

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 IPR2023-00739

U.S. Patent No. 10,888,601

**PETITIONER'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE**

Pursuant to the Board’s authorization (Ex. 3001), Petitioner submits this reply to Patent Owner’s Preliminary Response (“POPR”) (Paper 6) in IPR2023-00739.

I. Notwithstanding Patent Owner’s Disclaimer, the *Fintiv* Factors Weigh in Favor of Institution Because the Issues Here Do Not Overlap With Those in the Mylan Litigation

In response to this IPR, Patent Owner disclaimed nine claims of U.S. Patent No. 10,888,601 (the “’601 patent”): claims 15-16, 20, 23-24, 31-32, and 46-47. For context, Grounds I, IV, and V relate solely to the disclaimed claims (and other previously-disclaimed claims), and are thus no longer relevant. The remaining twelve Challenged Claims are claims 10-12, 17-19, 21, 25-28, and 33. They recite a dosing regimen of five monthly loading doses followed by maintenance doses administered every two months, along with multiple dependent limitations. Grounds II, III, and VI address these claims.

Patent Owner’s disclaimer had no material effect on the *Fintiv* analysis, despite Patent Owner’s argument to the contrary.

First, despite the disclaimer, ten of the twelve remaining Challenged Claims still will not be adjudicated in the Mylan Litigation. Only claims 11 and 19 are at issue there. Accordingly, no matter what happens in the Mylan Litigation, the validity of ten of the twelve Challenged Claims will go unaddressed. This alone should be dispositive. There remains no risk of duplication of effort as to those ten

Challenged Claims (*Fintiv* Factors 1-3) and the claims are not the same claims as presented in the district court (*Fintiv* Factor 4).

Recognizing this flaw in its argument, Patent Owner states that claims 11 and 19 “are representative of other challenged claims in this proceeding.” POPR at 4. But the ten non-overlapping Challenged Claims recite, *inter alia*, a different dosing regimen (claims 12, 21, and 28) than claims 11 and 19, as well as exclusion criteria (claims 17 and 25) that Patent Owner has argued render similar claims patentable. *See*, IPR2023-00442, Paper 7, 12-31 (’681 POPR). These claims thus do not necessarily overlap in scope with claims 11 and 19, and the Mylan Litigation will not address the validity of these claims at all. Tellingly, Patent Owner neither disclaimed these additional claims, nor represents to the Board that it will disclaim the remaining ten claims if claims 11 and 19 are invalidated in the Mylan Litigation. Accordingly, whether or not the Mylan Court invalidates claims 11 and 19, the remaining Challenged Claims will stand, and the Mylan Litigation will do nothing to resolve the validity of the full set of Challenged Claims.

Second, the current Petition presents multiple grounds of invalidity that are not at issue in the Mylan Litigation, both as to the ten non-overlapping claims as well as claims 11 and 19.

As to the non-overlapping claims, the validity of those claims has never been addressed by the district court in the Mylan Litigation and will never be addressed.

Thus the “same prior art and arguments” (*NHK Spring Co. v. Intrix-Plex Techs., Inc.*, IPR2018-00752, Paper 8, 20 (P.T.A.B. Sept. 12, 2018) (precedential)) cannot, by definition, be at issue in the Mylan Litigation. For instance, in Ground VI, which addresses claims 17 and 25, Petitioner presents an obviousness ground including the CATT and PIER Studies. The CATT and PIER studies are not part of any ground presented in the Mylan Litigation. *See* Ex. 1058 (Mylan Post-Trial Brief). Patent Owner ignores these ten claims completely in its *Fintiv* analysis.

Even as to claims 11 and 19, Petitioner presents significantly different prior art and arguments than Mylan. Mylan relied solely on the 2009 Press Release. *See* Ex. 1058 at 14-17. In Ground II, in contrast, Petitioner presents the 2009 Press Release in combination with Shams. In Ground III, Petitioner additionally relies on a combination with the Elman 2010 reference. Mylan did not present such a combination or rely on Shams or Elman 2010. *See id.*

Patent Owner, however, argues that in view of its disclaimer, the same prior art arguments are presented in the Mylan Litigation and this Petition. Specifically, Patent Owner states that “[b]oth Petitioner and Defendants start with the point that the 2009 Press Release disclosed multiple aflibercept dosing regimens for DME, including ‘initial doses spaced 4 week/1 month apart, followed by extended dosing intervals, such as 8 weeks/2 months.’” POPR at 43. But this argument misstates Mylan’s and Petitioner’s arguments.

