UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO., LTD.,
Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

Case No. IPR2025-00176

U.S. Patent No. 11,084,865

PETITIONER'S REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE

TABLE OF EXHIBITS

Exhibit	Description
1001-1114	*Previously Presented*
1115	PTAB Decision Granting Adverse Judgment After Institution of Trial in *Celltrion, Inc. et al. v. Regeneron Pharms., Inc.*, IPR2023-00462, U.S. Patent No. 10,464,992 (P.T.A.B. Feb. 21, 2024)
1116	PTAB Decision Granting Adverse Judgment After Institution of Trial in *Samsung Bioepis Co., Ltd. et al. v. Regeneron Pharms., Inc.*, IPR2023-00739, U.S. Patent No. 10,888,601 (P.T.A.B. July 30, 2024)
1117	PTAB Decision Granting Adverse Judgment After Institution of Trial in *Samsung Bioepis Co., Ltd. et al. v. Regeneron Pharms., Inc.*, IPR2023-00884, U.S. Patent No. 11,253,572 (P.T.A.B. July 23, 2024)
1118	PTAB Final Written Decision Determining Challenged Claims 1, 3-11, 13-14, 16-24, and 26 Unpatentable in *Samsung Bioepis Co., Ltd. et al. v . Regeneron Pharms., Inc.*, IPR2023-00442, U.S. Patent No. 10,130,681 (P.T.A.B. June 14, 2024)
1119	PTAB Final Written Decision Determining All Challenged Claims Unpatentable in *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2022-01226, U.S. Patent No. 10,888,601 (P.T.A.B. Jan. 9, 2024)
1120	37 C.F.R. 1.321(a) Disclaimer of U.S. Patent No. 10,888,601, Claims 15-16, 20, 23-24, 31-32, and 46-47
1121	37 C.F.R. 1.321(a) Disclaimer of U.S. Patent No. 10,888,601, Claims 10-12, 17-19, 21, 25-28, and 33
1122	37 C.F.R. 1.321(a) Disclaimer of U.S. Patent No. 10,888,601, Claims 3, 4, 13, 14, 22, 29, and 30
1123	37 C.F.R. 1.321(a) Disclaimer of U.S. Patent No. 11,253,572, Claims 1-30
1124	37 C.F.R. 1.321(a) Disclaimer of U.S. Patent No. 10,464,992, Claims 1-18
1125	Complaint filed in *Regeneron Pharms., Inc. v. Samsung Bioepis, Co., Ltd.*, Case No. 1:23-cv-94, Dkt. 1 (N.D.W. Va. Nov. 22, 2023)

Exhibit	Description
1126	Complaint filed in *Regeneron Pharms., Inc. v. Samsung Bioepis, Co., Ltd.*, Case No. 1:23-cv-106, Dkt. 1 (N.D.W. Va. Dec. 27, 2023)
1127	*Reserved*
1128	Regeneron August 9, 2024 Email Regarding Proposed Scheduling Order and Attachment submitted in *In Re: Aflibercept Patent Litigation*, MDL No. 1:24-md-3103-TSK (N.D.W. Va.)
1129	*Reserved*
1130	PTAB Decision Granting Institution in *Celltrion, Inc. v. Regeneron Pharms., Inc.*, IPR2023-00462, U.S. Patent No. 10,464,992 (P.T.A.B. July 20, 2023)
1131	*Reserved*
1132	*Reserved*
1133	Regeneron's May 10, 2024 Submission in *In Re: Aflibercept Patent Litigation*, MDL No. 1:24-md-3103-TSK (N.D.W. Va.)
1134	Executed Summons filed in *Regeneron Pharms., Inc. v. Samsung Bioepis, Co., Ltd.*, Case No. 1:23-cv-94, Dkt. 285 (N.D.W. Va. Oct. 17, 2024)
1135	Samsung Bioepis's February 3, 2025 Motion for Entry of Scheduling Order Pursuant to Rule 16 or, in the alternative, a Status Conference and Proposed Schedule Attached as Exhibit A filed in *Regeneron Pharms., Inc. v. Samsung Bioepis, Co., Ltd.*, Case No. 1:23-cv-94, Dkt. 318 (N.D.W. Va.)
1136	Celltrion, Formycon, and Samsung Bioepis's August 9, 2024 Email Regarding Updated Proposed Case Management Order and Attachment submitted in *In Re: Aflibercept Patent Litigation*, MDL No. 1:24-md-3103-TSK (N.D.W. Va.)
1137	*Reserved*
1138	April 22, 2025 Stipulation and Order Vacating Permanent Injunction Previously Issued by the Court Against Biocon Biologics Inc. and Mylan Pharmaceuticals Inc. and Dismissing All Claims and Counterclaims With Prejudice in *Regeneron Pharms., Inc. v. Mylan Pharms Inc. et al.*, Case No. 1:22-cv-61, Dkt. 874 (N.D.W. Va.)

