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.,	)	**REDACTED PUBLIC VERSION FILED FEBRUARY 23, 2024**
Defendant.	)	

PLAINTIFFS' OPENING BRIEF IN SUPPORT OF
MOTION FOR A PRELIMINARY INJUNCTION

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Pursuant to the Biologics Price Competition and Innovation Act ("BPCIA"), Plaintiffs Alexion Pharmaceuticals, Inc. and Alexion Pharma International Operations Ltd. (collectively, "Alexion"), respectfully request a Preliminary Injunction under 42 U.S.C. § 262(*l*)(8)(A) to prevent Defendant Samsung Bioepis Co. Ltd. ("Samsung") from launching its eculizumab biosimilar product, SB12, until a final decision on the merits in this case.

I. INTRODUCTION

SOLIRIS® (eculizumab) is a monoclonal antibody indicated for the treatment of rare blood diseases, including paroxysmal nocturnal hemoglobinuria ("PNH") and atypical hemolytic uremic syndrome ("aHUS"). SOLIRIS® works by binding with high "affinity" (*i.e.* tightness) and "specificity" (*i.e.*, directed to a single antigen) to the human protein "C5," a key component of the complement pathway. Without SOLIRIS® treatment, the body naturally cleaves C5 into components "C5a" and "C5b," which leads to downstream effects of the complement pathway, including hemolysis in PNH patients, and thrombotic microangiopathy in aHUS patients. When SOLIRIS® is administered, however, it binds to a critical location ("epitope") on C5 with sufficient affinity and specificity to prevent cleavage of C5, thus blocking the negative downstream effects of the complement pathway in PNH and aHUS patients, among others.

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"), 10,590,189 ("the '189 patent"), 10,703,809 ("the '809 patent"), 9,447,176 ("the '176 patent"), and 11,807,678 ("the '678 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 (D.I. 1). For purposes of this PI only and for the benefit

of the Court, Alexion seeks preliminary injunctive relief due to infringement of two claims: claim 1 of the '176 patent (Ex. A[1]) and claim 1 of the '189 patent (Ex. B) (collectively, the "PI Claims").[2]

The PI Claims cover methods of treating PNH and aHUS comprising administering pharmaceutical compositions of a non-naturally occurring, uniquely-engineered humanized antibody developed by Alexion and marketed as SOLIRIS®. The claimed sequence is unique because it is an unnatural hybrid of two different antibody structures, namely IgG2 and IgG4.

The FDA approved SOLIRIS® on March 16, 2007 as the first approved therapy to reduce hemolysis in patients with PNH. The FDA later approved SOLIRIS® on September 23, 2011 as the first therapy to inhibit complement-mediated thrombotic microangiopathy in patients with aHUS. Sales of Alexion's first-in-class terminal complement inhibitor, SOLIRIS®, are critical to Alexion. Imminent market entry of Samsung's SB12 biosimilar threatens to inflict devastating and irreparable harm to Alexion from price erosion, loss of market share, and reputational harm.

The equitable factors weigh in favor of a preliminary injunction against Samsung. ***First,*** Alexion is likely to succeed on the merits in showing that Samsung infringes both of the PI Claims. Likelihood of success on a single patent claim alone is all that is needed to warrant an injunction. As discussed below, if Samsung markets and sells its SB12 biosimilar product, it will infringe each of the PI Claims because Samsung's label will encourage and instruct medical professionals to use SB12 in a manner that practices each and every limitation of the claimed methods, either literally or under the doctrine of equivalents ("DOE"). Conversely, Samsung is not likely to show that either of the PI Claims are invalid.

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[1] All exhibits cited in the form "Ex. _" are submitted within the attorney Declaration of Andrew Cochran, filed contemporaneously herewith.

[2] Alexion expressly reserves the right to assert additional or other patents, and claims of those patents, as discovery progresses in this case.

Second, absent injunctive relief, Alexion will suffer severe and irreparable harm that will not be adequately compensated by monetary damages. A premature launch of Samsung's SB12 biosimilar product prior to a trial on the merits will cause unrecoverable price erosion and lost market share as well as significant damage to Alexion's reputation as an innovator.

Third, the balance of hardships favors Alexion as these substantial and irreparable harms to Alexion far exceed any harm to Samsung, who currently derives no revenue from SB12 in the United States.

Fourth, there is significant public interest in protecting Alexion's patent rights and investment in research and development in the treatment of rare blood diseases, which outweighs any benefit Samsung may attribute to its SB12 biosimilar product.