Mylan's primary argument is anticipation based on the disclosure of three monthly loading doses followed by a ***PRN dosing regimen*** in the 2009 Press Release. *See* Ex. 1058 at 14-17. Mylan thus does not start from a regimen that already discloses extended dosing intervals (as Petitioner does, as Patent Owner acknowledges). Instead, Mylan argues that based on the disclosed PRN regimen, three initial doses would be given, and then the additional two monthly doses and the recited extended 8-week dosing regimen would "be immediately apparent to one of ordinary skill" as a potential result of the monthly evaluations that are part of PRN dosing. *Id.* at 14. Thus Mylan argues these limitations are inherently disclosed by PRN regimen of the 2009 Press Release. *Id.* Mylan also presented a secondary obviousness argument based on that same PRN dosing regimen. *Id.* at 17.

In contrast, Petitioner's obviousness theory based on the 2009 Press Release does not start from the disclosed PRN regime. It starts instead from the disclosure in the 2009 Press Release relating to three monthly loading doses followed by extended-interval maintenance doses at 8-week intervals—not PRN. Ex. 1009. As the Petition points out, because this regimen already discloses extended-interval dosing after three monthly doses, the only difference between this disclosure and the dosing regimen of claims 10, 18, and 26 of the '601 patent is the number of initial monthly doses. To arrive at the claimed invention from this regimen requires only

trivial and routine modification—the addition of a single monthly injection between the last loading dose and first maintenance dose. *See, e.g.*, Petition at 4.

Even putting aside the prior art combinations not presented by Mylan, Petitioner’s fundamental argument is a substantially different and simpler obviousness theory than Mylan’s anticipation and obviousness theories based on a PRN dosing regimen. There is no risk of a “conflicting opinion” nor “inefficiency and duplication of efforts,” because the theories are wholly distinct, particularly as to the disclosure of extended dosing intervals. *Fintiv*, 2020 WL 2126495, at *3.

Third, there is no risk, as Patent Owner suggests, that a hypothetical appeal of the district court’s claim construction order, which found the exclusion criteria lack patentable weight, will result in conflicting opinions and inefficiency.

As explained in Ground VI, the Board (like the Mylan district court) determined the exclusion criteria lack patentable weight, and thus the claims reciting them are obvious for the same reasons set out in Grounds II and III of the Petition. Petition at 21-22, 54. As part of Ground VI, however, Petitioner alternatively argues that even if the exclusion criteria are given patentable weight, they are rendered obvious by a combination of the primary references and the exclusion criteria from the CATT and PIER Studies. *Id.* at 54. The Board has preliminarily found in connection with Petitioner’s ’681 IPR that the criteria are obvious in view of these studies. IPR2023-00442, Paper 10, 29-40 (Institution Decision). There is thus no

risk of a conflicting judgment. Either the Federal Circuit adopts the Board and Mylan Court’s claim construction; or, if the exclusion criteria are given patentable weight then the Petition already presents a second, alternative prior art grounds for finding those limitations obvious.

II. The Challenged Claims Do Not Require “Fixed,” “Predetermined” Dosing With No Patient Assessment

Throughout its POPR, Patent Owner argues that the Challenged Claims require “a fixed, extended dosing regimen.” According to Patent Owner, a “fixed approach provides for treatment on a *predetermined* schedule regardless of whether reaccumulated fluid has been detected, while assessment-based approaches take a fundamentally different approach by making injections conditional on patient characteristics.” POPR at 23 (emphasis added). Patent Owner thus claims that “[t]he claims recite a dosing regimen that is fixed, rather than based on individualized patient assessments, throughout the course of treatment, with a transition to extended (but still fixed) dosing after the fifth dose.” POPR at 28. Patent Owner attempts to distinguish Petitioner’s grounds on this basis. This argument fails for two reasons.

First, although it does not admit it, Patent Owner is engaging in claim construction. But Patent Owner identifies no claim language to construe, because there is no claim language that supports its interpretation of the claims. The claims do not recite that the method of treatment is “fixed” or “predetermined” at the start, nor that “assessment based approaches” that are “conditional on patient

characteristics” are excluded. There is no language in the Challenged Claims that require a “fixed” regimen. For example, claim 10 states:

A method for treating diabetic macular edema in a patient in need thereof, comprising intravitreally administering, to said patient, an effective amount of aflibercept which is 2 mg approximately every 4 weeks for the first 5 injections followed by 2 mg approximately once every 8 weeks or once every 2 months.

The claim does not require that the recited doses be “predetermined.” The claim would be practiced if a patient was assessed every month and only received doses according to the claimed dosing regimen. Patent Owner’s arguments improperly import limitations into the claim and should be rejected. *See, Superguide Corp. v. DirecTV Enterprises, Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004).