Exhibit	Description
1139	Celltrion, Formycon, and Samsung Bioepis's May 10, 2024 Proposed Case Management Order submitted in *In Re: Aflibercept Patent Litigation*, MDL No. 1:24-md-3103-TSK (N.D.W. Va.)

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Starting in January 2023, Petitioner filed or joined five prior IPR petitions against Patent Owner's ("PO") patents, including U.S. Patent No. 10,464,992 (the "'992 patent"), which is in the same family as the challenged '865 patent. Exs.1115-1119. PO alleged these patents cover its EYLEA® (aflibercept) product. The Board instituted all five IPRs. *Id.* And in each case, including the '992 IPR, the Board found the challenged claims unpatentable in a FWD, or PO disclaimed every challenged claim before a FWD was even reached. *Id*.; *see also*, Exs.1120-1124.

In November and December 2023, during the pendency of these IPRs, PO filed two related district court cases against Petitioner, asserting 40+ patents. Exs.1125-1126. PO was then granted a preliminary injunction ("PI") in June 2024 on a single patent—the '865 patent. Ex.2002. In opposition to the PI, Petitioner was allowed to submit only a single 25-page brief addressing all PI factors and multiple PO patents. *Id*. Petitioner was thus forced to limit its defenses, and accordingly did not raise any obviousness combinations as to the '865 patent during the PI proceedings. *Id*. Instead, Petitioner presented only two invalidity defenses based on obviousness-type double patenting and lack of written description. *Id.* In granting the PI, the district court did not conduct a hearing and relied heavily on its findings from a previous trial against Mylan. *Id.*, 11-166.

In its POPR, however, PO contends that in the PI decision against Petitioner, as well as the *Mylan* decision, the district court analyzed "virtually all of SB's cited

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prior art and arguments" (POPR, 2) and found three limitations to be nonobvious: glycosylation of aflibercept, a 40 mg/mL concentration, and the 98% stability limitation.[1] Thus, PO contends institution of this IPR is unnecessary as a matter of discretion and would contradict the decisions in the district court cases substantively.

PO's contention is false. Petitioner's grounds include multiple material prior art references that no court has considered and which disclose the three allegedly missing elements. Petitioner did not present any obviousness combinations at all during PI proceedings, and in the only trial on the merits relating to the '865 patent—the *Mylan* case—the court did not address two of Petitioner's three primary references. Ex.2001, 154-202. Specifically, the district court did not address any combination with *Wulff*, which teaches that aflibercept is glycosylated. *Id.* And Mylan also did not assert a second primary reference (the *2006 Presentations*) which teaches the 40 mg/mL concentration limitation. *Id.* And in the '992 IPR, the Board found that the 98% stability limitation was disclosed by Ground II, a highly similar obviousness combination to the one Petitioner asserts here. Ex.1130, 24-41.

