No. 24-1829

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

ALEXION PHARMACEUTICALS, INC. AND ALEXION PHARMA INTERNATIONAL OPERATIONS LTD.,

Plaintiffs-Appellants

v.

SAMSUNG BIOEPIS CO. LTD.,

Defendant-Appellee

On Appeal from the United States District Court
for the District of Delaware, No. 1:24-cv-00005-GBW

APPELLANTS' MOTION FOR AN INJUNCTION PENDING APPEAL

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June 21, 2024

CERTIFICATE OF INTEREST

Gerald J. Flattmann, Jr., counsel for Alexion Pharmaceuticals, Inc. and Alexion Pharma International Operations Ltd., certifies the following:

1. The full name of the parties represented by me are:

   Alexion Pharmaceuticals, Inc. and Alexion Pharma International Operations Ltd.

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

   N/A

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

   Alexion Pharmaceuticals, Inc. is a wholly-owned, indirect subsidiary of AstraZeneca plc. No other publicly-held corporation owns 10% or more of its stock.

   Alexion Pharma International Operations Ltd. is a wholly-owned, indirect subsidiary of AstraZeneca plc. No other publicly-held corporation owns 10% or more of its stock.

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

   Daniel M. Silver (McCarter & English, LLP)

   Alexandra M. Joyce (McCarter & English, LLP)

   Maliheh Zare (McCarter & English, LLP)

   Andrew M. Solomon (Cahill Gordon & Reindel LLP)

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. *See* Fed. Cir. R. 47.4(a)(5) and 47.5(b). (The parties should attach continuation pages as necessary).

N/A

Dated: June 21, 2024

/s/ Gerald J. Flattmann, Jr.

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

LIST OF EXHIBITS

Exhibit 12
U.S. Patent No 6,355,245

Exhibit 13
John P. Mueller et al., *Humanized Porcine VCAM-Specific Monoclonal Antibodies with Chimeric IgG2/G4 Constant Regions Block Human Leukocyte Binding to Porcine Endothelial Cells*, 34 Molecular Immunology 441 (1997)

Exhibit 14
U.S. Patent Application Publication No. 2005/0191298 A1 issued to Leonard Bell et al. (filed Feb. 3, 2005, published Sep. 1, 2005)

Exhibit 15
Paul J. Tacken et al., *Effective induction of naïve and recall T-cell responses by targeting antigen to human dendritic cells via a humanized anti—DC-SIGN antibody*, 106 Blood 1278 (2005)

Exhibit 16
Declaration of Arturo Casadevall (D.I. 20)

Exhibit 17
U.S.Patent Application Publication No. 2005/0271660 A1 issued to Yi Wang (filed May 11, 2005, published Dec. 8, 2005)

Exhibit 18
Declaration of Bernhardt L. Trout (D.I. 21)

Exhibit 19
Samsung's Answer and Counterclaims (D.I. 11)

Exhibit 20
Declaration of Jeffrey V. Ravetch, IPR2023-10169

Exhibit 21
Public Version of Cochran Declaration (D.I. 54)

Exhibit 22
Public Version of Declaration of Miquel Blasco (D.I. 55)

Exhibit 23
Provisional Application No. 61/198,803 filed on Nov. 10, 2008

Exhibit 24
Declaration of John Bissler (D.I. 41)

Exhibit 25
E-mails between Russell P. Rother of Alexion, Nathalie Varoqueaux, and Valerie Chatelet, dated between July 3-4, 2008

Exhibit 26
"Eculizumab dosing & PK/PD sample schedule, and suggested clinical laboratory assessments," dated July 2008

Exhibit 27
Public Version of Opening Brief in Support of Motion for Preliminary Injunction (D.I. 29)

Exhibit 28
Public Version of Reply Brief in Support of Motion for Preliminary Injunction (D.I. 53)

Exhibit 29
Public Version of Declaration of Vincent Thomas (D.I. 30)

Exhibit 30
World Intellectual Property Organization International Publication No. WO 97/11971 issued to John P. Mueller et al. (filed Sep. 27, 1996, published Apr. 3, 1997)