Moreover, the intrinsic evidence contradicts Patent Owner’s position. The specification explains that “the frequency at which the secondary and/or tertiary doses are administered to a patient can vary over the course of the treatment regimen.” Ex. 1001, 4:32-46. Contrary to Patent Owner’s position, it further explains that these adjustments are based on an assessment of the patient’s characteristics: “The frequency of administration may also be adjusted during the course of treatment by a physician *depending on the needs of the individual patient following clinical examination.*” *Id.* If such an adjustment results in extended 8-

week dosing after five initial monthly doses—i.e. based on an assessment that the patient has improved after five doses such that bi-monthly injections are sufficient—that falls within the scope of the claims.

Similarly, the dependent claims are inconsistent with a “fixed” dosing regimen as defined by Patent Owner. Claims 17, 25, and 33 recite exclusion criteria based on an assessment of the patient’s ocular condition before, during, and after treatment. A “predetermined” dosing regimen is the opposite of this approach. Similarly, claims 12, 21, and 28 recite **returning** to monthly dosing after beginning the extended dosing. Such a course of treatment makes no sense if predetermined, but would make sense if arrived at based on a clinical assessment of a patient that shows regression after trying extended dosing. *See, e.g.*, Claims 12, 21 and 28.¹

¹ Additionally, Patent Owner’s argument makes little sense in the clinical setting. As discussed in the Petition, it was and still is standard clinical practice for a physician to evaluate the patient’s ocular conditions and response to treatment before, during, and after treatment and adjust the injection schedule accordingly—treatment is not predetermined or fixed. Ex. 1002, ¶¶ 58-61 (“[T]he actual injection schedule is routinely optimized based on patient need and compliance, treatment risks and effects, and overall cost effectiveness.”).

A POSA thus would not interpret the recited method of treatment to exclude arriving at the claimed sequences of doses through a routine evaluation of the patient for improvement (or regression), consistent with clinical practice. Yet Patent Owner would read the claims as if such standard practice was disallowed, without any basis in the claims for doing so.

Patent Owner's claim construction requiring "fixed" or "predetermined" dosing is not supported by either the claims or the specification and should be rejected.

Second, even if Patent Owner is correct that the claims require "fixed" dosing (it is not), Petitioner's grounds are based on the 2009 Press Release's disclosure of a regimen that—by Patent Owner's own admission—is "fixed." As Patent Owner admits, "the 2009 Press Release does disclose an arm with *fixed* eight-week dosing (after three initial monthly doses)." (POPR at 34 (emphasis added)).

This precise disclosure is the primary basis for all of Petitioner's grounds. As Petitioner explained above, unlike Mylan (who relies on a PRN regimen which is arguably not "fixed" according to Patent Owner), Petitioner's argument is that a POSA would find the use of five initial monthly doses as claimed, rather than three as disclosed in the 2009 Press Release, obvious—either based on the 2009 Press Release alone, or in combination with Shams or Elman 2010. Patent Owner acknowledges that this is a disclosure of the sort of "fixed" dosing regimen it claims

is required. Thus, the claims are obvious even if Patent Owner's claim construction requiring "fixed" dosing is adopted.

Accordingly, for the reasons set forth in its initial Petition and above, Petitioner has established a reasonable likelihood that the Challenged Claims are unpatentable and respectfully requests institution of the Petition.

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Respectfully submitted,

By /Raymond N. Nimrod/
Raymond N. Nimrod (Reg. No. 31,987)
raynimrod@quinnemanuel.com
QUINN EMANUEL URQUHART
& SULLIVAN LLP
51 Madison Avenue, 22nd Floor
New York, NY 10010
Tel: (212) 849-7000
Fax: (212) 849-7100

Attorneys for Petitioner Samsung Bioepis

CERTIFICATE OF SERVICE

In accordance with 37 C.F.R. § 42.6(e), I hereby certify that on August 21, 2023, true and correct copies of Petitioner's Reply to Patent Owner's Preliminary Response and Exhibit 1058 were served via electronic mail to Patent Owner at the following email addresses of record:

Brausa, Adam R. ABrausa@mofo.com
Davis, Kira A KiraDavis@mofo.com
Weires, Rebecca RWeires@mofo.com
Durie, Daralyn J. DDurie@mofo.com
Regeneron-MoFo-IPR Regeneron-MoFo-IPR@mofo.com

DATED: August 21, 2023

Respectfully submitted,

By /Raymond N. Nimrod/

Raymond N. Nimrod (Reg. No. 31,987)
raynimrod@quinnemanuel.com
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
51 Madison Ave., 22nd Floor
New York, NY 10010
Tel: (212) 849-7000
Fax: (212) 849-7100