

2024-1965, -1966

**United States Court of Appeals
for the Federal Circuit**

REGENERON PHARMACEUTICALS, INC.,

Plaintiff-Appellee,

— v. —

MYLAN PHARMACEUTICALS INC., AMGEN USA, INC., BIOCON
BIOLOGICS INC., CELLTRION, INC., FORMYCON AG, AMGEN INC.,

Defendants,

SAMSUNG BIOEPIS CO., LTD.,

Defendant-Appellant.

*On Appeals from the United States District Court for the Northern
District of Virginia in Nos. 1:22-cv-00061-TSK-JPM, 1:23-cv-
00089-TSK-JPM, 1:23-cv-00094-TSK-JPM, 1:23-cv-00097-TSK-
JPM, 1:23-cv-00106-TSK-JPM, 1:24-cv-00039-TSK-JPM,
1:24-cv-00053-TSK, and 1:24-md-03103-TSK-JPM,
Chief Judge Thomas S. Kleeh*

**NONCONFIDENTIAL OPENING BRIEF FOR DEFENDANT-
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CELLTRION, INC., v. REGENERON PHARMACEUTICALS, INC.

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CELLTRION EXHIBIT 1063

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PATENT CLAIMS AT ISSUE

This appeal concerns claims 4, 7, 9, 11, 14-17, and 55 of U.S. Patent

No. 11,084,865. Claim 4 is representative:

1. A vial comprising an ophthalmic formulation suitable for intravitreal administration that comprises:
 - a vascular endothelial growth factor (VEGF) antagonist
 - an organic co-solvent,
 - a buffer, and
 - a stabilizing agent,wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4; and
wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography.
2. The vial of claim 1, wherein the concentration of said VEGF antagonist fusion protein is 40 mg /m l, and wherein said organic co-solvent comprises polysorbate.
4. The vial of claim 2, wherein said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20.

Appx196.

FORM 9. Certificate of Interest

Form 9 (p. 1)
March 2023

**UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT**

CERTIFICATE OF INTEREST

Case Number 2024-1965, 2024-1966
Short Case Caption Regeneron Pharms., Inc. v. Mylan Pharms. Inc.
Filing Party/Entity Samsung Bioepis Co., Ltd.

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2. Please enter only one item per box; attach additional pages as needed, and check the box to indicate such pages are attached.
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Date: 07/17/2024

Signature: /s/ Raymond N. Nimrod

Name: Raymond N. Nimrod

FORM 9. Certificate of Interest

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March 2023

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	2. Real Party in Interest. Fed. Cir. R. 47.4(a)(2).	3. Parent Corporations and Stockholders. Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☒ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Samsung Bioepis Co., Ltd.		Samsung Biologics Co., Ltd.
		Samsung C&T Corporation
		Samsung Electronics Co., Ltd.

☐ Additional pages attached

CELLTRION, INC., v. REGENERON PHARMACEUTICALS, INC.

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FORM 9. Certificate of Interest

Form 9 (p. 3)
March 2023

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

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☒ None/Not Applicable ☐ Additional pages attached

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Statement Regarding Confidential Material Omitted

Pursuant to Federal Circuit Rule 25.1(e) and the Protective Order issued in the U.S. District Court for the Northern District of West Virginia on February 23, 2023, Samsung Bioepis Co., Ltd. (“SB”) is filing a confidential version of this brief that highlights the material marked confidential, and a non-confidential version including appropriate redactions. In the non-confidential version of this brief, confidential material has been deleted on pages i, 6-7, 11-13, 17, 19, 23, 26-30, 45, 57, 60, 62-63. The general nature of the deleted material is (1) confidential information of SB regarding its SB15 product and agreements with a third party not involved in this litigation; and (2) confidential information of Regeneron Pharmaceuticals, Inc. regarding its EYLEA® product.

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STATEMENT OF RELATED CASES

The following cases may directly affect or be directly affected by this Court's decision in the pending appeal:

- *Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals Inc.*, No. 24-2002 (Fed. Cir.)
- *Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals Inc.*, No. 24-2009 (Fed. Cir.)
- *Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals Inc.*, No. 24-2019 (Fed. Cir.)
- *Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals Inc.*, No. 24-2058 (Fed. Cir.)
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- *Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals Inc.*, Nos. 23-1395, -1396 (Fed. Cir.)
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- *Regeneron Pharmaceuticals, Inc. v. Samsung Bioepis Co., Ltd.*, No. 1:23-cv-106 (N.D.W. Va.)
- *Regeneron Pharmaceuticals, Inc. v. Samsung Bioepis Co., Ltd.*, No. 1:23-cv-94 (N.D.W. Va.)
- *Regeneron Pharmaceuticals, Inc. v. Formycon AG*, No. 1:23-cv-97 (N.D.W. Va.)
- *Regeneron Pharmaceuticals, Inc. v. Celltrion, Inc.*, No. 1:23-cv-89 (N.D.W. Va.)
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- *Celltrion, Inc. v. Regeneron Pharmaceuticals, Inc.*, IPR2022-00257 (P.T.A.B.)

- *Apotex Inc. v. Regeneron Pharmaceuticals, Inc.*, IPR2022-00301 (P.T.A.B.)
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- *Chengdu Kanghong Biotechnology Co., Ltd. v. Regeneron Pharmaceuticals, Inc.*, PGR2021-00035 (P.T.A.B.)

PRELIMINARY STATEMENT

This is an appeal of a preliminary injunction entered by the U.S. District Court for the Northern District of West Virginia (Kleeh, J.) that prevents Defendant-Appellant Samsung Bioepis (“SB”) from launching its SB15 product to treat serious eye disorders, thereby allowing Plaintiff-Appellee Regeneron Pharmaceuticals, Inc. (“Regeneron”) to improperly extend its monopoly over its EYLEA® product based on trivial changes to patent claims that expired long ago.

SB15 is a biosimilar containing the active ingredient aflibercept. Aflibercept is a genetically engineered fusion protein that inhibits vascular endothelial growth factor (“VEGF”) (thus sometimes called a VEGF Trap) and is used to treat a variety of eye disorders, including wet age-related macular degeneration. The Food and Drug Administration (“FDA”) approved SB15 on May 20, 2024, but SB has been enjoined from launch, first by a temporary restraining order (“TRO”), and now by a preliminary injunction.

SB15’s reference product is EYLEA, which is manufactured and sold by Regeneron. EYLEA is an ophthalmic formulation with 40 mg/mL of VEGF Trap aflibercept. The aflibercept in EYLEA is produced by CHO cells and as a result has a particular glycosylation pattern. Regeneron launched EYLEA in 2011 and has maintained market exclusivity for thirteen years.

Regeneron’s fundamental composition of matter patent on aflibercept, U.S. Patent No. 7,070,959 (the “’959 patent”), expired in June 2023—a full twelve years after the product’s launch. Regeneron also filed and obtained a patent covering the precise formulation of EYLEA (U.S. Patent No. 9,340,594 (the “’594 patent”)). But that patent expired in 2021, even earlier than the composition of matter patent.

Regeneron now blocks others from the market through a network of 50-plus patents largely reciting known or obvious features of the same EYLEA product claimed in expired patents. Of particular relevance, Regeneron was granted a series of ten formulation patents in a single family (“Stability Family”), each of which shares the same five-and-one-half page specification (the “Common Specification”). The Stability Family patents all claim priority to a patent application filed in 2007. The Common Specification teaches six VEGF Trap formulations and provides stability and turbidity data for those formulations. The patent at issue here, U.S. Patent No. 11,084,865 (“the ’865 patent”), belongs to the Stability Family, as does the expired ’594 patent.

The expired ’594 patent claims recite Regeneron’s specific EYLEA formulation, which is set forth in Examples 3 and 4 of the Common Specification, and further recites that the formulation is “stable” at four months. When Regeneron sought claims to this “stable” aflibercept

formulation, Regeneron faced obviousness-type double patenting (“OTDP”) rejections over patents that already claimed aflibercept formulations. To overcome those rejections, Regeneron filed terminal disclaimers, including to a patent from a separate, earlier-expiring family. As a result, the ’594 patent expired in 2021.

In an attempt to extend the patent term on its EYLEA formulation, Regeneron prosecuted new applications with claims reciting the same formulations set forth in Examples 3 and 4, but added limitations requiring specific two-month stability of “at least 98%” and glycosylated aflibercept. Regeneron relied on the “at least 98%” two-month stability limitation to overcome an OTDP rejection over the ’594 patent, even though the alleged improved two-month stability was a feature of Examples 3 and 4 that formed the basis for the ’594 patent claims.

The district court enjoined SB from launching its biosimilar product based on the patent term of the ’865 patent, which extends many years beyond that of the ’594 patent claiming the EYLEA formulation. The injunction is legally erroneous in many respects.

First, the district court lacks personal jurisdiction over SB. In granting the preliminary injunction, the court found a “reasonable probability” that personal jurisdiction exists in West Virginia based solely on SB having filed

a Biologics License Application (“BLA”) for SB15. The court misread this Court’s decision in *Acorda Therapeutics Inc. v. Mylan Pharms. Inc.*, 817 F.3d 755 (Fed. Cir. 2016), as holding that an ANDA or BLA filer will be subject to personal jurisdiction in *every state* unless it can affirmatively prove that it has “carved any states out of the United States market.” *Acorda* is not so broad. Rather, in *Acorda*, it was undisputed that the defendant specifically intended to sell the accused product in the forum state upon FDA approval. Here, in contrast, Regeneron—despite having the opportunity to take jurisdictional discovery—adduced no evidence of any intent to sell SB15 in West Virginia, and it was error for the district court to relieve Regeneron of its burden by assuming such sales would take place.

Second, the district court erred as a matter of law in ruling that Regeneron was likely to succeed on the merits of SB’s OTDP and written-description challenges. The district court’s ruling that, despite its earlier expiration date, the ’594 patent is not available as an OTDP reference directly conflicts with this Court’s precedent and upends decades of patent prosecution practice. The court, moreover, erroneously disregarded the specification in determining the proper scope and disclosure of the ’594 patent reference claim (claim 5)(“Reference Claim”). As a result, the court nonsensically concluded that the ’865 patent claims are patentably distinct from the ’594 Reference

Claim even though the '865 claims and the '594 Reference Claim recite the *same* Example 3 and 4 formulation and thus have the *same* properties.