A preliminary injunction thus should be entered to preserve the status quo until Alexion's full set of claims can be adjudicated.

II. NATURE AND STAGE OF THE PROCEEDINGS

On July 7, 2023, Samsung provided its notice of commercial marketing of Samsung's SB12 biosimilar product pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. C. [redacted]

Alexion brought this patent infringement case against Samsung under the BPCIA on January 3, 2024. D.I. 1 at ¶ 1.

In a January 17, 2024 letter from Samsung's counsel, [redacted] Ex. D.

As discussed more below, this case is also proceeding in parallel with five *Inter Partes* Review ("IPR") trials before the Patent Trial and Appeal Board ("PTAB"), which Samsung filed in May and June 2023, including one IPR against the '189 patent. Samsung did not challenge the '176 patent by IPR. As also discussed below, Samsung will be estopped under 35 U.S.C. § 315(e)(2) from asserting at trial in this litigation any ground of invalidity that Samsung "raised or reasonably could have raised during" its five IPRs.

III. STATEMENT OF FACTS

Samsung submitted an abbreviated Biologics License Application ("aBLA") to the FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of SB12. Ex. C. Samsung has represented that it is seeking approval from the FDA to market its SB12 biosimilar for indications to treat PNH and aHUS. *Id.*

Samsung has refused to provide Alexion with a copy of its aBLA. *Id.* In order to be marketed as biosimilar to SOLIRIS® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), however, SB12 must be highly similar to SOLIRIS® with only minor differences in clinically inactive components, and with no clinically meaningful difference between SB12 and SOLIRIS® in terms of safety, purity, and potency. The European Medicines Agency (EMA) conducted a similarity assessment between Samsung's SB12 biosimilar—known as Epysqli in Europe—and SOLIRIS® and concluded that the two products share an "identical primary [amino acid] sequence." Ex. E at 11. Samsung's SB12 was granted marketing authorization by the European Commission (EC) on May 26, 2023, as a biosimilar to SOLIRIS®, for the treatment of patients with PNH. Ex. F at 17. Accordingly, SB12 contains either eculizumab or an antibody identical or highly similar to

Alexion's "eculizumab" as recited in claim 1 of the '176 patent and to the amino acid sequence of eculizumab recited in claim 1 of the '189 patent.

IV. ARGUMENT

The Court has broad discretion to "grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent." 35 U.S.C. § 283. The Federal Circuit has made it clear that preliminary injunctions should issue in patent cases where the legal requirements have been met in order to vindicate the property right granted to protect the innovations of patent owners. *See Trebro Mfg. v. FireFly Equip., LLC*, 748 F.3d 1159, 1170-71 (Fed. Cir. 2014).

When a patentee moves for a preliminary injunction, the Court must consider four factors: "(1) likelihood of success on the merits of the underlying litigation, (2) whether irreparable harm is likely if the injunction is not granted, (3) the balance of hardships as between the litigants, and (4) factors of the public interest." *Abbott Lab'ys* v. *Sandoz, Inc.*, 544 F.3d 1341, 1344 (Fed. Cir. 2008). Here, all four factors weigh in favor of granting the requested preliminary injunction.

A. Alexion Will Likely Succeed on the Merits

To show likelihood of success, "a patentee must prove that success in establishing infringement is 'more likely than not.'" *Trebro Mfg.*, at 1166. Alexion is likely to succeed on the merits because Samsung will (1) infringe at least one of the PI Claims, literally or under DOE; and (2) at least one infringed claim will withstand Samsung's invalidity challenges. *See Abbott Lab'ys v. Andrx Pharms., Inc.*, 473 F.3d 1196, 1201 (patentee "must show that it will likely prove that [defendants] infringe [] at least one valid and enforceable patent claim").

1. The PI Claims Are Infringed

A defendant directly infringes a method patent by using the patented method or by importing or selling a product made by using the patented method. 35 U.S.C. §§ 271(a), (g); *see id.* § 271(e)(2) (filing an aBLA is an "act of infringement"). A defendant can also be liable for indirect infringement by inducing another to directly infringe. *Id.* § 271(b). Induced infringement requires showing (1) direct infringement by another; and (2) "that the defendant possessed specific intent to encourage another's infringement." *See Vanda Pharm. v. W.-Ward Pharm.*, 887 F. 3d 1117, 1129 (Fed. Cir. 2018); *see also Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App'x 917, 926 (Fed. Cir. 2011) (holding "that the sale of a product specifically labeled for use in a patented method constitutes inducement to infringe that patent").