Accordingly, the prior findings against Petitioner and Mylan regarding the three allegedly missing limitations in the art are not just inapplicable to Petitioner's

[1] The Federal Circuit heard oral argument on *Mylan*'s appeal, but PO settled with *Mylan* before an opinion could issue. Ex.1138.

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carefully constructed grounds here, but are directly controverted by disclosures in the new references and the ’992 ID, as addressed in detail below. The Board should disregard PO’s invitation to rely on the irrelevant PI and *Mylan* decisions.

In its POPR, PO also misrepresents the state of the related district court cases, which have been pending but stagnant for over 20 months. The district court has not opened discovery, set a case schedule or a trial date, or even held a status conference since May 2024, prior to entering the PI. In fact, the district court has ignored Petitioner’s repeated requests for the case to proceed, while PO has advocated for delay. Exs.1110, 1135, 1128. It has thus become apparent that whatever schedules the parties may have previously proposed—all of which are now stale—the district court will not reach a decision on the 40+ asserted patents—including the ’865 patent—until well after a FWD here. Accordingly, if the Board institutes an IPR, Petitioner will not seek a trial date on the ’865 patent until after any FWD is due.

The ’865 patent is the only patent preventing Petitioner from launching its biosimilar product in the United States. Petitioner respectfully requests institution.

I. Institution Is Warranted Because Petitioner Presents New Prior Art References That Disclose Material Aspects of the Invention

In its POPR, PO primarily argues that Petitioner “raises obviousness challenges to the ’865 patent that multiple courts repeatedly have considered and rejected” including in (1) a trial between Mylan and PO and (2) PI proceedings between PO and Petitioner and two other parties. POPR, 1. Based on this premise,

PO argues that the Board should deny institution both as a discretionary matter and on substantive grounds.

Petitioner's obviousness challenges, however, rely on a combination of three primary references—*Fraser*, *Wulff*, and the *2006 Presentations*—that has never been previously asserted and was not the subject of any prior decision, despite PO's extraordinary claim that institution would require "reversal of at least seven judicial decisions" (POPR, 1). In the *Mylan* proceeding on which PO heavily relies, the district court's decision did not address any combination that included *Wulff* or the *2006 Presentations*. Ex.2001, 154-202. And in the PI proceedings, Petitioner did not even ***assert*** an obviousness combination, given the restrictions on the proceedings and need to address the full set of PI factors. Ex.2002.

PO, however, contends that the same three limitations that the district court found were not disclosed by the art in the *Mylan* and the PI decisions—glycosylation, a 40 mg/mL concentration, and the 98% stability limitation—doom Petitioner's grounds here. POPR, 26-63. But PO's contention ignores the substantial differences between Petitioner's obviousness combinations compared to those addressed in the district court's prior decisions. As set out below, Petitioner's grounds present new art that discloses or renders obvious the allegedly missing limitations.

First, PO contends that the district court and Federal Circuit found that a POSA would not be motivated to glycosylate aflibercept because a POSA allegedly

"understood that glycosylation of aflibercept—required by each challenged claim—was disfavored for an ophthalmic formulation." POPR, 2. PO argues the Board should find the same here. But Petitioner need not show motivation to glycosylate aflibercept because Petitioner relies on prior art that the POSA would understand discloses glycosylated aflibercept. Specifically, the *Wulff* reference teaches "[t]he VEGF trap was expressed in CHO cells," which by the priority date, were known and expected to glycosylate aflibercept at the five asparagine residues (Asn 62, 94, 149, 222, and 308). Pet., 38-40. Thus, a POSA would have understood the aflibercept disclosed in the primary reference (*Wulff*) ***was*** glycosylated—no motivation is needed to do more. *See General Electric Company v. Raytheon Technologies Corporation*, 983 F.3d 1334, 1351-52 (Fed. Cir. 2020). PO's argument (at 34-36) that aflibercept ***could*** be made without CHO cells is irrelevant; Petitioner's art makes clear that the aflibercept ***was*** produced in common CHO cells, and does not "criticize, discredit, or otherwise discourage" using such cells or glycosylated aflibercept. *See Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738-39 (Fed. Cir. 2013); *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1199 (Fed. Cir. 2014).