As to SB's written description defense, the district court first erred by permitting Regeneron to claim stability values of 99.4-100%—about 35% of the claimed range—when the inventors achieved at most 99.3% two-month stability. Furthermore, the POSA could not discern the lower bound of 98% from the two-month stability values disclosed in the examples (98.9-99.3%), all of which round to 99% and none of which supports the 98% lower bound. And the district court's OTDP finding that "VEGF Trap SEQ ID 4"—which is used in all the patent examples—"is not necessarily glycosylated" means that the skilled person reviewing the specification would find *no* examples identified as using glycosylated aflibercept and thus no support for any stability limitations for such formulations.

Third, the district court erred in failing to apply this Court's precedents requiring a nexus between Regeneron's alleged irreparable harm and SB15's alleged infringement of the "at least 98%" stability requirement. The 98% two-month stability limitation is a feature of every claim of the '865 patent on which Regeneron relied to distinguish its prior patent asserting generic four-month stability. Yet, Regeneron presented no evidence of any nexus between its purported injury and the 98% two-month stability feature, or that the 98%

CONFIDENTIAL MATERIALS OMITTED

stability limitation drives demand for SB's product. The undisputed evidence shows that customers will *not* know what stability level SB15 achieves at two months. Moreover, the FDA requires only 95% stability at two months for approval, and SB's BLA permits it to make and sell SB15 product having ^{Confidential Product Information} [REDACTED] two-month stability. On those undisputed facts, the 98% stability feature cannot drive demand.

For these reasons and as further explained below, this Court should reverse.

JURISDICTIONAL STATEMENT

The district court had subject-matter jurisdiction over this action pursuant to 28 U.S.C. § 1338. This Court has jurisdiction over the district court's orders granting a preliminary injunction pursuant to 28 U.S.C. § 1292(c)(1). SB timely filed notices of appeal on June 14, 2024, which it amended on July 11, 2024. Appx20867-78.

STATEMENT OF THE ISSUES

1. Whether Regeneron failed to establish a substantial probability of personal jurisdiction where SB has no contacts with the forum state and Regeneron adduced no evidence that SB intends to undertake any SB15 sales or direct any other acts in the forum state.

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2. Whether SB raised substantial questions of invalidity based on (a) OTDP over a reference patent claiming the same formulation and having the same properties as the claimed formulation of the '865 patent; and/or (b) lack of written description support for the “at least 98%” two-month stability limitation where the specification provides no stability values for any formulations identified as using glycosylated aflibercept as recited by the claims and also provides no support for the upper and lower bounds of the claimed range for any aflibercept formulation.

3. Whether Regeneron failed to establish a nexus between its alleged harm and the claimed feature of “at least 98%” two-month stability, where the FDA approved SB’s BLA on the basis that SB could sell SB15 Confidential Product Information products having two-month stability less than 98% (down to [REDACTED]), such that SB can sell SB15 without infringing the '865 patent claims and Regeneron would suffer the alleged harm even absent infringement.

STATEMENT OF THE CASE

A. Regeneron’s Stability Family Of Patents

Regeneron’s Stability Family of patents includes ten issued patents that all claim priority to an application filed in 2007. Appx185.

The Stability Family patents all share a five-and-a-half page Common Specification including eight examples. Appx185-92. The examples

describe six VEGF Trap liquid formulations and provide stability data (measured as % VEGF Trap Native Configuration using size-exclusion chromatography (“SEC”)) and turbidity data for the formulations after storage at 5 °C for various periods of time. Appx190-91. The examples are the only part of the specification that discloses stability values. Appx190-91. There is no generic disclosure of any two-month stability range. Appx187-90.

Examples 3 and 4 describe the precise EYLEA formulation. Appx191. Example 3 discloses the formulation stored in a vial, and Example 4 discloses a pre-filled syringe (“PFS”). Appx191. Stability is reported at various points through four months, including at two months. Appx191. Relevant to this appeal, at the two-month point, the tests report 99.1% and 99.2%, virtually the same stability for vial and PFS embodiments. Appx191.

None of the examples specifies whether the aflibercept used in the formulations is glycosylated. Appx190-91. The specification only mentions the word “glycosylation” once, stating that in a “specific embodiment” (not even a preferred embodiment), the aflibercept is “glycosylated at Asn residues 62, 94, 149, 222 and 308.” Appx189 (6:30-

37). Regeneron's expert testified, however, that the skilled person reading the Common Specification would conclude that aflibercept used in Examples 3 and 4 was glycosylated at the relevant locations. Appx15122-34 (161:14-175:7); *see* Appx11446 (fn. 8).

B. Regeneron's '594 Patent

On June 14, 2014, Regeneron filed the application leading to the issuance of the '594 reference patent, with claims based on the embodiments in Examples 3 and 4. Appx14883-960; Appx4542. Claim 5 of the '594 patent recites the precise formulation of Examples 3 and 4 and further specifies that the formulation is "stable for at least 4 months." Appx4542. Like the examples themselves, the Reference Claim does not expressly state that the aflibercept is glycosylated. Appx4542.

During prosecution of the '594 patent, the Examiner rejected the claims for OTDP over U.S. Patent No. 7,608,261 ("the '261 patent"). Appx14936-42. The '261 patent is part of the Stability Family, but it expired early and did not have a full twenty-year term based on its own terminal disclaimer over another Regeneron patent (U.S. Patent No. 7,531,173), which also was terminally disclaimed. Appx11596; Appx11472.

When faced with the OTDP rejection during prosecution of the '594 patent, Regeneron did not contend that the '261 was not a proper OTDP

reference patent because the '261 and '594 patents are in the same patent family. Appx14950. Instead, Regeneron filed a terminal disclaimer. Appx14943-53. As a result, the '594 patent issued with a shortened patent term that expired in March 2021. Appx11596; Appx14955-60; Appx4532.

C. Regeneron '865 Patent

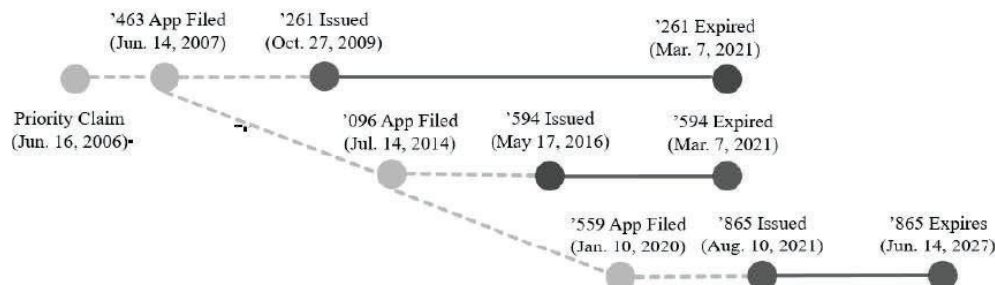
As the '594 patent neared expiration, Regeneron sought another patent—the '865 patent—also directed to the EYLEA formulation embodied in Examples 3 and 4. Appx4089-101. To distinguish over prior patent claims in the same family, Regeneron added three features based on the same Example 3 and/or 4 formulations of the '594 patent claims. Appx4100-01. The new claims specified that the aflibercept formulation had “at least 98%” two-month stability, was glycosylated, and was stored in a vial. Appx4100-01.

During prosecution of the '865 patent, the claims were initially rejected for OTDP over the claims of the '594 patent. Appx4107-09. Regeneron did not challenge the rejection on the ground that the '594 patent was not a proper OTDP reference, as it does now. Instead, Regeneron relied on the “at least 98%” stability limitation to purportedly distinguish the '865 claims from the '594 claims. Appx4112-13. Even though the '594 claims recite the same formulation of Examples 3 and 4 and also recite the four-month stability

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achieved by those examples, the Examiner withdrew the rejection and allowed the claims. Appx4122-25.

Filing, issue and expiry dates for the relevant patents in the Stability Family are shown below:



D. SB's SB15 Product And BLA

In February 2023, SB filed BLA No. 761350 with the FDA, seeking approval for its SB15 drug product as an interchangeable biosimilar to EYLEA. Appx255 (¶¶3-4). SB's BLA specifies that the SB15 is an intravitreally administered drug for the treatment of various angiogenic eye disorders. Appx2277; Appx2289. SB15 works by binding to VEGF and can be referred to as an VEGF antagonist. Appx2277; Appx2289; *see* Appx2123.

SB15's active ingredient is aflibercept. Appx2277; Appx2289. The proposed label states that SB15 is at a concentration of 40 mg/mL, with ^{Confidential Product Information} [REDACTED] sodium phosphate buffer, ^{Confidential Product Information} [REDACTED] polysorbate 20, [REDACTED] sucrose, and a pH of 6.2. Appx2277; Appx2289; *see* Appx2119 (¶¶2-3). Among a host of ^{Confidential Product Information} stability criteria, SB's BLA specifies the product must remain above [REDACTED]

purity at various points, including at two months. Appx2753, Appx2820; Appx2822.

In April 2023, FDA notified SB that the SB15 BLA had been accepted for review, thereby triggering SB's obligations under 42 U.S.C. § 262(l)(2)(A). Appx255 (¶4). Thereafter, the parties engaged in the "patent dance" required by 42 U.S.C. § 262(l)(3). Appx255; Appx259 (¶¶4, 18-19); Appx383-84 (¶5).

Following completion of the patent-dance exchanges, Regeneron and SB began the statutorily required negotiations over the patents to include in any patent infringement action. Appx262 (¶30). As part of those discussions, SB offered to discuss proper jurisdictions for any infringement suit. Appx1426-29. Regeneron refused. Appx620 (¶10).

In November 2023, SB served Regeneron with Notice of Commercial Marketing under 42 U.S.C. § 262(l)(8)(A), stating that commercial marketing of the biological product at issue in BLA No. 761350 would begin on or after May 18, 2024, following FDA approval. Appx20567. SB will not distribute, market, or sell SB15 in the United States but has instead contracted with Biogen who has exclusive rights to commercialize the product. Appx496 (¶11); Appx499-618.

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On May 20, 2024, SB received final approval from the FDA of its BLA for SB15 under the brand name OPUVIZ™ (aflibercept-yszy) in single-dose vial and vial kit. Appx20686-92. The FDA approved SB's BLA on the basis that SB's products would achieve at least ^{Confidential Product Information} [REDACTED] two-month stability. Appx20686-92; Appx2160-69. SB thus can make and sell non-infringing ^{Confidential Product Information} SB15 lots having less than 98% two-month stability (but at least [REDACTED]). The two-month stability criteria is not available to the public, and the product would be sold without reference to actual stability measurement for any batches. Appx11704-05 (¶83).