Plaintiffs-Appellants, Alexion Pharmaceuticals, Inc. and Alexion Pharma International Operations Ltd. (collectively, "Alexion") move pursuant to Fed. R. App. Pro. 8(a)(2) and Fed. Cir. R. 8 to enjoin the imminent marketing and sales by Defendant-Appellee Samsung Bioepis Co. Ltd. ("Samsung") of its SB12 biosimilar product to SOLIRIS® pending Alexion's appeal of its motion for preliminary injunction by Judge G. Williams of the U.S. District Court for the District of Delaware.[1]

Per Fed. Cir. R. 27(a)(2), Alexion's counsel have discussed this Motion with Samsung's counsel, and Samsung opposes this Motion. Alexion believes Samsung could launch its SB12 biosimilar product imminently in advance of a decision on appeal and asks for injunctive relief to maintain the status quo until then.

I. INTRODUCTION

This is a Biologics Price Competition and Innovation Act ("BPCIA") case involving Alexion's drug SOLIRIS® (eculizumab), a monoclonal antibody approved for the treatment of rare blood diseases, including paroxysmal nocturnal hemoglobinuria ("PNH") and atypical hemolytic uremic syndrome ("aHUS").

SOLIRIS® is covered by at least the following six patents: Nos. 9,732,149 ("the '149 patent"), 9,718,880 ("the '880 patent"), 9,725,504 ("the '504 patent"),

[1] Alexion's Opening Brief in the appeal is due July 3, 2024. *See* Dkt. 12.

10,590,189 ("the '189 patent"), 10,703,809 ("the '809 patent"), and 9,447,176 ("the '176 patent"). The SOLIRIS® patents claim the composition of the antibody by its unique sequence as well as methods of using the antibody to treat diseases, including PNH and aHUS. Alexion asserted all six patents in its Complaint (Ex. 3). For purposes of Alexion's Motion for Preliminary Injunction ("PI") at the District Court, Alexion sought injunctive relief due to infringement of two claims: claim 1 of the '176 patent (Ex. 4) and claim 1 of the '189 patent (Ex. 5) (collectively, the "PI claims").

Before this action was filed, Samsung filed IPR petitions against five of the six patents asserted against Samsung in Alexion's Complaint (Ex. 3), including an IPR petition against the '189 patent (IPR2023-01069 or, the "'189 IPR"). In December 2023, the Board instituted trial in Samsung's five IPRs.

Alexion filed its Motion for Preliminary Injunction (Ex. 2) on February 12, 2024. The U.S. District Court for the District of Delaware (Williams, J.) issued its Memorandum Order (Ex. 1) on May 6, 2024, denying Alexion's motion, and Alexion filed its Notice of Appeal (Ex. 6) on May 14, 2024.

Alexion fears Samsung will launch its SB12 biosimilar product while this appeal is still pending. Accordingly, Alexion filed a motion under Fed. R. Civ. Pro. 62(d) and 65(b) (Ex. 7) seeking a temporary restraining order and injunctive relief

pending appeal at the district court on May 17, 2023. That motion was denied on June 17, 2024.[2] Ex. 8.

II. LEGAL STANDARD

This Court may grant an injunction while an appeal is pending, Fed. R. App. Pro. 8(a)(2); Fed. Cir. R. 8, and considers four factors in connection therewith: (1) whether the movant has made a strong showing of likelihood of success on the merits; (2) whether the movant will be irreparably injured absent injunctive relief; (3) whether issuance of the injunction will substantially injure the other parties in the proceeding; and (4) whether the public interest favors an injunction. *See Hilton v. Braunskill*, 481 U.S. 770. 776 (1987); *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 2010 WL 3374123, at *1 (Fed. Cir. 2010). The first factor favors injunctive relief so long as the movant demonstrates "a substantial case on the merits provided that the harm factors militate in its favor." *Eli Lilly & Co.*, 2010 WL 3374123, at *1.