The '176 patent claims a method for treating aHUS with eculizumab. Samsung, directly and by inducement, has infringed and/or will infringe at least claim 1 of the '176 patent:

> 1. A method for treating atypical hemolytic uremic syndrome (aHUS), the method comprising administering to a patient in need thereof eculizumab in an amount effective to treat aHUS in the patient; wherein the eculizumab is intravenously administered to the patient under the following schedule:
>
> 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.

The '189 patent claims a method and formulation for treating PNH with eculizumab, including claim elements directed to eculizumab's uniquely-engineered amino acid sequence. Samsung, directly and by inducement, has infringed and/or will infringe at least claim 1 of the '189 patent:

> 1. A method of treating a patient suffering from paroxysmal nocturnal hemoglobinuria (PNH) comprising administering to the patient a

> pharmaceutical composition comprising an antibody that binds C5, wherein the antibody comprises a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4, and wherein the composition comprises a single-unit dosage form comprising 300 mg of the antibody in 30 mL of a sterile, preservative-free solution.

As a biosimilar to SOLIRIS®, Samsung seeks FDA approval for a label that specifies treatment methods that, if followed as expected, will infringe the methods described by the PI Claims. Thus, if the FDA were to approve of SB12 and its proposed label, Samsung will advertise and otherwise inform doctors, patients, and other healthcare providers that SB12 is available for use to treat aHUS and PNH as indicated in Samsung's label. As such, upon FDA approval, Samsung will induce the direct infringement by doctors, patients, and other healthcare providers, either literally or under DOE, through Samsung's proposed label for SB12. Where, as here, a product label and other materials "encourage, recommend, or promote infringement," the court must find inducement. *Sanofi v. Watson Lab'ys Inc.*, 875 F.3d 636, 644 (Fed. Cir. 2017); *see also Vanda*, 887 F.3d at 1129 (label recommended performing claims).

Samsung's European SB12 biosimilar, Epysqli, shares an "identical primary [amino acid] sequence" to SOLIRIS®, as shown by the EMA's similarity assessment. Ex. F at 23. Any differences between SB12 and SOLIRIS® are likely inconsequential. Further, Samsung will meet the formulation limitations of claim 1 of the '189 patent based on its approved Epysqli label, which describes Samsung's biosimilar composition as "[o]ne vial of 30 ml contains 300 mg of eculizumab," which "contains no preservatives," and is administered via a "sterile syringe." Ex. F at 2, 16-17. Also, the SOLIRIS® label, which Samsung's proposed label must be substantially similar to, includes a dosing regimen covered by claim 1 of the '176 patent. Ex. G. Thus, Samsung's SB12 will infringe the PI Claims either literally or under DOE.

Accordingly, Alexion is likely to succeed in proving infringement of the PI Claims.

2. The PI Claims Are Valid

An issued patent is presumed to be valid. 35 U.S.C. § 282. At the preliminary injunction stage, "the very existence of the patent with its concomitant presumption of validity satisfies the patentee's burden of showing a likelihood of success on the validity issue." *BlephEx, LLC v. Myco Indus.*, 24 F. 4th 1391, 1399 (Fed. Cir. 2022). If "an alleged infringer attacks the validity of a patent at the preliminary injunction stage . . . it bears the initial burden to come forward with . . . evidence to raise a substantial question of validity." *Id.*; *see Andrx*, 473 F. 3d at 1201. The patentee then "must persuade the court that, despite the challenge presented to validity, the patentee is nevertheless likely to succeed at trial on the validity issue." *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1377-79 (Fed. Cir. 2009).

Before this action was filed, Samsung filed IPR petitions against five of the six patents asserted against Samsung in Alexion's Complaint (D.I. 1).[3] 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

[3] Samsung did not challenge the validity of the '176 patent before the PTAB. Nor did Samsung's Answer and Counterclaims (D.I. 11) provide any specific allegations of invalidity of that patent.

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 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*, 544 F.3d at 1344 ("(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.[4]

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

[4] 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.

No. 18-172 (MN), 2021 WL 3015280, at *3 (D. Del. July 6, 2021) (citing four decisions by the Federal Circuit). 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.

In addition, and for the reasons stated in those IPR proceedings and here (*infra*), Alexion maintains that it has a reasonable likelihood of success on the merits with respect to validity.

a. The PI Claims Cover Breakthrough Methods of Treatment

The FDA approved SOLIRIS®: (1) on March 16, 2007, as the first approved therapy to reduce hemolysis in patients with PNH; and (2) on September 23, 2011, as the first approved therapy for patients with aHUS. *See* Ex. H; Ex. I. Alexion's inventions contained within the PI Claims were breakthrough approaches in the treatment of both aHUS and PNH, which are debilitating, ultra-rare, and life-threatening blood disorders.