E. The Proceedings Below

1. Regeneron's Complaint And SB's Motion To Dismiss

On November 21, 2023, Regeneron filed its first complaint against SB, asserting infringement of thirty-seven patents under 35 U.S.C. § 271(b), (c), (e), and/or (g). Appx253-380.

Once the parties completed the patent dance at the end of November, Regeneron filed a follow-on complaint in late December (Case No. 1:23-cv-106), alleging infringement under 35 U.S.C. § 271(e) of patents at issue in the original action, as well as fifteen additional patents. Appx381-463.

Soon thereafter, SB filed a motion to dismiss Regeneron's complaint for lack of personal jurisdiction. Appx464-94. Regeneron opposed solely on

the basis that specific personal jurisdiction exists. Appx1489-521. The district court has not ruled on SB's motion.

Immediately thereafter, Regeneron moved to establish a multi-district litigation ("MDL") for all aflibercept BPCIA cases, and to transfer its case against Amgen, Inc. ("Amgen") from the Central District of California to the Northern District of West Virginia under 28 U.S.C. § 1407. Appx206. On April 11, 2024, the Judicial Panel on Multidistrict Litigation granted the motion. Appx244. The MDL consists of six actions: separate actions against Amgen, Mylan/Biocon, Celltrion, and Formycon, as well as the two actions against SB. Appx244.

2. The Parties' Preliminary Injunction Filings And The Court's Orders

Regeneron filed its preliminary injunction motion on February 22, 2024. The parties engaged in briefing the preliminary injunction motion, with principal briefs limited to 25 pages. *See* Appx1891-924; Appx11427-62. Regeneron initially asserted that SB's launch of SB15 would infringe four of its asserted patents: the '865 patent and three patents directed to cell culture media. Appx1901-14. Regeneron later narrowed its preliminary injunction motion to claims 4, 7, 9, 11, 14-17, and 55 of the '865 patent. Appx20067; Appx20676.

The district court scheduled a hearing for early May, but then abruptly cancelled the hearing. Appx20439-40. After the parties jointly requested guidance regarding the hearing (Appx20431-32), the court held a status conference at which it requested simultaneous submission of “proposed orders,” with no opportunity to respond or object to the other party’s proposed order. Appx20663-64. In contrast to its 25-page opening brief, Regeneron submitted a 120-page proposed order with substantially expanded arguments.¹

On May 14, 2024, Regeneron sought a TRO to prevent launch of SB15, while the court continued to consider the preliminary injunction briefing that had been completed for a month. Appx20465-93. The court granted the TRO until May 31, 2024 (Appx20650-53), and then extended it until June 14, 2024 (Appx20703-05).

On June 14, 2024, without holding a hearing, the district court issued a decision and order granting Regeneron’s motion for a preliminary injunction. Its order adopted, nearly word-for-word, almost all 120 pages of Regeneron’s proposed order. Among other rulings, without resolving SB’s motion to dismiss that had been pending for several months, the court concluded that

¹ Regeneron emailed its 120-page proposed order to the district court, and thus it does not appear on the docket. Regeneron objected to including its proposed order in the appendix.

Regeneron had shown a reasonable probability of personal jurisdiction based on SB's BLA filing and relationship with Biogen. Appx22-27. The court also ruled that Regeneron had met its burden of establishing all four preliminary injunction factors, rejecting SB's defenses of OTDP and written description (Appx27-179) and concluding that Regeneron would be irreparably harmed by the launch of SB15 (Appx117-74).

On July 10, 2024, the court issued a short additional order specifying the terms of the injunction. Appx182-84.

SUMMARY OF THE ARGUMENT

I. The district court erred in concluding that Regeneron "had demonstrated that there is a reasonable probability of ultimate success upon the question of personal jurisdiction." Appx179. In so ruling, the court misapplied *Acorda* and concluded that personal jurisdiction exists in all 50 states for a defendant that files an application for FDA marketing approval unless the defendant can show it intends to carve out any state from its sales territory. *Acorda* does not support such a broad application of personal jurisdiction. In particular, in *Acorda*, this Court found personal jurisdiction based, not only on the defendant's FDA application, but also on the plaintiff's evidence of the defendant's specific intent to direct sales into the forum state after approval. 817 F.3d at 763.

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Here, in contrast, the district court assumed that West Virginia sales would take place unless SB could prove that they would not, thereby improperly relieving Regeneron of its burden of proving personal jurisdiction and flipping the burden to SB instead. Had the district court held Regeneron to its burden, the evidence showed that there is no personal jurisdiction over SB in West Virginia. SB has no contacts with West Virginia, no evidence of Third Party Confidential Business Information any expectation or intent that SB15 will be sold in the state, and no [REDACTED] over Biogen who has exclusive rights to commercialize SB15 in the United States. Indeed, reflecting the total lack of proof, Regeneron failed to present evidence that even Biogen intends to sell SB15 in West Virginia.

II. The district court erred in concluding that Regeneron is likely to succeed on the merits.

First, the district court erroneously ruled that SB's OTDP defense based on the prior expiration of the '594 patent lacked substantial merit. Disregarding this Court's controlling precedent, the court ruled that the '594 patent was not a proper OTDP reference to the '865 patent because the '865 patent and the '594 patent claim priority to the same application and thus have the same twenty-year statutory term. But the '594 patent did not have a twenty-year term; it issued with a shortened, terminally disclaimed term set to expire in 2021.

The court further ruled that, even if the '594 patent were a proper reference patent, the '865 patent is allegedly patentably distinct from the '594 Reference Claim based on the '865 claims elements requiring (i) at least 98% stability at two months, (ii) glycosylation, and (iii) a vial. But both patents recite the same formulation of the same embodiment described in Examples 3 and 4. The '865 patent claims simply recite additional properties of that same embodiment, so the '865 claims are not patentably distinct.

Second, the district court erroneously ruled that SB's written description argument regarding the "at least 98% native conformation" requirement lacked substantial merit. There is no generic disclosure of "at least 98%" two-month stability or any other stability ranges in the specification. Accordingly, the examples are the only potential source of written description support, but the specification only discloses specific values (99.1% and 99.2%) in Examples 3-4 that do not support the full claimed range of 98-100%. Even considering other examples, the specification show that inventors achieved at most 99.3% two-month stability. Nothing suggests that the inventors possessed an invention that could achieve two-month stability values of 99.4-100%, which corresponds to about 35% of the claimed range. Furthermore, the POSA could not discern the lower bound of 98% based on the two-month stability values disclosed in the examples

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(98.9-99.2%), all of which round to 99% and none of which support the 98% lower bound. Finally, the district court’s OTDP finding that (1) “VEGF Trap SEQ ID 4” (aflibercept) “is not necessarily glycosylated” (Appx80) and (2) the skilled person would have been motivated to use non-glycosylated aflibercept (Appx83) means that the POSA reviewing the specification would find *no* examples identified as using glycosylated aflibercept and thus no support for the stability limitation of the ’865 patent claims.

III. The district court erred in assuming a causal nexus existed between SB15’s alleged infringement and the alleged harm to Regeneron. The court reasoned that SB15 was not like complex, multi-featured products, where a connection between a specific patented feature and consumer demand must be shown, disregarding the many other features of SB15 that Regeneron contends infringe its other 50+ patents asserted in the litigation. The court further concluded that the nexus requirement was established because SB15 could not be manufactured without infringing the patent, disregarding that the ^{Confidential Product Information} FDA-approved BLA for SB15 allows for [REDACTED] stability at two months, so SB can manufacture SB15 without infringing the ’865 patent.

STANDARD OF REVIEW

This Court reviews issues of personal jurisdiction *de novo*. *Avocent Huntsville Corp. v. Aten Int’l Co.*, 552 F.3d 1324, 1328 (Fed. Cir. 2008).

This Court reviews an order granting a preliminary injunction for abuse of discretion. *Erico Int’l Corp. v. Vutec Corp.*, 516 F.3d 1350, 1353 (Fed. Cir. 2008). “An abuse of discretion in granting or denying a preliminary injunction may be found ‘by showing that the court made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings.’” *Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1335 (Fed. Cir. 2006) (quoting *Polymer Techs., Inc. v. Bridwell*, 103 F.3d 970, 973 (Fed. Cir. 1996)); see *Globetrotter Software, Inc. v. Elan Computer Grp., Inc.*, 236 F.3d 1363, 1367 (Fed. Cir. 2001) (when preliminary injunction rests on error of law “the legal issue is reviewed *de novo*”).

ARGUMENT

I. THE DISTRICT COURT LEGALLY ERRED IN RULING THAT REGENERON ESTABLISHED A REASONABLE PROBABILITY OF SUCCESS ON PERSONAL JURISDICTION

“A district court cannot enjoin a party if it does not have jurisdiction over that party.” *Celgard, LLC v. LG Chem, Ltd.*, 624 F. App’x 748, 751 (Fed. Cir. 2015).² Consequently, in the context of a preliminary injunction, a district

² This Court applies its own law to issues of personal jurisdiction “because the jurisdictional issue is ‘intimately involved with the substance of the patent laws.’” *Avocent*, 552 F.3d at 1328 (quoting *Akro Corp. v. Luker*, 45 F.3d 1541, 1543 (Fed. Cir. 1995)).

court must “[a]t a minimum ... determine that there is a *substantial probability* that it has jurisdiction over the claim that requires preliminary injunctive relief.” *Id.* (quoting *U.S. v. First Nat’l City Bank*, 379 U.S. 378, 390 (1965)) (cleaned up) (emphasis added). The required showing at the preliminary injunction stage is thus even stronger than the *prima facie* case necessary to survive a motion to dismiss. *See, e.g., Catalog Mkt’g Servs., Ltd. v. Savitch*, 1989 WL 42488, *2 (4th Cir. 1989); *Enterprise Int’l, Inc. v. Corporacion Estatal Petrolera Ecuatoriana*, 762 F.2d 464, 471 (5th Cir. 1985); *Visual Scis., Inc. v. Integrated Commc’ns Inc.*, 660 F.2d 56, 59 (2d Cir. 1981). In undertaking this analysis, a district court must “make factual findings adequate enough to permit intelligent appellate review.” *Visual Scis.*, 660 F.2d at 59; *see Celgard*, 624 F. App’x at 751-52.

The “West Virginia long-arm statute is coextensive with the full reach of due process,” and therefore “the statutory inquiry [for personal jurisdiction] necessarily merges with the Constitutional inquiry” under the Due Process Clause. *In re Celotex Corp.*, 124 F.3d 619, 627-28 (4th Cir. 1997) (cleaned up). A three-factor test governs whether exercising specific personal jurisdiction comports with due process: “(1) whether the defendant purposefully directed its activities at residents of the forum; (2) whether the claim arises out of or relates to the defendant's activities with the forum; and

(3) whether assertion of personal jurisdiction is reasonable and fair.” *Xilinx, Inc. v. Papst Licensing GmbH & Co. KG*, 848 F.3d 1346, 1353 (Fed. Cir. 2017) (cleaned up).