III. SUMMARY OF THE ARGUMENT

Alexion will likely succeed on the merits. Among other errors, the district court's Memorandum Order (Ex. 1) incorrectly found that Samsung raised a substantial question of validity as to each of the PI claims without substantive

[2] Although the district court in its Oral Order (Ex. 8) characterized Alexion's motion as a "motion for reconsideration with respect to the Court's prior injunction," it was in fact a motion for injunction pending appeal, which satisfies the standard under Fed. R. App. Pro. 8(a)(1).

analysis of Alexion's arguments; failed to consider whether Samsung's invalidity arguments will meet the clear and convincing standard required at trial; and did not properly evaluate Alexion's IPR statutory estoppel argument. Moreover, Alexion established infringement of the PI claims, and Samsung did not address Alexion's infringement allegations (Ex. 9 at 7, n. 3).

Although the Memorandum Order does not address the remaining preliminary injunction factors, Alexion satisfied its burden as to these factors in the original briefing because:

(1) Alexion will suffer irreparable harm that cannot be adequately compensated by money damages if Samsung is not enjoined. If Samsung launches its biosimilar product, Alexion will lose significant dollar sales and market share; suffer net price erosion; experience significant disruption to their workforces; lose research and development efforts into additional uses for SOLIRIS®; and will incur harm to their reputation and goodwill that cannot be reversed even if Samsung's product is later withdrawn from the market.

(2) The balance of hardships favors Alexion. Alexion will suffer irreversible harm if Samsung launches its generic product, whereas Samsung, who has not yet marketed that product, will suffer little, if any, harm if an injunction is granted.

(3) The public interest weighs in Alexion's favor. Protecting valid patents incentivizes innovators, like Alexion, to make substantial investments in developing pharmaceuticals.

IV. ARGUMENT

A. Alexion is Likely to Succeed on Appeal

This Court has explained that the trial court's decision process for determining whether a "substantial question" of invalidity has been raised at the preliminary injunction stage "requires the court to assess the potential of a clear and convincing showing in the future." *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1380 (Fed. Cir. 2009) (internal quotation marks omitted). Here, it does not appear that the district court considered whether any of Samsung's arguments will rise to the clear and convincing standard "at trial" as required. *Id.* at 1379-1380. If the district court had considered Samsung's arguments according to the proper burden and timeframe, it would have found that Samsung failed to raise any substantial questions as to the validity of the PI claims.

1. The District Court Incorrectly Found a Substantial Question of Validity Regarding Claim 1 of the '189 Patent

The district court attributed undue weight to the '189 IPR institution decision and failed to recognize that IPR institution decisions are preliminary and require far less than clear and convincing evidence. *See* 35 U.S.C. § 314(a) (institution of an IPR requires only a "reasonable likelihood that the petitioner would prevail with

respect to at least 1 of the claims challenged in the petition"). Moreover, PTAB decisions are not binding on district courts. *See, e.g.,Tinnus Enters., LLC v. Telebrands Corp.*, 846 F.3d 1190, 1202 n.7 (Fed. Cir. 2017) ("The PTAB's [final written] decision is not binding on this court, and … it does not persuade us that the district court abused its discretion in granting the preliminary injunction."); *see also Liqwd, Inc. v. L'Oreal USA, Inc.*, 2018 WL 11189633, at *3 (D. Del. 2018) ("The PTAB's decision invalidating the '419 patent is not binding on the court"); *Genuine Enabling Tech., LLC v. Sony Corp.*, 2020 WL 1140910, at *7 (D. Del. 2020) ("The PTAB's construction is not binding on this Court"). Rather than engage independently with Alexion's arguments in defense of the PNH claim, the district court deferred entirely to the institution decision. The institution decision, however, is incorrect for a number of reasons.

Namely, according to Samsung, years before the March 15, 2007 priority date of the '189 patent, several prior art publications, when reverse-engineered, allegedly disclosed outright the exact amino acid sequence of "eculizumab." That is incorrect. Instead, a POSA as of March 15, 2007 would have understood ***only*** that Alexion had developed a humanized monoclonal antibody named "eculizumab," which bound to human C5 and blocked its cleavage. A POSA at that time would ***not*** have known that "eculizumab" had the claimed uniquely-engineered, ***hybrid IgG2/IgG4*** sequence. Nothing in the prior art before March 15, 2007 teaches or discloses the

full unique hybrid IgG2/IgG4 sequence without the benefit of hindsight. Instead, the existing literature as of March 15, 2007 consistently and repeatedly directed a POSA to an ***IgG4*** antibody described in Thomas (Ex. 10) for the structure and sequence of "eculizumab."

