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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

YEDA RESEARCH AND DEVELOPMENT CO. LTD.,
Patent Owner.

Case IPR2015-00643
Patent 8,232,250 B2

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and TINA E. HULSE, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

INTRODUCTION

Mylan Pharmaceuticals Inc. ("Petitioner") filed a Corrected Petition (Paper 7 ("Pet.")), seeking an *inter partes* review of claims 1–20 of U.S. Patent No. 8,232,250 B2 ("the '250 patent," Ex. 1001). Yeda Research and Development Co., Ltd. ("Patent Owner") timely filed a Preliminary Response. Paper 10 ("Prelim. Resp."). We have jurisdiction under 35 U.S.C. § 314.

For the reasons provided below, we determine that, having established a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim, Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). We institute an *inter partes* review of claims 1–20 of the '250 patent.

Related Proceedings

The parties have been litigating over the '250 patent in the following two district court cases: *Teva Pharmaceuticals USA, Inc. v. Mylan Pharmaceuticals Inc.*, 14-cv-01278 (D. Del., Oct. 6, 2014), and *Teva Pharmaceuticals USA, Inc. v. Mylan Pharmaceuticals Inc.*, 14-cv-00167 (N.D. W. Va., Oct. 7, 2014). Pet. 1, 2; Paper 6, 2. The '250 patent is also the subject of several other district court cases that do not involve Petitioner. Pet. 1, 2; Paper 6, 2.

The ’250 Patent

The ’250 patent is directed to a method of alleviating a symptom of relapsing-remitting multiple sclerosis (“RRMS”) using glatiramer acetate (“GA”). Ex. 1001, Abstract, 2:55–64. RRMS is a form of multiple sclerosis (“MS”), an autoimmune disease that affects the central nervous system. *Id.* at 1:18–20, 1:31. “Patients suffering from RRMS experience sporadic exacerbations or relapses, as well as periods of remission.” *Id.* at 1:32–33.

GA is a mixture of polypeptides that do not all have the same amino acid sequence. *Id.* at 1:65–2:16. Before the ’250 invention, the FDA approved 20 mg GA daily injection (under the tradename Copaxone®) for treating patients with RRMS. *Id.* at 2:17–20. The ’250 patent discloses an effective low frequency dosage regimen of GA administration to patients suffering from RRMS. *Id.* at 2:47–51.

Illustrative Claim

Claims 1, 15, and 19 are independent claims. Claim 1 is illustrative. It reads:

> 1. A method of alleviating a symptom of relapsing-remitting multiple sclerosis in a human patient suffering from relapsing-remitting multiple sclerosis or a patient who has experienced a first clinical episode and is determined to be at high risk of developing clinically definite multiple sclerosis comprising administering to the human patient a therapeutically effective regimen of three subcutaneous injections of a 40 mg dose of glatiramer acetate over a period of seven days with at least one day between every subcutaneous injection, the regimen being sufficient to alleviate the symptom of the patient.

Claim 15 is similar to claim 1, except it is directed to a method of increasing the tolerability of GA treatment in an RRMS patient, and requires the regimen to do so. Claim 19 is also similar to claim 1, except it is directed to a method of reducing frequency of relapses in an RRMS patient, and requires the regimen to do so.

Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claims	Basis	Reference(s)
1–13, 19, 20	§ 102(b)	Pinchasi[1]
1–20	§ 103	Pinchasi
1–20	§ 103	Pinchasi and the 1996 SBOA[2]
1–20	§ 103	Pinchasi and Flechter[3]

The earliest priority of the challenged claims is August 20, 2009. Ex. 1001, 1:4–7. Thus, according to Petitioner, Pinchasi, the 1996 SBOA, and Flechter all qualify as prior art under 35 U.S.C. § 102(b). Pet. 18, 20, 21.

In support of its patentability challenge, Petitioner relies on the Declarations of Dr. Stephen J. Peroutka (Ex. 1003) and Dr. Ari Green (Ex. 1004).