Personal jurisdiction is assessed as of the filing date of the complaint. For claims (such as those here) based on an artificial act of infringement under 35 U.S.C. § 271(e) resulting from an application seeking FDA approval to market a drug or biological product, a court may consider the defendant’s future conduct planned as of the filing date regarding the product that is the subject of the FDA application. *Acorda*, 817 F.3d at 759-60, 763.

Here, it is undisputed that SB itself has no contacts with West Virginia. The district court’s determination that Regeneron nevertheless satisfied its burden of showing a reasonable probability of personal jurisdiction is wrong as a matter of law.

A. SB Lacks Any Contacts With West Virginia

It is undisputed that SB itself has never had any presence in West Virginia, either generally or with respect to SB15 specifically. SB is a Korean biopharmaceutical company headquartered in Incheon, South Korea without any facilities or employees in the United States, let alone West Virginia. Appx495 (¶¶4-5). SB is not registered to do business in West Virginia, has

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not done business with any entities located in West Virginia, and has not designated an agent for service of process in West Virginia. Appx496 (¶8).

SB itself has not distributed, marketed, or sold *any* product in West Virginia. Rather, SB contracts with one of two U.S. companies—Biogen and Organon, neither of which has been shown to be incorporated in or have any places of business in West Virginia—to commercialize its products in the United States. Appx495-Appx496 (¶¶6, 8). Under those contracts, SB develops and manufactures the biosimilar products and delivers them to Biogen or Organon, which are exclusively responsible for commercialization of the products wherever they choose in the United States—including all Third Party Confidential Business Information [REDACTED], [REDACTED] and [REDACTED]. Appx495-Appx496 (¶6).³ SB15 will be no different, as Biogen has the exclusive rights to commercialize the product in the United States. Appx520; Appx1392.

The only sale of SB15 that SB will make in the United States will take Third Party Confidential Business Information place in [REDACTED] to a Massachusetts corporation (Biogen). Appx1709 (257:8-23); Appx21391. The district court did not find otherwise.

³ SB has a U.S. subsidiary, Samsung Bioepis United States, Inc. (“SB USA”), incorporated in Delaware. Appx496 (¶9). The district court made no findings that SB USA’s contacts should be charged to SB, but even if they were SB USA also does not market or sell any of SB’s biosimilar products in the United States. *Id.*

Thus, SB has no contacts whatsoever with West Virginia, much less the minimum contacts required to establish personal jurisdiction. *See International Shoe v. Washington*, 326 U.S. 310, 316 (1945).

B. SB’s BLA Filing Does Not Support Personal Jurisdiction In West Virginia

Brushing past SB’s lack of contacts with West Virginia, the district court nevertheless found specific personal jurisdiction—and it did so without providing any analysis.⁴ Based on its recitation of background facts (Appx6-7) and the legal framework for personal jurisdiction (Appx22-27), however, the court appears to have relied on but misapprehended this Court’s decision in *Acorda Therapeutics Inc. v. Mylan Pharms. Inc.*, 817 F.3d 755 (Fed. Cir. 2016), to conclude that an ANDA or BLA filer whose product will later be marketed, sold, and distributed in the United States is subject to personal jurisdiction in *every state* unless the filer can prove that it has “carved any states out of the United States market.” Appx7; Appx25 (quoting *Acorda* for proposition that “‘the minimum-contacts standard is satisfied’ where a non-resident defendant files an abbreviated new drug application (‘ANDA’) ‘for

⁴ The district court referenced its earlier TRO (Appx27), but that order likewise had only a bare conclusion and lacked any legal analysis (Appx20652-53).

the purpose of engaging in ... allegedly wrongful marketing conduct in' the forum state") (alterations in original).

Contrary to the district court's ruling, *Acorda* does not hold that the mere past act of submitting an FDA application subjects the filer to personal jurisdiction in all 50 states, and it is hard to fathom how any such rule would comport with due process. Rather, in *Acorda* this Court held that personal jurisdiction existed because the defendant (Mylan) *both* sought "approval to sell its generic drugs throughout the United States, including in Delaware [the forum state], *and* it [wa]s undisputed that Mylan plan[ned] to direct sales of its generic drugs into Delaware." 817 F.3d at 763 (emphasis added). Indeed, it was "of particular importance" to this Court that Mylan had admitted that it "*intend[ed] to direct sales of its drugs into Delaware*, among other places, once it ha[d] the requested FDA approval to market them." *Id.* at 758 (emphasis added). And this Court additionally noted Mylan's admissions that it "does some business in every State, either directly or indirectly," it was "registered to do business in Delaware," with its certificate of registration indicating it intended to engage in "pharmaceutical manufacturing, distribution and sales," and it had appointed an agent to accept service of process in Delaware. *Id.* at 763.

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Thus, in *Acorda*, personal jurisdiction turned not just on the filing of the FDA submission, but also on the planned forward-looking acts that the defendant undisputedly intended to undertake in the forum state after receiving FDA approval. Here, unlike Mylan in *Acorda*, Regeneron submitted no evidence that SB has any plans or intent to distribute, market, or sell SB15 in West Virginia. Appx496-97 (¶11). Nor did the district court identify any such evidence or make any such finding.

C. There Is No Evidence That Biogen Intends To Market SB15 In West Virginia Or That SB Could Exercise [REDACTED] Over Biogen's Marketing Decisions

The district court also erred to the extent it ruled that *Biogen's* future commercialization activities support personal jurisdiction over SB. Again citing *Acorda*, 817 F.3d at 763, the court stated that “the minimum-contacts requirement is satisfied even where the defendant ‘does not sell its drugs directly into’ the forum state but rather contracts with a wholesaler or distributor to market the drugs in the state.” Appx25. The court stated that “SB had established a robust U.S. distribution channel for SB15” by Third Party Confidential Business Information “designat[ing] Biogen as the exclusive distributor authorized to [REDACTED], [REDACTED], Third Party Confidential Business Information and [REDACTED] SB15 in the United States, including West Virginia.” Appx6-

7. The district court erred in two key respects.

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First, the district court never found, let alone identified any evidence, that Biogen intends to market, sell, or distribute SB15 in or to West Virginia. This is fatal to Regeneron’s attempts to establish personal jurisdiction over SB based on Biogen’s activities. *See, e.g., Celgard, LLC v. SK Innovation Co., Ltd.*, 792 F.3d 1373, 1382 (Fed. Cir. 2015) (affirming dismissal for lack of personal jurisdiction where there was “no evidence establishing that [the accused] products actually enter the forum state”); *Glam & Glits Nail Design, Inc. v. iGel Beauty, LLC*, 2021 WL 4125873, *4 (C.D. Cal. Aug. 2, 2021) (rejecting unsupported allegations of jurisdiction where the plaintiffs failed to “make any showing of proof” that the accused products “were eventually sold” in the forum state).

Unlike in *Acorda* where there was a finding that the defendant “plan[ned] to direct sales of its generic drugs into” the forum state, 817 F.3d at 763, the district court here merely *assumed* Biogen would make West Virginia sales because the agreement between SB and Biogen did not “carv[e] any states out of the United States market.” Appx7.⁵ In doing so, the district court improperly shifted the burden to SB to prove Biogen would not make

⁵ The district court also erroneously stated that “SB does not deny that it will [REDACTED], [REDACTED], and [REDACTED] SB15 in West Virginia **through Biogen.**” Appx6-7 (emphasis in original). SB explicitly disputed this fact. Appx469; Appx484-85; Appx11201-02.

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sales in West Virginia, as opposed to requiring Regeneron to meet its burden of proving that Biogen intended to do so. *See Catalog Mkt'g*, 1989 WL 42488, at *2; *Enterprise Int'l*, 762 F.2d at 471; *Visual Scis.*, 660 F.2d at 59; *SK Innovation*, 792 F.3d at 1377-78 (plaintiffs bear burden of affirmatively establishing personal jurisdiction).⁶

Because there is no evidence that Biogen intended to make any West Virginia sales, there likewise is no evidence that SB expects or intends Biogen to make any such sales. Indeed, the district court made no such finding.

Second, even if Biogen did intend to make West Virginia sales, the district court never found, let alone cited any evidence, that SB could [REDACTED] where Biogen chose to market SB15 or that SB shared that intent. The agreement between SB and Biogen confirms that Biogen has [REDACTED] over, and [REDACTED] with respect to,” all aspects of SB15’s U.S. commercialization, including [REDACTED], [REDACTED] and [REDACTED]. Appx505;

⁶ The other cases cited by the district court (Appx26-27) are likewise distinguishable on this basis. In *Apicore US LLC v. Beloteca, Inc.*, 2019 WL 1746079 (E.D. Tex. April 18, 2019), the agreement between the defendant and its distributor required the distributor to sell the defendant’s generic product in the United States, indisputably including the forum state. *Id.* at *2, 4. In *Helsinn Healthcare S.A. v. Hospira, Inc.*, 2016 WL 1338601 (D.N.J. April 5, 2016), the defendant sold its drug products through its wholly owned subsidiary that it admitted would “market, sell, and distribute [its drug] product in the state.” *Id.* at *6, 8 (internal quotations omitted).

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Appx536. In this way, Biogen is not a distributor working under the direction
Third Party Confidential Business Information
and [REDACTED] of SB, as existed in *Acorda* and other cases cited by the district
court.⁷ Rather, Biogen is an independent entity that negotiated the exclusive
Third Party Confidential Business Information
rights and [REDACTED] over the U.S. commercialization of SB15 in an arms-length
transaction.

Contrary to this plain language in SB's agreement with Biogen, the
Third Party Confidential Business Information
district court stated that "SB retains significant [REDACTED] over and involvement
in Biogen's U.S. commercialization activities through various contractually-
established mechanisms." Appx6-7. The court did not specify what
"mechanisms" it was referring to and cited no evidence other than the
agreement itself, which explicitly refutes the court's finding by giving
Third Party Confidential Business Information
exclusive [REDACTED] over commercialization to Biogen. The district court clearly
erred to the extent it concluded otherwise.