Moreover, the PI Claims are valid under 35 U.S.C. §§ 101 and 112. The claims are each directed to a "specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome." *See Vanda*, 887 F. 3d at 1136. The PI Claims together allow physicians to "change the course of aHUS and make a remarkable difference for patients," and use "the most important advance that has been made in the treatment of [PNH]." *See* Ex. I at 2; Ex. H at 1.

b. Samsung's Expected Arguments

Alexion anticipates that Samsung will reiterate the arguments it made against the '189 patent's validity in its IPR Petition.[5] Notably, however, IPRs operate under a different standard

[5] IPR2023-01069 (U.S. Patent No. 10,590,189) ("the '189 IPR"). Alexion's Patent Owner

than the clear and convincing standard that Samsung must meet to prevail in this litigation. And the Board's institution decisions are preliminary only and not binding. Further, the '189 patent is presumed valid and Samsung will be estopped under Section 315. *See* Section IV.A.2 *supra.* Thus, it is not necessary for Alexion to address Samsung's predicted arguments. Alexion does so only out of an abundance of caution.

Namely, according to Samsung's hindsight-driven arguments in the IPRs, 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 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. Instead, the existing literature as of March 15, 2007 consistently and repeatedly directed a POSA to an ***IgG4*** antibody described in Thomas (Ex. K) 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. L) and Evans (Ex. M) (obviousness); (2) Evans and Mueller[6] (Exs. N, O) (obviousness); and (3) Bell (Ex. P) (inherent anticipation). Samsung also relies on Tacken (Q) as a secondary reference.

Preliminary Response in the '189 IPR (attached as Ex. J) provides a full explanation of each of Samsung's arguments and Alexion's responses.

[6] Samsung relies on two Mueller references: Mueller 1997 (a research article); and Mueller PCT (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. IPR2023-01069, EX1003 at ¶¶ 62, 124.

Samsung's reading of these references is flawed. As a concise preview, Bowdish does not provide ***any*** disclosure of an antibody consisting of the claimed sequence. Casadevall Decl., App'x. B, ¶¶ 158-161. Evans does not describe ***any*** full-length ***humanized*** antibodies for binding C5, let alone the claimed antibody. *Id.*, ¶¶ 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. *Id.*, ¶ 155. Bell does not disclose the claimed amino acid sequence, which was unknown, not publicly disclosed, and was unavailable to anyone but Alexion (and those bound to confidentiality to Alexion) as of Bell's publication. *Id.*, ¶¶ 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. *Id.*, ¶¶ 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." *Id.*, ¶¶ 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 further in the Declaration of Dr. Arturo Casadevall, filed contemporaneously herewith, Samsung's arguments thus amount to little more than a post-hoc narrative that reconstructs the claimed sequences piecemeal and in hindsight, a fact that the

Board itself has acknowledged. Casadevall Decl., App'x B, ¶¶ 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 bits of the claimed sequence 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 will raise in this case 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. R), 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. S, 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. Trout Decl., App'x B, ¶¶ 76-91, 80-90. Moreover, as further explained in the Declaration of Dr. Bernhardt Trout, filed contemporaneously herewith, 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. *Id.*, ¶¶ 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 Board is likely to confirm the patentability of claim 1 of the '189 patent..

Samsung's Counterclaims allege inequitable conduct against the '189 patent based on Alexion's submission of an amino acid sequence to the Chemical Abstract Society ("CAS"). D.I. 11 at 41-59. These allegations fail as a matter of law. *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1291 (Fed. Cir. 2011). The CAS sequence submitted in 1999 is not the claimed sequence. Exs. T, U. This undisputed fact nullifies Samsung's position. And Samsung was fully aware of this undisputed fact before making its serious allegations of fraud: its Counterclaims cite to the prosecution history of Alexion's European Pat. No. 3 167 888, during which Alexion repeatedly showed that the 1999 CAS sequence was not the claimed sequence. And Samsung's alleged inequitable conduct arguments against the '189 patent's parents based on Tacken and Mueller PCT fail, as both references are directed to completely different antibodies.

Additionally, during prosecution of the '176 patent, claim 1 overcame rejections under Sections 102 and 103, due in part to the claim's novel dosing schedule. Samsung is therefore unlikely to succeed in proving the invalidity of claim 1 of the '176 patent.