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[1] Pinchasi, WO 2007/081975 A2, published July 19, 2007 (Ex. 1005).
[2] Summary Basis of Approval for the New Drug Application for 20 mg daily Copaxone ® (NDA #20-622) (Ex. 1007).
[3] S. Flechter et al., *Copolymer 1 (Glatiramer Acetate) in Relapsing Forms of Multiple Sclerosis: Open Multicenter Study of Alternate-Day Administration*, 25 CLINICAL NEUROPHARM. 11–15 (2002) (Ex. 1008).

ANALYSIS

Claim Construction

In an *inter partes* review, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, No. 2014-1301, 2015 WL 4097949, *8 (Fed. Cir. July 8, 2015). Under that standard, and absent any special definitions, we assign claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

"Comprising"

Each independent claim recites a method "comprising" administering a therapeutically effective "regimen of three subcutaneous injections of a 40 mg dose of glatiramer acetate over a period of seven days with at least one day between every subcutaneous injection." Petitioner argues that the use of "comprising," an open-ended transition, allows the claims to encompass three or more subcutaneous injections over a period of seven days. Pet. 14–15. Petitioner also argues that the term "regimen" does not "close" the claims. *Id.* at 16. Instead, "the use of the indefinite article 'a' before 'regimen' reinforces that the independent claims are each open-ended and allow for additional, unrecited elements to fall within the scope of the

claim." *Id.* Thus, Petitioner concludes, the claims encompass "every-other-day dosing, in which three doses are administered during the first 7-day period . . . and four doses are administered during the second 7-day period." *Id.* at 15.

Patent Owner counters that Petitioner "improperly uses the 'comprising' transition to reach into subsequent individual method step limitations and render []each of them open-ended." Prelim. Resp. 28. In addition, Patent Owner points out that, during prosecution, the examiner rejected the claims as anticipated by Flechter, which discloses administration of GA "in an alternate-day administration schedule for up to two years." *Id.* at 24–25 (citing Ex. 1002, 67). In response, the applicant amended the claims to require a therapeutically effective "regimen," and argued that the alternate-day administration in Flechter would "result[] in four administrations every other successive seven day period," and thus, cannot anticipate the claimed regimen "requiring administration 3 times during a seven day period." *Id.* at 25–26 (citing Ex. 1002, 151, 161). As a result, Patent Owner contends, the applicant expressly limited the claims to a three-injections-weekly regimen and disclaimed the alternate-day administration. *Id.* at 25.

Based on the current record, we find Patent Owner's argument more persuasive. Even though we must give a term its broadest reasonable interpretation, the construction may not be so broad that it becomes "unreasonable under general claim construction principles." *See Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1298 (Fed. Cir. 2015). Here, we

agree with Patent Owner that, although the term "comprising" allows for additional steps in the claimed method, the term does not "reach into each [limitation] to render every word and phrase therein open-ended." *Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337, 1343 (Fed. Cir. 2007). Thus, we are not persuaded that, as Petitioner asserts, the term "comprising" requires us to construe the claims to encompass more than three injections over a period of seven days.

In addition, when construing claim terms, we "also consult the patent's prosecution history in proceedings in which the patent has been brought back to the agency for a second review." *Proxyconn*, 789 F.3d at 1298. Here, we agree with Patent Owner that, during prosecution, the applicant clearly disavowed administering the drug on alternate days by amending and distinguishing its claims over the prior art.

Accordingly, at this stage of the proceeding, we determine that under the broadest reasonable interpretation, the claims do not encompass an alternate-day administration schedule (i.e., one that administers the drug three times in one week and four times the next).

Claim 3

It appears that there is a typographic error in claim 3 as it does not specify which claim it depends from. Petitioner argues that "[b]ased on its position, and from the language of claim 2 and the following dependent claims, claim 3 depends from claim 1." Pet. 17. We are not persuaded.

First, the doctrine of claim differentiation creates a presumption that each claim in a patent has a different scope. *Free Motion Fitness, Inc. v. Cybex Int'l, Inc.*, 423 F.3d 1343, 1351 (Fed. Cir. 2005). Claim 12, reciting the same additional limitation as that of claim 3, depends from claim 1. Indeed, claims 3 and 12 read:

> 3. The method of claim wherein the 40 mg dose of glatiramer acetate is in a prefilled syringe for self administration by the human patient.
> 12. The method of claim 1, wherein the 40 mg dose of glatiramer acetate is in a prefilled syringe for self administration by the patient.