For these reasons, the "stream-of-commerce" theory would not support
personal jurisdiction here. The standard for such a theory is unsettled, as
"neither this [C]ourt, nor the Supreme Court, has decided whether stream-of-
commerce jurisdiction requires merely placing goods into the stream of

⁷ See *Acorda*, 817 F.3d at 763; see also *Apicore*, 2019 WL 1746079 at
*2 (undisputed that defendant intended its distributor would sell accused
product in forum state); *Helsinn*, 2016 WL 1338601 at *6 (finding personal
jurisdiction where distributor was defendant's wholly owned subsidiary).

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commerce with the expectation that they would be purchased in the forum state, or if ‘something more’ is required, *i.e.*, the purposeful direction of activities toward the forum.” *SK Innovation*, 792 F.3d at 1380; *see Asahi Metal Indus. Co. v. Superior Ct. of Cal.*, 480 U.S. 102 (1987) (competing pluralities regarding the stream-of-commerce theory).

Personal jurisdiction is lacking here under either formulation because Regeneron failed to adduce any evidence showing that SB is even “aware that [its] product [will be] marketed in the forum State.” *Asahi*, 480 U.S. at 117. Thus, Regeneron also necessarily cannot establish that SB is purposefully directing activities toward West Virginia. *See id.* at 112. Indeed, given that Biogen has exclusive ^{Third Party Confidential Business Information} [REDACTED] of the U.S. [REDACTED] and [REDACTED] efforts for SB15 (*see supra*, at pp. 12, 28), SB has no ability to purposefully direct those efforts anywhere, let alone into West Virginia. *See, e.g., Hanson v. Denckla*, 357 U.S. 235, 253 (1958) (“The unilateral activity of those who claim some relationship with a nonresident defendant cannot satisfy the requirement of contact with the forum State”); *Costa v. FCA US LLC*, 542 F. Supp. 3d 83, 95 (D. Mass. 2021) (no personal jurisdiction where defendant-manufacturer “ha[d] no further involvement in the distribution chain once it” sold the accused product to partner, and “purposeful availment cannot be established based on the unilateral actions of others”) (internal citations

omitted); *DNA Genotek Inc. v. Spectrum DNA*, 224 F. Supp. 3d 359, 364-65 (D. Del. 2016) (no personal jurisdiction where defendant only manufactured infringing product, and then “ha[d] no control over what happen[ed] to the accused products once shipped to” its commercialization partner).

Thus, Regeneron failed to establish a substantial probability of personal jurisdiction over SB. This Court may reverse on this basis alone.

II. THE DISTRICT COURT LEGALLY ERRED IN RULING REGENERON IS LIKELY TO SUCCEED ON THE MERITS

The burden is always on the party seeking a preliminary injunction to show that it is likely to succeed on the merits. Thus, “[a] patent holder seeking a preliminary injunction bears the burden of establishing a likelihood of success on the merits with respect to the patent’s validity.” *Entegris, Inc. v. Pall Corp.*, 490 F.3d 1340, 1351 (Fed. Cir. 2007) (internal citation omitted). “If the alleged infringer raises a ‘substantial question’ regarding invalidity, *i.e.*, asserts an invalidity defense that the patentee cannot prove ‘lacks substantial merit,’ the preliminary injunction should not issue.” *Id.* (quoting *Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1364 (Fed. Cir. 1997)).

Regeneron did not show that either SB’s OTDP or written-description invalidity defenses lack substantial merit.

A. The '865 Patent Is Likely Invalid For Obviousness-Type Double Patenting Over The '594 Patent

This Court “review[s] a court’s conclusion on double patenting without deference because double patenting is a matter of what is claimed, and therefore is treated like claim construction upon appellate review.” *Amgen Inc. v. F. Hoffman-LA Roche Ltd*, 580 F.3d 1340, 1352 (Fed. Cir. 2009) (cleaned up); see *In re Basell Poliolefine Italia S.P.A.*, 547 F.3d 1371, 1375 (Fed. Cir. 2008) (“Double patenting is a question of law that we review *de novo*.”).

“[I]t is a bedrock principle of our patent system that when a patent expires, the public is free to use not only the same invention claimed in the expired patent but also obvious or patentably indistinct modifications of that invention.” *Gilead Scis., Inc. v. Natco Pharma Ltd.*, 753 F.3d 1208, 1214 (Fed. Cir. 2014). “And that principle is violated when a patent expires and the public is nevertheless barred from practicing obvious modifications of the invention claimed in that patent because the inventor holds another later-expiring patent with claims for obvious modifications of the invention.” *Id.*

That is the exact situation here. With its patent on the EYLEA formulation having expired in 2021, Regeneron obtained another patent on that same formulation that expires in 2027. By adding claim elements specifying properties of the formulation it had already claimed, Regeneron

improperly recaptured the '594 patent term that it had dedicated to the public through its disclaimer. Appx142-43. The district court erred in ruling that SB's OTDP defense lacks substantial merit.

1. The '594 Patent Qualifies As A Reference Patent

A patent qualifies as an OTDP reference patent if it is commonly owned and expires earlier than the patent at issue. *Gilead*, 753 F.3d at 1216 (expiration dates “guarantee[] a stable benchmark” by which to determine whether OTDP applies); *Abbvie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1374 (Fed. Cir. 2014) (“[T]he doctrine of obviousness-type double patenting [applies] where two patents that claim the same invention have different expiration dates.”) The '594 patent already expired and is commonly owned, so it is a proper reference patent for OTDP purposes.

The district court erroneously ruled that the '594 patent does not qualify as an OTDP reference patent because it and the '865 patent “share the same parent patent and have the same statutory term.” Appx57. That ruling has no basis in this Court's precedent. There is no OTDP exception for patents in the same family (*i.e.*, who share a parent patent).⁸ And OTDP references are

⁸ If the district court were correct, then patents in the same family could not even be *considered* as OTDP references during patent prosecution. That would upend long-standing PTO practice in which such rejections are

determined based on expiration date, not priority date. *Gilead*, 753 F.3d at 1214-1215.

Under this Court’s OTDP precedent, the question is not whether the ’865 patent gives Regeneron more than twenty years of patent life. The question is whether the ’865 patent claims formulations (or obvious variants of formulations) that were claimed in another patent that expires before the ’865 patent. *E.g.*, *Abbvie*, 764 F.3d at 1373 (“It is designed to prevent an inventor from securing a second, later expiring patent for the same invention.”) It is in that circumstance that a patent holder is removing from the public domain formulations over which it has already enjoyed its patent monopoly. *E.g.*, *Gilead*, 753 F.3d at 1215 (“[T]he primary ill avoided by enforcement of the double patenting doctrine is restriction on the public’s freedom to use the invention claimed in a patent and all obvious modifications of it *after that patent expired.*”) (emphasis added).

Regeneron, like all other patent holders, “is not entitled to an extra six years of monopoly solely because it filed a separate application unless the two inventions are patentably distinct.” *Abbvie*, 764 F.3d at 1374. “A crucial purpose of ODP is to prevent an inventor from securing a second, later-

commonly made and overcome by filing terminal disclaimers (as was done in both the ’594 and ’865 prosecutions).

expiring patent for non-distinct claims.” *In re Collect, LLC*, 81 F.4th 1216, 1226 (Fed. Cir. 2023); *see Abbvie*, 764 F.3d at 1372 (“It cannot be, that a patentee can have in use at the same time two valid patents for the same invention; and if he can successively take out at different times new patents for the same invention, he may perpetuate his exclusive right during a century.”) (internal quotation omitted).

The district court also erred in concluding that the ’865 patent does not extend the ’594 patent’s statutory term because the ’594 patent was rendered unenforceable due to a terminal disclaimer. Appx59. To the contrary, “[w]hen a patent issues subject to a terminal disclaimer, the patentee [] has not just agreed to forgo some amount of its enforceable term, but has in fact reduced the term itself by effectively eliminating the disclaimed portion from the original patent.” *In re Yamazaki*, 702 F.3d 1327, 1333 (Fed. Cir. 2012). Thus, “when [a] patent issued with its terminal disclaimer in effect, that disclaimer became part of the original [] patent and served to define its term, regardless of any further term that might have been otherwise available in the absence of the disclaimer.” *Id.* at 1331. The ’865 patent thus indisputably extends the ’594 patent term because it expires six years after the ’594 patent.

The district court relied primarily on *Merck Sharp & Dohme Corp. v. Teva Pharms. USA, Inc.*, 217 F. Supp. 3d 782 (D. Del. 2016), to conclude that

a patent that expires due a terminal disclaimer cannot serve as an OTDP reference for another patent in the same family. But *Merck* is not controlling precedent, and it cannot undo this Court’s binding precedent that a patent qualifies as an OTDP reference based on its expiration date. *Gilead*, 753 F.3d at 1214-15; *Abbvie*, 764 F.3d at 1372-74. Moreover, *Merck* involved the factually distinguishable circumstance of a reference patent that issued *after* the challenged patent. *See* 217 F. Supp. 3d at 787.

The ’594 patent is thus a proper OTDP reference against the ’865 patent claims.

2. The ’865 Claims Are Not Patentably Distinct From ’594 Patent Claim 5

“The obviousness-type double patenting analysis involves two steps: First, the court construes the claim[s] in the earlier patent and the claim[s] in the later patent and determines the differences. Second, the court determines whether those differences render the claims patentably distinct.” *Abbvie*, 764 F.3d at 1374 (cleaned up).

The ’865 patent claims cover the same EYLEA Example 3 and 4 formulation as the ’594 Reference Claim, but also specify that (i) the formulation achieves “at least 98%” stability at two months, (ii) the aflibercept active ingredient is glycosylated, and (iii) the formulation is in a vial. Appx196-97. The district court erred in concluding that the mere

recitation of additional properties of the Example 3 and 4 formulation taught in the '594 patent and claimed in the Reference Claim renders the '865 patent claims patentably distinct. And it likewise erred in concluding that it would not have been obvious to package the claimed formulation in a vial, despite Example 3's teaching that the formulation was prepared and stored in a vial.

(a) A Reference Patent's Specification Is Relevant To The OTDP Analysis

The district court committed a fundamental legal error that pervades its analysis with respect to all three limitations: it failed to consider the '594 patent specification in its OTDP analysis. Although a patent's specification cannot be by itself considered *as prior art* in the OTDP context, that does not mean, as the district court apparently concluded (Appx82; Appx97), that the specification cannot be used at all. *See In re Vogel*, 422 F.2d 438, 441 (C.C.P.A. 1970) (“[T]he patent disclosure may not be used as prior art” but “[t]his does not mean that the disclosure may not be used at all.”) To the contrary, the specification “may also be used to answer the question whether claims merely define an obvious variation of what is earlier disclosed and claimed.” *Basell*, 547 F.3d at 1378.