B. Alexion Will Suffer Irreparable Harm

Samsung's launch of SB12 will irreparably harm Alexion. "Price erosion, loss of good-will, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm." *Celsis In Vitro v. CellzDirect*, 664 F.3d 922, 930 (Fed. Cir. 2012); *Research Found. of State Univ. of N.Y. v. Mylan Pharms., Inc.*, 723 F. Supp. 2d 638, 658 (D. Del. 2010). Availability of damages does not negate irreparable harm, given the market is inherently uncertain and not all harm is measurable. *See Hybritech v. Abbott Lab'ys*, 849 F.2d 1446, 1456-57 (Fed. Cir. 1988) ("[B]ecause the principal value of a patent is its statutory right to exclude, the nature of the patent grant weighs against holding that monetary damages will always suffice to make the patentee whole."); *Abbott*, 544 F.3d, 1361-62 ("loss of market opportunities cannot be quantified or adequately compensated").

1. Price Erosion

The direct competition between Alexion and Samsung will drive down the price of both companies' products, which will, in turn, lead to irreversible price erosion of Alexion's SOLIRIS® product. Price erosion constitutes irreparable harm because third-party payors for pharmaceutical products resist any attempts to return to pre-entry prices "once they experience paying a much lower price for [defendant]'s generic version of it." *Research Found.*, 723 F. Supp. 2d at 658. When a biosimilar enters the U.S. market, it is "typically priced at a 30% discount to the brand name biologic drug to which it is structurally similar." Thomas Decl., ¶ 20[7]. Alexion estimates

[7] The Declaration of Vincent Thomas, filed contemporaneously herewith, provides

that a biosimilar introduction in 2025 would result in price erosion [redacted] [redacted] *Id.*, ¶¶ 17, 30 . Alexion expects similar impact on the pricing and sales of its related drug, Ultomiris®, which is approved to treat PNH and aHUS. *Id.*, ¶ 20. Ultomiris' mechanism of action is the same as that of SOLIRIS®, but offers a more convenient dosing schedule and potentially other associated benefits for patients. *Id.*, ¶ 19. A premature launch of Samsung's SB12 biosimilar product, will likely, "erode Alexion's pricing power for Soliris ***and Ultomiris,*** which are the company's key drugs." *Id*, ¶ 20.

Further, even if Samsung is forced to exit the market after a premature launch, Alexion will not have the ability to unilaterally restore the pre-Samsung launch price because market pricing will remain low. *Id.*, ¶¶ 15-17 . Thus, the expected price erosion supports a finding of irreparable harm. *See Sanofi-Synthelabo v. Apotex*, 470 F.3d 1368, 1382 (Fed. Cir. 2006) (irreparable harm of "irreversible price erosion in light of a complex pricing scheme that is directly affected by the presence of the generic product in the market," as "it is nearly impossible to restore [patentee's drug] to its pre-launch price").

2. Lost Sales and Market Share

In addition, a launch of Samsung's SB12 biosimilar product will inevitably cause Alexion to lose significant market share. "[D]irect competition between [the parties] . . . weighs in favor of finding irreparable harm." *Apple v. Samsung*, 809 F.3d 633, 641 (Fed. Cir. 2015). Biosimilar introduction generally leads "clinicians to reconsider their treatment choices as more options become available," and biosimilars designated as "interchangeable" can be "substituted for the reference product without the intervention of the healthcare provider." Thomas Decl., ¶ 14. Also,

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economic analysis and conclusions regarding irreparable harm.

the Inflation Reduction Act (IRA) incentivizes physicians to use biosimilars by establishing an 8% add-on payment rate for biosimilars under Medicare Part B. *Id.* Alexion estimates that the entry of Samsung's biosimilar "would reduce Alexion's market share by [redacted] and erode the market share of SOLIRIS® [redacted] *See id.*, ¶¶ 15-16. Moreover, [redacted] resulting in further market fragmentation and loss of market share for Alexion. *See Abbott*, 544 F.3d at 1361 (affirming finding that generic manufacturer's sales would cause irreparable harm even though two other generic manufacturers were already on the market).