Despite facially citing several references, Samsung's IPR positions principally rely on four references and three core arguments and combinations: (1) Bowdish (Ex. 11) and Evans (Ex. 12) (obviousness); (2) Evans and Mueller[3] (obviousness); and (3) Bell (Ex. 14) (inherent anticipation). Samsung also relies on Tacken (Ex. 15) as a secondary reference.

Samsung's reading of these references is flawed. As a concise preview, Bowdish does not provide ***any*** disclosure of any antibody consisting of the claimed sequence. Ex. 16 at ¶¶ 158-161. Evans does not describe ***any*** full-length ***humanized*** antibodies for binding C5, let alone the claimed antibody. Ex. 16 at ¶¶ 154-157. The only full-length anti-C5 antibody disclosed in Evans is a ***mouse*** antibody that is very different from the claimed ***humanized*** antibody. Ex. 16 at ¶ 155. Bell does not disclose the claimed amino acid sequence, which was unknown, not publicly

[3] Samsung relies on two Mueller references. Mueller 1997 (Ex. 13) (a research article); and Mueller PCT (Ex. 30) (a published patent application). The two are cumulative of each other and disclose similar subject matter. Samsung's IPR declarant, Dr. Ravetch, stated that Mueller PCT is a "companion patent application describing the same work" as Mueller 1997. Ex. 20 at ¶¶ 62, 124.

disclosed, and was unavailable to anyone but Alexion (and those bound to confidentiality to Alexion) as of Bell's publication. Ex. 16 at ¶¶ 204-208. Both Mueller and Tacken are directed to completely different antibodies and contain, at best, peripheral and ambiguous clues about eculizumab's constant region, which cannot contradict the art's clear teaching that "eculizumab" had Thomas's IgG4 structure. Ex. 16 at ¶¶ 143-146, 165-167. Notably, both Bell and Tacken, among several other references before March 15, 2007, cite to Thomas for the structure and sequence of "eculizumab." Ex. 16 at ¶¶ 122-123, 146, 209.

Each of Samsung's arguments is based on an erroneous premise—that a POSA would have somehow known the specific and unique hybrid IgG2/IgG4 amino acid sequence of the claimed antibody eventually commercialized as Alexion's groundbreaking orphan disease therapy known today as SOLIRIS®. But this premise ignores how a POSA would actually view the art as of March 15, 2007 and ignores the overwhelming evidence in the literature that described "eculizumab" by pointing a POSA to Thomas's natural IgG4 sequence.

Before March 15, 2007, the unique amino acid sequence of SOLIRIS® was not publicly known or disclosed in the art. As explained by Alexion's expert, Dr. Arturo Casadevall, Samsung's arguments thus amount to little more than a post-hoc narrative that reconstructs the claimed sequences piecemeal and in hindsight. Ex. 16 at ¶¶ 139-173, 192-262. A POSA would not have combined the art to arrive at

the claimed sequences on one's own back in 2007 and would have had no reasonable expectation that they would work as they do. *Id*. Across its arguments, Samsung impermissibly culls and combines bits of multiple and unrelated references in hindsight to reconstruct the claimed sequences. Such hindsight-driven analysis—starting with the claimed sequence and working backwards to reconstruct it—is always improper. *See, e.g., Graham v. John Deere Co.*, 383 U.S. 1, 36 (1966) (warning against "slipping into use of hindsight" and "the temptation to read into the prior art teachings of the invention in issue"); *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2017) (warning against "the distortion caused by hindsight bias" and "arguments reliant upon *ex post* reasoning").

Much like its obviousness arguments, Samsung's anticipation theory using Bell requires a POSA to combine portions of the claimed sequences from other prior art documents. These arguments are thus Samsung's recycled obviousness arguments shoehorned into an alleged inherent anticipation argument. *See, e.g., Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1335 (Fed. Cir. 2002) ("[A]nticipation requires that each limitation of a claim must be found in a single reference . . . [and] does not permit an additional reference to supply a missing claim limitation.").