Specifically, a court can look to the specification's description of the embodiment claimed in the reference patent. As this Court's predecessor explained in *Vogel*, “it is most difficult, if not meaningless, to try to say what

is or is not an obvious variation of a claim” because “[a] claim is a group of words defining only the boundary of the patent monopoly.” 422 F.2d at 442. “The disclosure, however, sets forth at least one tangible embodiment within the claim, and it is less difficult and more meaningful to judge whether that thing has been modified in an obvious manner.” *Id.* Using the specification to interpret the claims in this way does not contravene the “cases forbidding its use as prior art ... since only the disclosure of the invention claimed in the patent may be examined.” *Id.*

This Court’s analysis in *Basell* is also instructive. There, the reference claim required olefins but did not specify any particular olefins, and the challenged claim required the specific olefin ethylene. 547 F.3d at 1377-78. This Court affirmed the PTO’s OTDP determination, noting that the specification of the reference patent “refers to ethylene, propylene, butene, and other olefins which indicates that those olefins were intended to fall within the meaning of the claims.” *Id.* at 1378. And this Court rejected the patent applicant’s argument that the PTO erred in considering the specification, explaining that “a patent’s disclosure may be used to determine whether an application claim is merely an obvious variation of an invention claimed in a patent.” *Id.*

The district court here thus was required to consider the ’594 patent

specification in its OTDP analysis.

(b) The 98% Stability Limitation Is An Obvious Variant of '594 Claim 5

The district court erred in ruling that the 98% stability limitation in the '865 patent is likely sufficient to overcome SB's OTDP challenge. Appx55-56. That limitation is simply an additional property of the composition claimed in the '594 reference patent and thus, as a matter of law, does not render the '865 patent distinct.

The '594 reference claim specifies that the formulation is generically "stable" at four months based on the stability data in Examples 3 and 4 but does not provide a specific stability value. Appx69-70. The '865 claims require that the same formulation is at least 98% stable at two months. Appx196-97. The district court concluded that the generic term "stable" in the reference claim does not require any particular value, and thus includes values above and below 98%. Appx76. Accordingly, under the district court's construction, the '594 reference claim covers, but is not limited to, formulations that are at least 98% stable at two months.

As in *Basell*, one can look to the specification to determine what stabilities are achieved by Examples 3 and 4, which are the embodiments disclosed for the formulation of the '594 Reference Claim. The '594 patent claims the Example 3 and 4 formulation and generically requires stability

through four months. And just as in *Basell*, where the specification made clear that the specific ethylene compound is one of the olefins generically covered by the reference claim, the Common Specification here shows that the specific two-month stability values recited in the '865 patent claims are encompassed by the generic four-month stability requirement in the '594 patent claim.

This Court's precedent requires courts to examine the specification in circumstances where the reference and challenged claim cover the same composition but recite different properties. *Sun Pharm. Indus., Ltd. v. Eli Lilly & Co.*, 611 F.3d 1381, 1385-89 (Fed. Cir. 2010) (summarizing precedent). In one common circumstance, this Court has held courts "*must* consider the specification because the disclosed uses of [a] compound affect the scope of the claim for obviousness-type double patenting purposes." *Id.* at 1387 (emphasis added); *see Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.*, 518 F.3d 1353, 1363 (Fed. Cir. 2008); *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1385-86 (Fed. Cir. 2003). In such cases, this Court has looked to the disclosure of utility in the reference specification and held challenged claims that recited the disclosed utility were invalid for OTDP, even though the reference claims were silent as to utility. *See Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, 689 F.3d 1368, 1379-

80 (Fed. Cir. 2012) (summarizing); *Abbvie Inc.*, 764 F.3d at 1380 (relying on shared disclosure of study results to confirm lack of unexpected properties).

Here, as explained above, the '594 Reference Claim recites the Example 3 and 4 formulation, which achieved 99.2% and 99.1% stability, respectively, at two months. Thus, both examples with a formulation that embodies the Reference Claim have two-month stability values that meet the '865 claims. Plainly, the inventors are claiming the same formulation in the '594 Reference Claim and in the '865 patent, but the '865 patent recites additional features disclosed in the examples for those formulations. Under this Court's precedent, those additional features are not patentably distinct. *See, e.g., Sun Pharm.* 611 F.3d at 1385-89; *Pfizer*, 518 F.3d at 1363, *Geneva*, 349 F.3d at 1385-86.

(c) Glycosylated Aflibercept Is An Obvious Variant Of '594 Claim 5

The district court additionally erred in ruling that the glycosylated aflibercept limitation in the '865 patent is likely sufficient to overcome SB's OTDP challenge. Appx55-56. That too is just an additional property of the composition claimed in the '594 reference patent.

The '594 Reference Claim requires "VEGF Trap SEQ ID 4," which is aflibercept, but does not specify whether the aflibercept is glycosylated. Appx55. The district court ruled that the Reference Claim generically covers

glycosylated and unglycosylated aflibercept (Appx80), as Regeneron admitted (Appx2089 (“the reference claims of the ’594 patent comprise both glycosylated and nonglycosylated versions of the claimed VEGF antagonist”)).

The Common Specification teaches that in a specific embodiment, aflibercept is glycosylated at five specific sites. Appx189.⁹ And although the eight examples in the Common Specification do not teach whether the aflibercept used in the formulation is glycosylated, Regeneron’s expert testified that the skilled person would understand that the aflibercept used in each of those formulations is glycosylated at all five sites. Appx15122-34 (161:14-175:7); *see* Appx11446 (fn. 8). Based on that testimony—which the district court credited to reject SB’s written description defense—a POSA would necessarily understand *based on the Common Specification* that Examples 3 and 4 use aflibercept glycosylated at those five specific sites.¹⁰

Thus, because it is undisputed that the ’594 Reference Claim embodies the Example 3 and 4 formulation, the specification makes clear that the ’594 patent’s claimed formulation encompasses aflibercept glycosylated at the five

⁹ There is no other teaching in the specification regarding glycosylated aflibercept or how to obtain glycosylation at those five sites.

¹⁰ SB does not contend for purposes of this appeal that the reference claim is limited to glycosylated aflibercept.

specific sites based on Regeneron’s expert testimony (which the district court credited). The ’865 patent simply restricts the claimed formulation to those in which aflibercept is glycosylated, *including at the five sites*. The glycosylated aflibercept recited in the ’865 patent claims is thus an obvious variant of the ’594 patent claims. *See, e.g., Basell*, 547 F.3d at 1378.

Nor is the district court correct that “the POSA would not have been motivated to use glycosylated aflibercept for an ophthalmic formulation” because the skilled person would not have expected glycosylated aflibercept to work in ophthalmic formulations. Appx83. This determination cannot be reconciled with the specification. *See supra*, at p. 32. But if the court were correct on this point, then as explained below the ’865 patent claims are invalid for lack of written description support because the POSA would not find in the specification two-month stability values for any formulations identified as using glycosylated aflibercept. *See infra*, Part II.B.1

(d) A Vial Is An Obvious Variant Of ’594 Claim 5

The district court also erred in concluding that changing the container recited in the claim from a PFS to a vial renders the ’865 claims patentably distinct. Appx55-56. The ’594 Reference Claim 5 claims the formulation of Examples 3 and 4 stored in a PFS. Example 3 explicitly teaches that the formulation was prepared and stored in a PFS, while Example 4 teaches

storing the same formulation in a PFS. The Reference Claim thus renders obvious the two specific storage forms taught in Examples 3 and 4. *Basell*, 547 F.3d at 1378-79.

Moreover, an ophthalmic formulation of course must be packaged in some type of container. It is undisputed that vials are one such container and that vials were well known and commonly used. Appx107. The district court concluded that the vial likely would not have been obvious because a PFS is more desirable than a vial. But SB does not have to establish that a vial is the best option; it need only be an obvious option. *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738 (Fed. Cir. 2013).

Under the district court's reasoning, Regeneron is entitled to six more years of patent life on its EYLEA formulation because the claims happen to require a vial and not a PFS. There is nothing inventive about filling a liquid formulation into a vial. Appx11444-45; Appx13028; Appx13058-60; Appx3833-88. And in any event PFS is an improvement over a vial. Appx13028; Appx13058-59; Appx2090-91; Appx1978-79. It is legal error to allow Regeneron to extend its monopoly by specifying an older and less advanced delivery system.

(e) Objective Evidence Does Not Support Nonobviousness

The district court's secondary considerations analysis (Appx108-10)

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also rests on legal error. *First*, the court relied on evidence of industry skepticism, unexpected results and copying related to EYLEA, and found that nexus was established because “the objective evidence is tied to Eylea and Eylea is an embodiment of the asserted claims” of the ’865 patent. Appx109. *But EYLEA is an embodiment of both the ’865 claims and the reference claims.* Thus, the district court relied on properties of the reference claim formulation (EYLEA) to conclude that the challenged claim formulation (also EYLEA) would not have been obvious over the reference claim. This nonsensical ruling is legally erroneous. *See, e.g., In re Huai-Hung Kao*, 639 F.3d 1057, 1074 (Fed. Cir. 2011) (“[S]econdary considerations do not compel a holding of nonobviousness” where patentee “has not provided any evidence of secondary considerations with a nexus to the novel components of [the] claim[s]”).

Second, the district court erroneously concluded that the “at least 98% stability” limitation constitutes evidence of secondary considerations because the POSA would understand that “there’s a relatively lower risk of inflammation” with a formulation achieving that level of stability. Appx109-10. There is no evidence that 98% two-month stability had superior clinical results as compared to, for example, [REDACTED] stability. Indeed, the FDA’s approval of SB15 with stabilities as low as [REDACTED] confirms that there is no

significant difference. Appx2753, Appx2820; Appx2822. In any event, a POSA's expectation that a more stable formulation will result in "relatively less inflammation" does not speak to whether the claimed formulation, with at least 98% stability at two months, would have been obvious over a formulation stable at four months.

The district court thus erred for all these reasons in relying on supposed secondary considerations evidence to conclude that the claimed formulations are patentably distinct.

B. The '865 Patent Is Likely Invalid For Failure To Provide Adequate Written Description Support

The focus of the written description requirement is "whether the specification notifies the public about the boundaries and scope of the claimed invention *and* shows that the inventor possessed all the aspects of the claimed invention." *Nuvo Pharmaceuticals (Ireland) Designated Activity Co. v. Dr. Reddy's Labs., Inc.*, 923 F.3d 1368, 1382 (Fed. Cir. 2019) (internal quotations omitted, emphasis in original). "In the case of a claimed range, a skilled artisan must be able to reasonably discern a disclosure of that range." *Indivior UK Limited v. Dr. Reddy's Labs. S.A.*, 18 F.4th 1323, 1328 (Fed. Cir. 2021).¹¹

¹¹ Written description is a question of fact reviewed for clear error. *Biogen International GMBH v. Mylan Pharmaceuticals Inc.*, 18 F.4th 1333, 1340-41 (Fed. Cir. 2021).