Second, PO argues (at 2-3) that courts have previously found that "the POSA understood the prior art to teach away from using the 40 mg/mL aflibercept concentration upon which SB's obviousness challenge is premised." PO further claims (at 27), incorrectly, that Petitioner "points to no prior art teaching or

suggesting a 40 mg/mL ophthalmic formulation of aflibercept." But the *2006 Presentations* disclose that a 4 mg intravitreal dose of aflibercept was known to be safe, effective, and well-tolerated—a teaching not found in any previous obviousness combination considered by the district court. Exs.1011-1013; Pet., 29-31, 49-51. As Petitioner establishes in its grounds, moreover, 0.1 mL was widely accepted as the safe maximum intravitreal injection volume at the time. Pet., 29-31, 49-51; Ex.1048, 932; Ex.1049, 106. A POSA would have thus understood that given these established values—a 4 mg dose in a maximum 0.1 mL injection volume—the *2006 Presentations* describe administration of an intravitreal injection with a 40 mg/mL concentration (i.e. 4 mg / 0.1 mL), consistent with the concentration of known intravitreal agents at the time. Pet., 29-31, 49-51. This significant disclosure was not considered in any previous proceeding.

Third, PO argues (at 47–60) that the stability limitation is not inherent, again drawing from the district court's findings regarding different prior art, in different proceedings. But those proceedings did not evaluate the stability of the Modified Fraser/Wulff formulation. Ex.2001-2004. Here, by contrast, Petitioner shows that the claimed stability is an inherent property of the obvious Modified Fraser/Wulff formulation because that formulation falls within the ranges tested by PO (with supporting data confirming the claimed stability) and is also obvious. Pet., 40-48.

Considerably more relevant than the decisions on which PO relies is the

Board's ID addressing the claims of the '992 patent, which recited the identical 98% stability limitation. Petitioner's theory is highly similar to Ground II of the '992 IPR, which the Board found raised a substantial question of patentability. Ex.1130, 24-41. There, the Board found that the stability limitation was inherent in *Fraser*'s formulation, relying on *Dix* as the supporting reference—just as Petitioner does here. *Id.* The Board additionally found "that a [POSA] would have been able to achieve the claimed stability limitations by making the VEGF TrapR1R2 formulation" described in Petitioner's art, and that a POSA also "would have been able to optimize" the formulation "in order to achieve the claimed stability." *Id.*, 40. PO subsequently disclaimed the '992 patent—rather than letting the Board reach a FWD—because those rulings were correct. Exs.1115, 1124.

Moreover, unlike the district court, "the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977).[2] PO asserts a previously confidential declaration from one of its inventors—whom Petitioner has

[2] PO argues (at 55-56) *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1375 (Fed. Cir. 2016) held that *In re Best* did not apply to IPRs, but the Federal Circuit did not address *In re Best* in *Magnum Oil*, and the Board did not agree with PO on this point in the '992 ID. Ex.1130, 39-40.

not deposed—allegedly proves the Modified Fraser/Wulff formulation lacks the claimed inherency under *In re Best*. But PO makes no showing that the formulation it relies on matches the Modified Fraser/Wulff formulation, rendering the testing data irrelevant to the inherency inquiry. *See In re Best*, 562 F.2d at 1255-56. Moreover, the inventor's testing conditions—25ºC, 37ºC, 45ºC, freeze/thaw, and vortex—differ from the claimed 5ºC storage conditions and were not maintained for the claimed two-month period. Ex.2024, 5-6. In contrast, the '865 patent and *Dix* report ≥98% native conformation for formulations encompassing the Modified Fraser/Wulff formulation under the claimed conditions. Pet., 40-48. Thus, while Petitioner's evidence addresses both the relevant formulation and storage conditions, PO's does not. Moreover, PO did not raise this evidence in the PI proceedings until after Petitioner's opposition, denying Petitioner the opportunity to respond. The Board should decline PO's request to accept untested factual assertions without trial.

