Samsung Cannot Show that Claim 1 is Obvious in View of Noris (2005) and the SOLIRIS® Label (2007)

Samsung's argument relies on post-hoc knowledge of the '176 patent's novel dosing schedule to treat aHUS. Samsung overstates the weight of Noris's teaching towards eculizumab in treating aHUS. As Samsung acknowledges, a POSA reading Noris in 2008 would have been met with a non-specific "***hope[]*** that ***the above complement inhibitors*** . . . will be useful in [aHUS] patients." D.I. 39, Ex. 3 at 1044 (emphasis added). Samsung seems to attach that ***hope*** solely to eculizumab, and ignores the two other compounds mentioned in the same paragraph. Of the three complement inhibitors that Noris "***hoped***" "***could*** represent a therapeutic target in [aHUS] patients," *id.* (emphasis added), two of them never made it to the market or were FDA approved for any indication, let alone for the treatment aHUS. D.I. 51 at ¶ 75; D.I. 50, Ex. A, 89:13-91:18 (admitting that he does "not have knowledge of pexelizumab," or TP10, "do[es] not know" if either are FDA approved or commercially available, and cannot "recall at this time" if he has used either to treat aHUS patients). But Noris, in 2005 without the benefit of hindsight, did not attribute any particular expectation of success to eculizumab over the other "hopeful" therapies. *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019) ("These references provide no more than hope—and hope that a potentially promising drug will treat a particular cancer is not enough to create a reasonable expectation of success in a highly unpredictable art such as this.").

Samsung cannot incorporate eculizumab's eventual success in the treatment of aHUS into the teachings of Noris. This type of hindsight thinking has no place in an obviousness inquiry. *See Insight Vision Inc.* v. *Sandoz, Inc.*, 783 F.3d 853, 859 (Fed. Cir. 2015). As Samsung's expert, Dr. Bissler concedes, a POSA "would have the ***suspicion*** that [eculizumab] would be an excellent choice, but biology is complicated." D.I. 50, Ex. A, 62:6-14. The authors of Noris clearly appreciated such complications by limiting their conclusions to nothing more than a hope in the absence of definitive clinical data. *See* D.I. 51 at ¶ 75.

Samsung relies on the basic fact that "eculizumab was known to inhibit" C5, which is "downstream from the known complement defects in both PNH and aHUS responsible for hyperactivation." D.I. 38 at 15. Dr. Bissler agrees, however, that a POSA would know that eculizumab's effectiveness at treating any given disease involving hyperactivation of complement "would depend on more details about the disease." D.I. 49, Ex. A, 125:17-24. Without more than Noris's "hope," a POSA as of 2008 would have had no reasonable expectation that eculizumab would be effective to treat aHUS in any given individual patient. *See* D.I. 51 at ¶ 76.

2. Samsung Cannot Show that Claim 1 is Anticipated by Chatelet (2008)

Samsung contends that Dr. Blasco's opinions regarding the '176 patent and its priority date should be given no weight primarily because Dr. Blasco "is not a native English speaker" and "his deposition was conducted in Spanish." Op. Br. at 11. Samsung, however, takes Dr. Blasco's deposition out of context by ignoring that he "speak[s] English fluently in the medical realm without issue" and chose to have his deposition, which was his first ever deposition, taken in Spanish to "be as accurate as possible in [his] opinions." Cochran Decl., Ex. A at 14:3-11. Samsung therefore inappropriately conflates a preference for Spanish with a lack of proficiency in English. It would be improper to discount Dr. Blasco's analysis of the documentary evidence

solely on the basis that he is multilingual with a preference for his native language. Dr. Blasco's opinions on the disclosure of the '803 provisional are set forth in his declaration, which he reiterated and supported in his deposition. *See, e.g.*, Cochran Decl., Ex. A at 49:15-50:4; 53:1-7.

[redacted]

[redacted]

IV. ALEXION WILL SUFFER IRREPARABLE HARM

Samsung does not dispute that its launch of SB12 will cause Alexion to suffer price erosion or lost market share. Instead, Samsung insists that those injuries should be ignored because Alexion has licensed another eculizumab biosimilar and faces competitive pressure from other branded products. But "the fact that a patentee has licensed others under its patents does not mean that unlicensed infringement must be permitted while the patents are litigated." *Abbott Lab'ys* v. *Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008).