Here, it is undisputed that the specification for the '865 patent does not contain any generic disclosure of “at least 98%” two-month stability or a range of 98-100% for formulations with glycosylated aflibercept. The only potential source of written description support for the claimed range is the examples, which the district court relied on to conclude SB had not raised a substantial question of invalidity. Appx111. But the examples disclose “VEGF Trap SEQ ID No. 4,” which the district found encompasses “at least thirty possible glycosylated forms of aflibercept” “in addition to the non-glycosylated form.” Appx82. As a result, the POSA reviewing the Common Specification would not find any two-month stability values for formulations identified as using glycosylated aflibercept. The district court further erred in finding that the two relevant two-month stability values in the examples (99.1% and 99.2%) allow the skilled person to discern a range that extends from 98% to 100%.

1. Under The District Court’s OTDP Findings, There Is No Written Description Support For Glycosylated Aflibercept Formulations With The Claimed Stability

A substantial question exists as to SB’s written-description challenge in light of the district court’s own OTDP findings.

The examples teach formulations of “VEGF Trap (SEQ ID NO:4)” (aflibercept) but say nothing about whether the aflibercept is glycosylated. In fact, there is only a single disclosure of the word “glycosylated” in the entire

specification. In the section entitled “VEGF Antagonists,” the specification states: “In a specific embodiment, the fusion protein comprises amino acids 27-457 of SEQ ID NO:4 and is glycosylated at Asn residues 62, 94, 149, 222 and 308.” Appx189. This generic disclosure precedes the examples and is not connected in any way to them.

In its OTDP analysis, the district court found that, as of the priority date, the skilled person would understand that “VEGF Trap SEQ ID NO: 4” as used in the ’594 patent claims “is not necessarily glycosylated” and covers at least thirty different glycosylated forms of aflibercept and non-glycosylated aflibercept. Appx80; Appx82. The district court further found that, of those options, the POSA would have been motivated to use *non-glycosylated* aflibercept in connection with the Reference Claim. Specifically, in assessing OTDP in view of the ’594 Reference Claim, the district court found “the prior art’s teachings would have motivated the POSA against using glycosylated aflibercept.” Appx84; *see* Appx87 (“[T]he Court finds that the prior art would motivate a POSA against using glycosylated aflibercept in formulations for ophthalmic use.”); Appx90 (“These immunological concerns would further motivate the POSA against using glycosylated aflibercept.”).

That means the skilled person would not have known whether any of the examples referring to “VEGF Trap SEQ ID NO: 4” (aflibercept) used non-

glycosylated or glycosylated aflibercept. As a result, under the district court's own OTDP findings, a POSA reading the specification would find *no* disclosure of any two-month stability values for the claimed glycosylated aflibercept formulations. The Common Specification thus would provide no written description support for the '865 patent claims, which recite glycosylated aflibercept formulations achieving at least 98% stability. This alone is a sufficient basis to set aside the district court's likelihood-of-success determination.

2. There Is No Written Description Support For The Claimed Range's Upper End Of 99.4-100% Stability

Even if the district court's OTDP findings do not establish error as to written description, the district court clearly erred in finding written-description support for the 99.4-100% portion of the claimed range, which constitutes about 35% of the claimed range. It is undisputed that the two-month stability data in the Common Specification went only as high as 99.3% (Appx190-192), and, with respect to the claimed formulation, Regeneron achieved at best 99.2% (Appx114). Nothing in the Common Specification suggests that Regeneron possessed an invention using the formulation of Examples 3 and 4 that could achieve two-month stabilities in the range of 99.4-100%. A POSA thus would recognize that the inventors attempted to

achieve high stability but could *not* achieve two-month stability greater than 99.3%.

The written description requirement is meant to prevent patentees from claiming inventions that they did not invent. *See, e.g., Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (“[T]he specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed.”) But under the district court’s ruling, formulators who develop embodiments with two-month stability in the range of 99.4-100% would be blocked by a patent that could not achieve that high stability.

The district court concluded that Regeneron need not establish written description support for the 100% upper bound based on Dr. Tessier’s testimony that “practically, ‘*most proteins* are not purified to [100%].” Appx112. The district court then found that Regeneron only need establish written description support for a “maximum percent native conformation” that is “somewhat less than 100%” and is “limited by what a person skilled in the art would understand to be workable.” Appx112-13. That analysis is flawed in two respects.

First, Dr. Tessier did not testify that *afibercept* cannot achieve values of 100%, nor did he testify that 99.3% is the maximum achievable value for

aflibercept. The cited testimony was that “*most proteins* are not purified to [100%],” Appx112, which does not support the district court’s conclusion that it was impossible to achieve 100% or other values in the range of 99.4-100% for aflibercept. To the contrary, Dr. Tessier’s use of the word “most” instead of “all” suggests that it is possible. In fact, Dr. Tessier testified that “there are examples where you see very high purity” and “[s]ometimes people write it as a hundred percent.” Appx20252.

Second, even assuming it is not possible to achieve 100% stability at two months such that Regeneron need not show written description support up to 100%, Regeneron still has not shown any of its formulations achieving stability values greater than 99.3%. The district court stated that Regeneron only need show support for “somewhat less than 100%,” and specifically up to “whatever the [POSA] would understand to be workable,” but the district court never explained what value that is. Appx112-13. The examples disclose at most 99.3% native conformation aflibercept at two months, and there is no evidence that 99.3% native conformation is the maximum that one could achieve in practice. There is no disclosure in the specification indicating that the inventors possessed any embodiments that achieve 99.4% or more stability. The claims thus lack written description support for the portion of the range above 99.3%, even if it does not extend up to 100%.

The district court also legally erred in concluding that the claims “need not by supported by an embodiment at that upper limit; the patent need only ‘enable[] [the POSA] to approach that limit.’” Appx113. That conflates written description and enablement.¹² “Teaching how to make and use an invention does not necessarily satisfy the written description requirement”; “the fact that an invention may be enabled does not mean it is adequately described, and vice versa.” *Nuvo*, 923 F.3d at 1382.

In any event, there is no evidence that disclosure of 99.3% native conformation enables the skilled person to obtain higher values of native conformation aflibercept. To the contrary, Dr. Tessier testified that “higher purity levels are much more difficult to achieve than the lower purity levels” because “each additional 0.1 percentage point represents a huge decrease in the level of degradation products.” Appx13097. The district court erred by ignoring that evidence.

¹² The district court cited *Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361 (Fed. Cir. 2007), as alleged support for its conclusion. But the quoted portion of *Andersen* explicitly related to enablement, not written description. 474 F.3d at 1375-76. Even to the extent *Andersen* conflated the written description and enablement requirements, this Court later confirmed their separateness. *Ariad*, 598 F.3d at 1351.

3. There Is No Written Description Support For A Lower Bound Of 98% Stability

The district court also clearly erred in concluding that there is written description support for the 98% lower bound of the range. The 98% lower bound is critical in this case because it is the claim element on which Regeneron relied to distinguish the '594 patent during prosecution and obtain an additional six years of patent life on its EYLEA formulation. But there is no way to discern the lower bound of 98% stability from the Common Specification. The claims are invalid for lack of written description support on this basis as well.

The question here is not whether Regeneron could achieve stability values of 98%. The question is whether, based on the disclosure in the examples of stability values around 99%, the POSA could “reasonably discern” the 98% lower boundary of the claim range. *Indivior*, 18 F.4th at 1328. Here, there is no basis whatsoever for the 98% lower bound in the specification, so the POSA could not reasonably discern the claimed range.

No part of the specification teaches a lower bound of 98%. All of the examples achieved 99% stability (stated as a whole number as recited in the claim) at two months. Appx190-192. Regeneron plucked the 98% number out of thin air.

The district court found support for 98% because “98% is simply the highest whole number achieved in each example (all of which met the claim limitation).” Appx116. But that is indisputably erroneous. *All* of the cited examples achieved 99% stability stated as a whole number. Appx190-92.

Furthermore, only two of the examples have the claimed aflibercept concentration and excipients. The two-month stability data for those examples are 99.1% and 99.2%. Appx191. Those two values are the only potential written description support for the stability values achieved by the claimed formulation. There is no way the skilled person could reasonably discern a lower bound of 98% stability from disclosure of 99.1% and 99.2% stability values.

The district court also found that the patent “contained multiple disclosures of native conformations throughout the range of 98% to 100%.” Appx116. It is true that over the twenty-four months of stability testing described for some of the examples, the formulations exhibit stability values ranging from 99.5% at *time zero* to 97.6% at twenty-four months. Appx191. But the claims require 98-100% stability *at two months*. The inventors’ possession of formulations with 98% stability after twelve months or twenty-four months does not allow a POSA to discern a lower boundary of 98% for two-month stability. Indeed, Example 2, the formulation that achieved 97.6%

stability after twenty-four months, achieved 98.5% stability after three months, which again rounds to 99% as a whole number. Appx190-91. Accordingly, none of the examples would allow a POSA to discern a lower boundary of 98% for two-month stability. The claims are thus likely invalid.

III. THE DISTRICT COURT LEGALLY ERRED IN RULING REGENERON SATISFIED THE CAUSAL NEXUS REQUIREMENT FOR IRREPARABLE HARM

“[T]o satisfy the irreparable harm factor in a patent infringement suit, a patentee must establish both of the following requirements: 1) that absent an injunction, it will suffer irreparable harm, and 2) that a sufficiently strong causal nexus relates the alleged harm to the alleged infringement.” *Apple Inc. v. Samsung Elecs. Co., Ltd.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012) (“*Apple II*”). Here, the district court found both requirements were satisfied, concluding that Regeneron had established likely irreparable harm and a casual nexus between that asserted harm and infringement of the ’865 patent. Appx118; Appx162-63. Although both rulings are erroneous, SB challenges only the casual nexus ruling on appeal. That error provides an independent basis to reverse the preliminary injunction. *See, e.g., Apple Inc. v. Samsung Elecs. Co.*, 678 F.3d 1314, 1324 (Fed. Cir. 2012) (“*Apple I*”) (“We hold that the district court was correct to require a showing of some causal nexus

between [the defendant]’s infringement and the alleged harm to [the plaintiff] as part of the showing of irreparable harm.”)