As another preview, the Board found the facts in the IPRs to be analogous to both *In re Crish*, 393 F.3d 1253 (Fed. Cir. 2004) ("*Crish*"), and *Nichols Inst.*

Diagnostics, Inc. v. Scantibodies Clin. Lab., Inc., 195 F. App'x 947 (Fed. Cir. 2006) ("*Nichols*"), and relied on each to find a reasonable likelihood that claim 1 of the '189 patent is anticipated. The Board misapplied *Crish* and *Nichols*, which are readily distinguishable for similar reasons. In both, the claimed sequence (*Crish*) and the claimed antibody (*Nichols*) were known and publicly available as of the priority date of the patents. The facts here are different because the claimed sequence was neither known nor publicly available as of the March 15, 2007 priority date. Nor does Samsung's hindsight-driven argument that the claimed sequence could allegedly be reverse-engineered from many disparate sources place the facts here within the same context as *Crish* and *Nichols* for at least two reasons. First, the claimed sequence was not known, not publicly disclosed, and not available to anyone but Alexion (and those bound to confidentiality to Alexion). Second, Samsung's argument is not an anticipation argument because it necessarily relies on multiple references. *See, e.g., Teleflex*, 299 F.3d at 1335; *see also Therasense, Inc. v. Becton Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010) ("Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim."). Thus, *Crish* and *Nichols* are both distinguishable.

The Examiners at the Patent Office apparently agree that Samsung's arguments are flawed. In 2019, Amgen filed IPRs against the parent patents of the '189 patent. After Amgen filed its IPRs, ***the entire IPR records***, including all

papers, references, and expert declarations and deposition transcripts, were submitted to and considered by the Examiners during the prosecution of the '189 patent. Samsung's art and arguments in its IPRs are duplicative of those raised in the Amgen IPRs. Thus, all of the prior art references that Samsung relies on in its IPRs were submitted to and thoroughly considered by the Examiners during the prosecution of the '189 patent. The Examiners of the '189 patent thus spent years becoming familiar with the same art and arguments Samsung has raised, and yet, granted the '189 patent's claims to the same novel and inventive sequence.

Further, Samsung has not shown in any of its arguments that the prior art disclosed the formulation, administration, and patient condition limitations of claim 1 of the '189 patent. For example, Samsung fails to show how the "single unit dosage form comprising 300 mg of the antibody in 30 mL of a sterile, preservative-free solution" claim limitation would have been obvious to a POSA without hindsight. Samsung relies on Bell and another reference, Wang (Ex. 17), for these elements, and implicitly concedes that neither discloses "a 300 mg single-use dosage form" or a "30 ml of a 10 mg/ml antibody solution." Ex. 17 at 41-42. Bell also fails to identify the dosage unit or concentration of the administered composition, and Wang fails to teach the specific 10 mg/ml antibody concentration. Ex. 18 at ¶¶ 76-91, 80-90. Moreover, as further explained in the Declaration of Dr. Bernhardt Trout, filed in the underlying PI briefing, the approach to formulating an antibody involves

many factors, including the antibody's stability, the effects of the formulation on the antibody, the concentration, the formulation type, and the route of administration. Ex. 18 at ¶¶ 43-56. Neither Bell nor Wang provide any insights into how a POSA would navigate these factors to arrive at the claimed formulation. For these additional reasons, the district court erred in deferring to the Board's institution decision without undertaking its own analysis.

Further, the district court did not assess Samsung's inability to make a clear and convincing showing as to the invalidity of the '189 patent at trial, where Samsung will be estopped by statute from relying on its IPR arguments. Without those arguments at its disposal, and without having raised any other arguments for the invalidity of claim 1 of the '189 patent, Samsung cannot meet the clear and convincing burden for invalidating claim 1 of the '189 patent ***at trial***. Alexion's estoppel argument raises a serious question of law that the district court failed to fully address: The IPR estoppel mandated by statute supersedes judge-made law regarding the equities at the preliminary injunction stage. Although the district court concluded that Alexion "oddly suggests" Samsung should be enjoined based on IPR estoppel (Ex. 1), this suggestion is the logical consequence of the IPR estoppel statute and preliminary injunction case law requiring a court to consider what could potentially happen ***at trial***.