3. Reputational Harm

Alexion will suffer reputational harm if Samsung launches its infringing biosimilar. Alexion has a reputation as an innovator of safe and effective PNH and aHUS treatments and perpetually seeks to improve the standard of care, for example, by developing Ultomiris® and "educating prescribers on the benefits of Ultomiris as compared to SOLIRIS® due to the dosage regime and other potential associated benefits to such patients." Thomas Decl., ¶ 34. The entrance of SB12 will "impact the rate at which patients may switch from Soliris to Ultomiris," and the differences between SB12 and SOLIRIS® may be difficult to communicate to the public, cause confusion among physicians and patients, and harm Alexion's reputation as the innovator of eculizumab. *See id.*; *Douglas Dynamics v. Buyer Prods.*, 717 F.3d 1336, 1344-45 (Fed. Cir. 2013 (irreparable harm to patentee's "reputation as an innovator" if competitors were allowed to use the invention).

4. Causal Nexus

An injunction is proper because a causal nexus exists between Samsung's infringement and Alexion's irreparable harm—*i.e.*, there is "some connection between the patented features and

demand for the infringing product[].” *Apple*, 809 F.3d at 639, 641; *Genband US v. Metaswitch Networks*, 861 F.3d 1378, 1384 & n.2 (Fed. Cir. 2017) (“[C]ausal nexus and consumer demand may be apparent from the simple fact of infringing sales.”).

The harm to Alexion ties directly to Samsung’s infringement. Samsung could not launch its SB12 biosimilar but for infringement of Alexion’s patents. Each of the irreparable harms discussed above will be a direct result of Samsung targeting hospitals and GPOs with a lower cost equivalent of SOLIRIS® that they would only use based on their association with Alexion’s products. *See Mylan Inst., LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 872-73 (Fed. Cir. 2017) (causal nexus shown where defendant could not make its product without infringing the patents).

C. The Balance of Hardships Weighs in Favor of Alexion

The balance of hardships strongly favors Alexion. Without injunctive relief, Alexion will suffer the irreparable harms described above and lose the value of its hard-earned intellectual property reflecting decades of investment and innovation. Samsung, on the other hand, will suffer minimal harm from an injunction delaying the launch of SB12, because SB12 has not yet gained FDA approval. Samsung, therefore, does not currently derive revenue from sales of SB12. *See M/A-COM Tech. v. Laird*, 2014 WL 2727198, at *7 (D. Del. June 13, 2014) (balance of hardships favors patentee where defendant “presently derives no revenue from [accused product] sales”). The only potential harm to Samsung is the “time-shifting” of revenue, which carries little weight. *See Research Found.*, 723 F. Supp. 2d at 661 (citing *Glaxo v. Apotex*, 64 Fed. App’x 751, 756 (Fed. Cir. 2003) (affirming injunction because “[patentee] would lose the value of its patent while [generic manufacturer] would only lose the ability to go on the market and begin earning profits earlier”)); *LEGO v. ZURU*, 799 F. App’x 823, 832 (Fed. Cir. 2020) (“It is axiomatic that an infringer. . . cannot complain about the loss of ability to offer its infringing product.”) For these

reasons, the balance of hardships favors an injunction. *See Abbott*, 544 F.3d at 1362 ("preserving the status quo" because "[patentee] will lose much more if this Court did not enjoin [generic's] infringing conduct").

D. The Public Interest Is Best Served By Injunctive Relief

The public interest favors an injunction. The public interest is best served by protecting those investments and enforcing valid patents. *See Pfaff v. Wells Elecs.*, 525 U.S. 55, 63 (1998); *Impax Lab'ys v. Aventis Pharm.*, 235 F. Supp. 2d 390, 396 (D. Del. 2002). Protecting Alexion's patents will incentivize further innovation. *See Abbott*, 544 F.3d at 1362-63 ("significant public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid pharmaceutical patents.") (internal quotation marks omitted). An injunction preserving the status quo will not harm the public, but rather, ensure continued patient access to safe and effective treatment. Alexion remains committed to providing SOLIRIS® to patients. Any public benefit Samsung attributes to selling its infringing product is outweighed by "the public interest in recognizing [Alexion's] patent rights, and more generally promoting continued, large-scale investment in research and development of new pharmaceuticals." *Research Found.*, 723 F. Supp. 2d at 663. Indeed, public policy does not support "eliminating the exclusionary rights conveyed by pharmaceutical patents" or "excuse infringement of valid pharmaceutical patents." *See Pfizer Inc. v. Teva Pharms.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005). Thus, the public interest in allowing Alexion's case to be heard outweighs the temporary delay in availability of potentially cheaper drugs.

V. CONCLUSION

For the foregoing reasons, Alexion respectfully requests that this Court grant its Motion for a Preliminary Injunction.

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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 February 12, 2024 on the following counsel in the manner indicated below.

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