II. The *Fintiv* Factors Favor Institution

In its POPR, PO contends that the related district court cases are in an advanced state and will reach resolution before a FWD. This is false.

First, no trial date has been set, and "without a trial date... [there is] no need to engage in a full analysis of the *Fintiv* factors, as there is no basis for Patent Owner's argument for discretionary denial." *Beckman Coulter, Inc. v. Sirigen II Limited*, IPR2022-01203, Paper 12 at 18.

More specifically, following the PI order in June 2024, Petitioner promptly sought to advance the underlying district court case—requesting a status conference and scheduling order to advance to an actual trial on the merits, as is common in cases where a PI is granted on a preliminary, limited record. Exs.1110, 1135. But the case has remained effectively stayed. All appeals, including the trial judgment against Mylan, have now been resolved, yet the district court still has not held a status conference, entered a case schedule, or set a trial date (*Fintiv* factors 1-3).

While both parties first proposed schedules in May 2024 (Ex.1139 and Ex.1133, 34-37), the district court never acted on any of them, and the proposals are now completely out-of-date, with many proposed deadlines having long since passed. Petitioner has subsequently proposed two additional schedules, both of which are also now stale and were never adopted by the district court. Exs.1135-1136. Given the district court's inaction, Petitioner proceeded instead with an IPR and has not proposed a new schedule. And, as set out above, Petitioner commits that, when allowed to submit a new schedule, if institution is granted, it will not seek a trial date on the '865 patent before the FWD is due.

Second, as set out above in Section I, Petitioner's grounds are entirely new. Thus, the "same prior art and arguments" are not at issue in the district court actions (*Fintiv* factors 3-4). Furthermore, there will be little overlap in the claims addressed here and at the district court. In *Mylan*, the district court limited trial to 12 claims (in

3 patents)—far fewer than the 48 challenged here. Exs.2001; Ex.1112, 1-9; Ex.1113, 5; Ex.1114, 9:3-11. Moreover, the challenged claims reciting a PFS presentation were neither adjudicated in the *Mylan* case nor are they currently in Petitioner's case.

To avoid any risk of overlap or duplication, however, Petitioner further stipulates that, if the Board institutes, Petitioner will not pursue an invalidity defense in the parallel litigations (C.A. Nos. 1-23-cv-00094, -106, and MDL No. 1:24-md-3103) that the claims subject to the instituted IPR are invalid based on the grounds that were raised or any grounds Petitioner reasonably could have raised in this IPR. *See Sotera Wireless, Inc. v. Masimo Corp.*, IPR2020-01019, Paper 12. Therefore, there is no risk of "conflicting decisions" nor "inefficiency and duplication of efforts."

Finally, PO accuses (at 10–11) Petitioner of "undue delay" in filing this Petition. But PO did not serve Petitioner with the complaint until October 16, 2024. Ex.1134. Petitioner filed its Petition just one month later, after it became clear the district court did not intend to act quickly—and well within the statutory deadline. Prior to that time, Petitioner expected the district court to move immediately to the merits after the PI, given the preliminary nature of its decision, which was based on a limited record and limited defenses. Once it was apparent the court was effectively staying the matter, Petitioner brought the instant petition. That is not a delay.

Accordingly, for the reasons set forth in its Petition and above, Petitioner respectfully requests institution on all challenged claims.

DATED: April 23, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

In accordance with 37 C.F.R. § 42.6(e), I hereby certify that on April 16, 2025, true and correct copies of Petitioner's Reply to Patent Owner's Preliminary Response were served via electronic mail to Patent Owner at the following email addresses of record:

Eylea@wc.com
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DATED: April 23, 2025

Respectfully submitted,

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