To construe claim 3 as depending directly from claim 1 would result in two identical claims in a single patent, a highly unlikely event.

In addition, claim 3 issued from new claim 21 added during prosecution, which depends from claim 2. Ex. 1002, 154.

Furthermore, based on the current record, we agree with Petitioner that regardless of whether claim 3 depends from claim 1 or claim 2, the unpatentability of claim 3 does not change. Thus, for purpose of this Decision, we treat claim 3 as depending directly from claim 2 and indirectly from claim 1. *See, e.g.*, *Novo Indus., L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1354 (Fed. Cir. 2003).

Level of Ordinary Skill in the Art

Petitioner contends that one of ordinary skill in the art would have had (1) several years of experience in the pharmaceutical industry or in practicing medicine; (2) experience with the administration or formulation of

therapeutic agents, dosing schedules and frequencies, and drug developmental study and design; and (3) a Ph.D. in pharmacology or be a physician with experience in clinical pharmacology. Pet. 13. Patent Owner asserts that a skilled artisan would have had knowledge of and experience with both MS and GA. Prelim. Resp. 33–34. We find Patent Owner's argument more persuasive.

Indeed, one of Petitioner's declarants, Dr. Green, states that one of ordinary skill in the art would have "direct experience administering therapeutic agents for the treatment of MS, as well as familiarity with the dosing schedules and frequencies of the different therapeutic agents available for MS treatment." Ex. 1004 ¶ 27.

Accordingly, we adopt Petitioner's definition of a person of ordinary skill in the art, with the addition that that person would also have experience with MS and GA.

Prior Art Disclosures

Pinchasi relates to a method of alleviating a symptom of an RRMS patient. Ex. 1005, 9.[4] The method comprises periodically administering by subcutaneous injection a 40 mg dose of GA. *Id.* Pinchasi discloses that the GA can be administered daily or every other day. *Id.* It also discloses that the alleviated symptom can be the frequency of relapses. *Id.*

[4] Unless stated otherwise, we cite to the page numbers provided by the parties in the lower right hand corner of the exhibits, pursuant to 37 C.F.R. § 42.63(d)(2). For purposes of clarity, we suggest the parties do the same in future filings.

The 1996 SBOA is a compilation of documents relating to the approval for the New Drug Application ("NDA") for 20 mg Copaxone®. Ex. 1007. It includes a review and evaluation of clinical data submitted by the sponsor of the NDA, Teva Pharmaceuticals, USA ("Teva"). *Id.* at 24–124. It also includes a review of the pharmacology and toxicology studies submitted by Teva. *Id.* at 125–292. The NDA was approved on December 20, 1996. *Id.* at 4.

Flechter reports the results of a multicenter study treating patients with relapsing MS with 20 mg doses of Copolymer 1 (i.e., GA) on alternate days. Ex. 1008, 1. Flechter states that the results of the trial "suggest that alternate-day treatment with Copolymer 1 is safe, well tolerated, and probably as effective as daily Copolymer 1 in reducing relapse rate and slowing neurologic deterioration." *Id.* at 5.

Patentability Analysis

Anticipation by Pinchasi

Petitioner argues that Pinchasi discloses each limitation of claims 1–13, 19, and 20. Pet. 22–34. Specifically, Petitioner argues that Pinchasi discloses administering GA by injection every other day, and thus, satisfies the limitation requiring three injections over seven days with at least one day in between every injection. Pet. 24–25. As explained above, however, we do not construe the claims so broadly. *See* supra at 5–7. Because at this stage of the proceeding, we do not construe the claims to encompass the alternate-day administration, we conclude that Petitioner has failed to

establish a reasonable likelihood that it would prevail in showing that Pinchasi anticipates claims 1–13, 19, and 20.

Obviousness over Pinchasi and the 1996 SBOA

Petitioner asserts that claims 1–20 would have been obvious over Pinchasi and the 1996 SBOA. Pet. 51–55. Based on the current record, we determine that Petitioner has established a reasonable likelihood it would prevail in this assertion.