Before this action was filed, Samsung filed IPR petitions against five of the six patents asserted against Samsung in Alexion's Complaint (Ex. 3).[4] In December 2023, the Board instituted trial in Samsung's five IPRs. Final written decisions in those proceedings should thus issue in or around December 2024, which will be before a trial can occur in this litigation.

After a final written decision issues in the five IPRs, Samsung will be estopped from asserting in this litigation all the invalidity defenses it "raised or reasonably could have raised" in those IPRs. 35 U.S.C. § 315(e)(2); *Intuitive Surg., Inc. v. Ethicon LLC*, 25 F.4th 1035, 1041 (Fed. Cir. 2022) ("[E]stoppel is triggered when an IPR proceeding results in a final written decision."). Estoppel applies whether or not Samsung's challenges at the PTAB are successful (which Alexion contends they will not be). Moreover, even if Samsung were to receive a favorable final written decision from the Board in December 2024 (which it will not), this litigation will proceed to trial on all remaining issues, including infringement, for three reasons: (1) trial will occur before a final decision on appeal in the IPRs; (2) "the Board's final written decision does not cancel claims; the claims are cancelled when the Director issues a certificate confirming unpatentability, which occurs only after 'the

[4] Samsung did not challenge the validity of the '176 patent before the PTAB. Nor did Samsung's Answer and Counterclaims (Ex. 19) provide any specific allegations of invalidity of that patent.

time for appeal has expired or any appeal has terminated,'" *United Therapeutics Corp. v. Liquidia Tech.*, 74 F.4th 1360, 1372 (Fed. Cir. 2023) citing 35 U.S.C. § 318(b); and (3) "an IPR decision does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights," *id. citing XY, LLC v. Trans Ova Genetics, L.C.*, 890 F.3d 1282, 1294 (Fed. Cir. 2018). Given that a trial will occur ***in this litigation*** before any decision on appeal in the IPRs, but after the Board's final written decisions, Samsung will be estopped from relying on the invalidity defenses it raised or reasonably could have raised in those IPRs during trial ***in this litigation***. And trial in this litigation is the relevant inquiry for determining likelihood of success on the merits for purposes of a preliminary injunction. *See Abbott Lab'ys v. Sandoz, Inc.*, 544 F.3d 1341, 1344 (Fed. Cir. 2008) ("(1) likelihood of success on the merits ***of the underlying litigation***") (emphasis added). The upshot here is that all of Samsung's invalidity defenses that it raised or reasonably could have raised in its IPRs have no legal bearing on these preliminary injunction proceedings.[5]

Nor will Alexion be collaterally estopped from continuing to assert its infringement positions concerning the five patents challenged by IPR in this

[5] Alexion acknowledges that estoppel under Section 315 will apply only to the '189 patent and the other four patents challenged by Samsung by IPR. It will not apply to the '176 patent, which Samsung did not challenge by IPR.

litigation, which holds true even in the unlikely event of a victory by Samsung at the PTAB in a final written decision. "Federal Circuit case law suggests that an IPR decision does not have preclusive effect until that decision is either affirmed or the parties waive their appeal rights." *TrustID, Inc. v. Next Caller Inc.*, C.A. No. 18-172 (MN), 2021 WL 3015280, at *3 (D. Del. July 6, 2021) (citing: *XY, LLC v. Trans Ova Genetics*, 890 F.3d 1282, 1294 (Fed. Cir. 2018); *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377 (Fed. Cir. 2018); *Papst Licensing GMBH & Co. KG v. Samsung Elecs. Am., Inc.*, 924 F. 3d 1243, 1249 (Fed. Cir. 2019); *Fresenius USA, Inc. v. Baxter Int'l, Inc.*, 721 F.3d 1330, 1344 (Fed. Cir. 2013)). Though "allowing Plaintiff to proceed at trial on claims that have been found by the PTAB to be invalid while at the same time preventing Defendant from asserting prior art defenses against these claims based on estoppel under § 315(e)(2) seems counterintuitive," "it is a permissible result that follows from the statute and the relevant case law." *Id.* at *4.

For these reasons, Alexion is likely to succeed on appeal with respect to the district court's finding of a substantial question of validity as to the PNH claim.