Moreover, an injunction is proper because a causal nexus exists between Samsung's infringement and Alexion's irreparable harm. Samsung's causal nexus defense incorrectly states the law and the evidence. *See* Op. Br. at 18-19. A patentee need only show "*some connection* between the patented feature and demand for the infringing product[]." *Apple Inc.* v. *Samsung*

Elecs., 809 F.3d 633, 639, 641 (Fed. Cir. 2015). Here, the claims of the PI Patents cover methods of treating patients with complement disorders using novel compositions and dosing regimens of eculizumab. Thus, the patented methods contribute to a desired clinical benefit in patients rather than some other factor, such as marketing, that drives consumer demand for SOLIRIS®. *Mylan Institutional LLC* v. *Aurobindo Pharma Ltd.*, 857 F.3d 858, 872-73 (Fed. Cir. 2017) (nexus where demand for the product stems from the patented features). Samsung's focus on branded competition as Alexion's "primary threat" is irrelevant. Op. Br. at 18. Samsung cites no authority to establish that its market entry must be the sole or largest threat to its market share to show a causal nexus. *Id.* at 18-19. Therefore, Alexion has satisfied its low-threshold burden to show a connection between Samsung's infringement and the anticipated harm.

Alexion has also identified concrete harms related to Samsung's potential at-risk launch of its SB12 biosimilar product. Samsung leans heavily on Alexion's prior settlement agreement with Amgen as proof that a biosimilar launch will not cause harm to Alexion. These arguments are misplaced. An unexpected acceleration of competition is in large part what creates the uncertainty and irreparable nature of harm to Alexion. In fact, Samsung's expert, Dr. Rao, concedes it is in Alexion's best interest to market ULTOMIRIS® to replace SOLIRIS® (D.I. 42 at ¶¶ 15, 59) but fails to acknowledge that accelerating competition will have an impact on Alexion's ability to do so in the short term. Alexion's inability to predictably execute on a harm-limiting plan put in place to account for a single biosimilar entry will lead to unexpected harm in the face of a second, accelerated generic entry, and will have long-term impacts that will not be possible to fully calculate by trial.

Samsung also conflates the [redacted] as proof that damages would be calculable. That clause, however, is a means by which Alexion and [redacted]

[redacted] the uncertainty that will be created in the event of another biosimilar market entry. *See* D.I. 50, Ex. D, 63:15-64:7.

V. SAMSUNG HAS NOT SHOWN THE OTHER FACTORS WEIGH IN ITS FAVOR

The balance of hardships weighs in Alexion's favor. Samsung fails to identify a single hardship it will face following the grant of a preliminary injunction, because Samsung will suffer minimal harm from an injunction delaying the launch of its SB12 product, [redacted]. Instead, Samsung simply concludes, without support, that the "balance of the equities and hardships tips strongly in Samsung's favor," Op. Br. at 19, before quickly turning to downplay Alexion's legitimate harms. Without Alexion's innovations related to SOLIRIS®, however, no patients would have the option of eculizumab and its eventual biosimilars.

Further, Samsung does not argue that an injunction will adversely affect patient care. Instead, Samsung simply appeals to the prospect of "less expensive drugs for the public at large." Op. Br. at 20. But the public interest in "obtaining lower-priced pharmaceutical compounds cannot justify entirely eliminating the exclusionary rights covered by pharmaceutical patents." *See Mylan Inst. LLC*, 857 F.3d at 865; *Impax Lab'ys, Inc.* v. *Aventis Pharm.*, 235 F. Supp. 2d 390, 397 (D. Del. 2002) (same).

VI. CONCLUSION

For the foregoing reasons, Alexion respectfully requests that this Court grant its motion for injunction pending appeal and temporary restraining order pending resolution of this motion.

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CERTIFICATE OF SERVICE

The undersigned counsel hereby certifies that true and correct copies of the foregoing document were caused to be served on June 7, 2024 on the following counsel in the manner indicated below.

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