A. There Is No Casual Nexus Because Regeneron Would Suffer The Alleged Harm Regardless Of Any Infringement

To satisfy the causal nexus requirement, the patentee cannot simply “establish some insubstantial connection between the alleged harm and the infringement and check the causal nexus requirement off the list.” *Apple II*, 695 F.3d at 1375. “The patentee must rather show that the infringing feature”—here, the 98% stability limitation—“drives consumer demand for the accused product.” *Id.*

Such a causal nexus is critical to the irreparable harm inquiry because it “informs whether the patentee’s allegations of irreparable harm are pertinent to the injunctive relief analysis, or whether the patentee seeks to leverage its patent for competitive gain beyond that which the inventive contribution and value of the patent warrant.” *Apple II*, 695 F.3d at 1375. “Sales lost to an infringing product cannot irreparably harm a patentee if consumers buy that product for reasons other than the patented feature.” *Apple I*, 678 F.3d at 1324. In other words, “a likelihood of irreparable harm cannot be shown if sales would be lost *regardless of the infringing conduct.*” *Id.* (emphasis added).

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Here, a causal nexus is lacking because, if SB is allowed to launch SB15, Regeneron's EYLEA sales would be lost to SB15 *regardless* of whether SB15 meets the limitation of all asserted claims requiring a stability of 98% over two months. SB's approved BLA *does not* require SB15 to achieve more than 98% stability at two months; SB15 need only achieve [REDACTED] stability at two months. Appx2753, Appx2820; Appx2822. Thus, SB can manufacture—and Biogen can sell—lots of SB15 that are only [REDACTED] stable at two months and that therefore do not infringe the '865 patent.

Regeneron presented no evidence that it would lose sales only to SB15 lots that achieve 98% stability (allegedly infringing) yet would not lose sales to SB15 lots that achieve only [REDACTED] stability (not infringing). Those latter lots would not infringe the '865 patent, but consumers—who do not even know the two-month stability of a given lot (Appx11704-705 (¶83); Appx15555)—would purchase such non-infringing lots just like they would purchase the allegedly infringing 98% stable SB15 lots. Indeed, Regeneron presented no evidence that doctors would care one whit about whether SB15 exceeded 98% stability after two months in deciding to procure SB15. Thus, "*sales would be lost regardless of the infringing conduct*," and Regeneron failed to show the requisite nexus. *Apple I*, 678 F.3d at 1324.

B. The District Court’s Irreparable Harm Ruling Rests On A Series Of Legal Errors

In nevertheless concluding that Regeneron satisfied the irreparable harm factor, the district court made a series of rulings that directly contravene this Court’s casual-nexus precedents. None of those rulings provide any basis for affirmance.

1. The Casual Nexus Requirement Applies To All Preliminary Injunctions

The district court legally erred in concluding that “Regeneron need not show the specific connection between the patented feature and demand” because the casual nexus requirement applies only in the context of “multi-featured products” like “smartphones and tablets.” Appx163. As this Court explained in *Apple Inc. v. Samsung Elecs. Co.*, 735 F.3d 1352 (Fed. Cir. 2013) (“*Apple III*”), “the causal nexus requirement is part of the irreparable harm factor,” and it “applies regardless of the complexity of the products.” *Id.* at 1362-63. Causal nexus “may be more easily satisfied (indeed, perhaps even conceded) for relatively ‘simple’ products” like “windshield wiper blades” or “orthopedic nails.” *Id.* at 1362. But it still must be established.

The district court thus erred in ruling that Regeneron had satisfied its burden by showing that its harms result from launch of an ophthalmic formulation with aflibercept as the active ingredient regardless of whether it

achieves the claimed 98% stability. Appx165-67. The court had concluded that “the nexus inquiry has ‘little work to do’ because SB15 ‘contains no feature relevant to consumers’ purchasing decisions other than what the patent claims,’ which is the drug product.” Appx163. The court thus found causal nexus because the ’865 patent covers the aflibercept drug product, and that is what drives demand. But that is error because the ’865 patent does not generically claim the drug product. Regeneron’s ’959 patent, which covered aflibercept, expired, as did its ’594 patent on the EYLEA formulation. Appx57; Appx13509. The ’865 patent requires 98% stability at two months, so that is the feature for which Regeneron must establish causal nexus. *See supra*, Part III.A.

The district court’s statement that the ’865 patent claims “cover SB15 itself — a 40 mg/mL ophthalmic formulation containing aflibercept that has recited purity recited in the claims—not a ‘feature’ or ‘attribute[] of the finished consumer good’” in fact illustrates the error. Appx163-64. The purity recited in the claims of course *is a feature or attribute* of the finished SB15 consumer good. This 98% stability feature is what must drive demand for SB15 to meet the causal nexus requirement. *See supra*, Part III.A.

But the district court did not look to whether the 98% stability feature drove demand. Instead, it found that EYLEA’s and SB15’s safety, “efficacy,”

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and the frequency of dosing drove demand. Appx166-67. This too was legal error. Regeneron cannot establish causal nexus by pointing to multiple features of EYLEA *unrelated* to the '865 stability requirement that Regeneron contends drive demand for EYLEA and then showing that SB15, as a biosimilar, shares those features. Regeneron must establish that the actual features *claimed in the '865 patent* drive demand for SB15. *See, e.g., Apple II*, 695 F.3d at 1374; *Apple I*, 678 F.3d at 1324.

None of EYLEA's features that the court identified as driving demand—safety, efficacy, and dosing schedule—is claimed in the '865 patent or has anything to do with the 98% stability required by that patent. Any alleged harm Regeneron will suffer due to unclaimed aspects of SB15 is irrelevant to irreparable harm. In fact, based the BLA approval, the FDA has ^{Confidential Product Information} determined that the SB15 batches having two-month stability as low as [REDACTED] are safe, efficacious, and achieve the specified dosing schedule. And doctors and patients are unaware of any alleged differences in two-month stability when making purchasing decisions.

The district court attempted to tie the stability limitation to safety, citing its prior decision in *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 2024 WL 382495, (N.D.W. Va. Jan. 31, 2024) for the proposition that that “the stability of the claimed compositions, including the required 98% native

conformation, indicated to the POSA that there's a relatively lower risk of inflammation." Appx110. Even if a *skilled person* would expect two-month stability data to have some bearing on inflammation, that would not establish causal nexus. Regeneron needed to show that *customers* will purchase SB15 because of its 98% stability data. *See, e.g., Apple I*, 678 F.3d at 1324. There is absolutely no evidence in the record to that effect. To the contrary, as discussed, the evidence shows that doctors and patients are not even aware of the specific stability criteria of EYLEA or SB15. Appx15554-55. Thus, Regeneron cannot show that the 98% stability feature drives demand for EYLEA.

2. *Aurobindo* Does Not Provide A Pharma-Specific Nexus Test

The district court also erroneously viewed *Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858 (Fed. Cir. 2017) as providing a pharma-specific causal nexus test. Appx162. *Aurobindo* does no such thing. Rather, there this Court concluded that "the district court's determinations were not clearly erroneous" because "there was a causal nexus between [the defendant's] infringement and [the patentee's] harm." *Aurobindo*, 857 F.3d at 872. In doing so, this Court explained that the defendant's product "would not be on the market" without infringing the asserted patents, *id.*; that the defendant needed to infringe the asserted "process and purity" patents to

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“make the [] product described in its ANDA,” *id.*; and that the defendant had admitted copying the process patent, *id.* at 873.

Aurobindo applies—and is entirely consistent with—the causal nexus standard discussed above. Just as in the *Apple v. Samsung* cases, the patentee was required to show that the injury it alleges would result from infringement of the asserted patent. *See Aurobindo*, 857 F.3d at 872-73. Because the defendant could not make and sell its product without infringing, any harm the patentee suffered necessarily resulted from infringement.

The district court analogized this case to *Aurobindo* by stating that “without infringing the ... patents” SB “would not be able to make the ... product described in” its BLA. Appx162. That is clear error. As discussed above, SB can make that product without infringing the ’865 patent by Confidential Product Information achieving [REDACTED] stability (but less than 98% stability) at two months. *See supra*, at p. 12.¹³ Furthermore, it is undisputed that 98% two-month stability

¹³ The district court also erroneously relied on Regeneron’s expert testimony that SB “could not ‘simply alter the SB15 formulation to attempt to avoid infringement’” because any change to the formulation would require “additional testing and other product changes, with no guarantee that a non-infringing product would work as intended.” Appx165. SB does not need to change the *formulation* of SB15 to avoid infringement. Confidential Product Information SB already has FDA approval to make SB15 with two-month stability values between [REDACTED] and 98% instead of 98% or greater.

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is not required for FDA approval. Appx2087-88 (Regeneron's expert admitting only 95% stability at two months is required for FDA approval). And not even Regeneron promised to achieve 98% stability at two months; its Confidential Product Information EYLEA specification permits [REDACTED] stability. Appx2087-2088 (¶387); *see, e.g.*, Appx6674; Appx6677; Appx6680; Appx6681.

3. Regeneron's Loss Of Its Monopoly Has No Casual Nexus To Any Alleged Infringement

Finally, Regeneron contends, and the district court agreed, that it will be irreparably harmed when it loses its EYLEA monopoly after biosimilars are permitted to launch. Appx118. But that generic harm from any biosimilar launch is not sufficient for Regeneron to enjoin SB15 when there is no evidence that Regeneron will suffer any harm resulting *from infringement* of the '865 patent at issue here. *See, e.g., Apple II*, 695 F.3d at 1374-75 (“[E]ven if the competitive injury that results from selling [SB15] is substantial, *the harm that flows from the alleged infringement (the only harm that should count) is not.*”) (emphasis added). This Court's precedent requires Regeneron to establish that *launch of SB15 specifically*—not biosimilars in general—is likely to cause irreparable harm *because SB15 allegedly meets the 98% stability limitation*. *See, e.g., Apple II*, 695 F.3d at 1374; *Apple I*, 678 F.3d at 1324. Regeneron presented no evidence that its generalized alleged harms have anything to do with whether SB15 achieves 98% stability. Regeneron's

generic alleged harms result from launch of a biosimilar, not from any infringing feature in that biosimilar.¹⁴

CONCLUSION

The preliminary injunction orders should be reversed.

Respectfully submitted,

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¹⁴ The district court's analyses of the balance-of-equities and public-interest factors depended on its erroneous likelihood-of-success and irreparable harm rulings (*see* Appx167-77), and thus provide no support for the preliminary injunction.