2. The District Court Erroneously Found a Substantial Question of Validity Regarding Claim 1 of the '176 Patent

In the proceedings below, Samsung raised two invalidity arguments with respect to claim 1 of the '176 patent. The district court erroneously found "that each of these theories raise[d] a substantial question of invalidity." Ex. 1 at 5. First,

Samsung argues that the claim is obvious over the combination of Noris (2005) and the SOLIRIS® label (2007). As the district court acknowledged, Noris (2005) indicates a "hope[]" that eculizumab could be used to treat aHUS patients. Ex. 1 at 5. But mere "hope" that eculizumab would be useful in treating aHUS patients, could in no way satisfy the clear and convincing standard at trial, and therefore does not raise a "substantial question."

A POSA would not have had a reasonable expectation of success in using eculizumab to treat aHUS, solely because of the drug's success in treating PNH. A reasonable expectation of success is a "higher bar" than "hope" or "cautious optimism." *See 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."); *see also Sanofi-Aventis U.S. LLC v. Sandoz, Inc.*, No. 20-804-RGA, 2023 WL 4175334 (D. Del. June 26, 2023) (finding non-obviousness due to no reasonable expectation of success where prior art was merely "hope[ful]" and "optimis[tic]" that a drug would be effective in treating one cancer based on previous success in treating a related cancer).

Samsung provides only attorney argument to read a "reasonable expectation of success" into Noris's limited conclusion. Ex. 9 at 15. 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." Ex. 9 at 15. Even putting aside Samsung's incorrect proposition that PNH and aHUS are both caused by similar complement defects leading to hyperactivation, Samsung's expert, Dr. Bissler, agrees 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." Ex. 21-A at 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* Ex. 22 at ¶ 76.

Second, Samsung argues that the claim is anticipated by Chatelet (2008). Though the district court stated that Chatelet (2008) "raises a substantial question of invalidity," the district court did "not reach" any substantive analysis regarding Chatelet (2008). Rather than address the merits of Samsung's position, the district court simply "note[d] that the ***existence*** of a second invalidity theory strengthens the Court's conclusion that there is a substantial question of validity." Ex. 1 at 5, 7 n.2. (emphasis added). Without any substantive analysis, the district court's statements cannot support the denial of Alexion's motion and requires a remand so the district court may substantively address it. Chatelet (2008) however, is not prior art, and therefore cannot anticipate the aHUS claim.

The '176 patent is entitled to a priority date of the '803 Provisional's filing date on November 10, 2008, which is the same date that Samsung alleges the Chatelet (2008) abstract was purportedly published.[6] The '176 patent's entitlement to that priority date disqualifies Chatelet (2008) as prior art.

The '803 Provisional discloses each and every limitation of claim 1:

aHUS Claim (Claim 1 of the '176 Patent)	**Exemplary '803 Provisional Disclosure**
1. A method for treating atypical hemolytic uremic syndrome (aHUS),	"The above-described compositions are useful in, *inter alia*, methods for treating or preventing aHUS in a subject. . ." Ex. 23 at 37:25-26.
the method comprising administering to a patient in need thereof eculizumab	"[A] human can be intravenously administered an anti-C5 antibody (e.g., eculizumab) . . ." Ex. 23 at 39:5-6.
in an amount effective to treat aHUS in the patient;	"The terms "therapeutically effective amount" or "therapeutically effective dose," . . . are intended to mean an amount of agent (e.g., an inhibitor of human complement component 5) that will elicit the desired biological or medical response (e.g., an improvement in one or more symptoms of aHUS)." Ex. 23 at 39:30-40:2.
wherein the eculizumab is intravenously administered to the patient under the following schedule:	"[A] human can be intravenously administered an anti-C5 antibody (e.g., eculizumab) . . ." Ex. 23 at 39:5-6.

[6] Samsung alleges Chatelet (2008) was published on November 10, 2008. Alexion contests that allegation and Samsung's supporting evidence. For purposes of this Reply, however, it is a moot point because Chatelet (2008) does not qualify as prior art.

at least 600 mg of eculizumab once per week for four consecutive weeks; and beginning at week five, maintenance doses of at least 900 mg eculizumab every two weeks thereafter.	"[A] dose of about 600 (e.g., about 625, 650, 700, 725, 750, 800, 825, 850, 875, 900, 925, 950, or 1,000 or more) mg every week, optionally, for two or more (e.g., three, four, five, six, seven, or eight or more) weeks. Following the initial treatment, the human can be administered the antibody at a dose of about 900 mg about every 14 . . . days, e.g., as a maintenance dose." Ex. 23 at 39:5-11.

Samsung contends that a POSA reading the '803 Provisional "would not understand 'about 900 mg' to adequately describe 'at least 900 mg,' which has no upper bound." Ex. 9 at 16. But Samsung ignores the '803 Provisional's "about 600" lexicography, which expressly teaches "about 600" to encompass "e.g., about 625, 650, 700, 725, 750, 800, 825, 850, 875, 900, 925, 950, or 1,000 or more," in the sentence immediately preceding the maintenance dose of "about 900 mg." *See* Ex. 22 at ¶ 57; Ex. 23 at 39:6-9. A POSA reading the "about 900 mg" limitation as it appears in the '803 Provisional, would therefore understand a numerical dose preceded by "about" to be interchangeable with "at least" as claimed in the '176 patent. *See* Ex. 22 at ¶ 57. Further, absent express direction to construe "about 900 mg" different than the surrounding instances of "about," a POSA would assume a consistent usage of the term rather than arbitrarily supply its own construction, as Dr. Bissler contends. *See* Ex. 22 at ¶ 58; Ex. 24 at ¶ 80.

Moreover, Samsung's assertion that the work of Dr. Chatelet "was conducted independent of Alexion" (Ex. 9 at 18) is factually incorrect, as Alexion invented the dosing schedule and provided it to Dr. Chatelet before her abstract was published. As shown by a series of e-mails on July 3-4, 2008 (Ex. 25), Dr. Chatelet received a document from Alexion on July 4, 2008 titled "Eculizumab dosing & PK/PD sample schedule . . ." containing the dosing schedule of claim 1 of the '176 patent. Ex. 26 at 6 n. 2; *see* Ex. 22 at ¶ 64. Thus, even if the '176 patent were not entitled to the priority date of the '803 provisional (it is), Chatelet 2008 is, at best, 35 U.S.C. § 102(a) art[7] and the facts prove that the inventors had possession of the dosing regimen before Chatelet's publication.

For these reasons, Alexion is likely to succeed on appeal with respect to the district court's finding of a substantial question of validity as to the aHUS claim.

B. The Remaining Irreparable Harm, Balance of Hardships, and Public Interest Factors Favor Alexion

The district court did not address these factors. If it had, it would have found that Alexion firmly established each of the factors based on Alexion's preliminary injunction memoranda (Ex. 27, Ex. 28), and the Declaration of Vince Thomas (Ex.

[7] Chatelet (2008) cannot be 102(b) art. At best, it was published exactly one year to the day before the filing of the application leading to the '176 patent. Even if the '176 patent were not entitled to the priority date of the '803 provisional, Chatelet was not published "***more than*** one year prior to the date of the application for patent" as required by Section 102(b) (pre-AIA).

29). Alexion asks this Court consider the briefing and declarations that the district court improperly failed to consider. *See Hybritech Inc. v. Abbott Lab'ys*, 849 F.2d 1446, 1451 (Fed. Cir. 1988) (the four factors, "taken individually, are not dispositive; rather, the district court must weigh and measure each factor against the other factors").

V. CONCLUSION

Accordingly, Alexion respectfully requests that this Court grant its Motion.

Dated: June 21, 2024

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CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

This Motion complies with the word length limits permitted by Federal Rule of Appellate Procedure 27(d)(2)(A), as it contains 4967 words. This Motion also complies with the type size and typeface requirements under Federal Rule of Appellate Procedure 27(d)(1)(D)-(E), because it has been prepared in a proportionately spaced typeface using Microsoft Word Times New Roman 14-point font.

CERTIFICATE OF SERVICE

I certify I served a copy of the foregoing on counsel of record on June 21, 2024, by Electronic Means (by E-mail and CM/ECF).

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