Regarding claim 1, Petitioner argues that Pinchasi provides a method for alleviating a symptom in an RRMS patient, wherein the symptom is the "frequency of relapses." *Id.* at 23–24 (citing Ex. 1005, 9:2–4, 9:12–13). Petitioner also refers to Pinchasi for teaching the subcutaneous injection of 40 mg of GA in each dose, the same amount recited in claim 1. *Id.* at 24 (citing Ex. 1005, 6:2–8). Based on the current record, we are persuaded that Petitioner has shown sufficiently that Pinchasi teaches each limitation of claim 1, except the requirement of three doses per seven day period.

Regarding the dosing frequency, Petitioner notes that a reviewer of the 1996 SBOA "recommend[ed] that [Teva] evaluate the necessity of daily [subcutaneous] injections as opposed to more infrequent intermittent administration of the drug." *Id.* at 53 (citing Ex. 1007, 252). In addition, according to Petitioner, the 1996 SBOA teaches that the half-life for Copaxone® is approximately 80 hours in a monkey, which "was a reliable model" for creating dosing schedules for human. *Id.* at 52 (citing Ex. 1007, 197; Ex. 1003, ¶ 120). Thus, Petitioner argues, a person of ordinary skill in

the art would have understood that the "injection frequencies could be reduced as far as approximately once every 80 hours while maintaining the same safety and tolerability profiles." *Id.* at 53 (citing Ex. 1003 ¶¶ 132–33). Accordingly, Petitioner asserts that a skilled artisan "would have expected both 40 mg GA three times over a 7-day period and 20 mg daily to provide the same therapeutic profile to a patient." *Id.* at 54 (citing Ex. 1003 ¶ 134).

Furthermore, Petitioner argues that one of ordinary skill in the art would have been motivated to modify Pinchasi's alternate-day injection schedule to three times in seven days to (1) reduce the number of injections and thereby reduce the frequency of side effects (*id.* at 46–47 (citing Ex. 1003 ¶¶ 100–03; Ex. 1004 ¶¶ 93, 94)); and (2) to allow for a more convenient dosing schedule (i.e., medicating on the same days of each week), which would improve patient compliance (*id.* at 47 (citing Ex. 1004 ¶¶ 93, 94)).

Patent Owner challenges Petitioner's evidence to establish the 1996 SBOA as prior art under § 102(b). Prelim. Resp. 47–48. According to Patent Owner, "Mylan presents no evidence [to show] the SBOA was indexed or publicly accessible at the relevant time, or if it was, in what form." *Id.* at 48. We are not persuaded.

To qualify as a printed publication within the meaning of § 102(b), a reference "must have been sufficiently accessible to the public interested in the art" before the critical date. *In re Cronyn*, 890 F.2d 1158, 1160 (Fed. Cir. 1989). A reference is considered publicly accessible if it was disseminated or otherwise made available to the extent that persons

interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it. *In re Lister*, 583 F.3d 1307, 1311 (Fed. Cir. 2009). Here, to show that the 1996 SBOA is prior art under § 102(b), Petitioner relies on a declaration from Marlene S. Bobka, the president of FOI Services, Inc. Ex. 1007, 1. Ms. Bobka states that FOI Services "maintains a private library of over 150,000 FDA documents," all of which are "faithful reproductions of the original [FDA] documents." *Id.* She also states that FOI Services sells the documents individually. *Id.* She further states that the 1996 SBOA was provided to Petitioner in the form of the compilation (attached as Exhibit A to Exhibit 1007) on July 17, 2007. *Id.*

At this stage of the proceedings, we are persuaded that Petitioner has set forth sufficient evidence that the 1996 SBOA was sufficiently accessible to the public at least by July 17, 2007. Thus, for purposes of this Decision, we determine that the 1996 SBOA constitutes prior art under § 102(b).

Patent Owner also challenges Petitioner's conclusion that, based on data generated from monkeys, a skilled artisan would have understood the injection frequency "could be reduced as far as approximately once every 80 hours." Prelim. Resp. 42 (citing Pet. 52–53). According to Patent Owner, the monkey study in the 1996 SBOA measured "not GA, but rather just the 'precipitable radiolabel.'" *Id.* (citing Ex. 1007, 198).

Patent Owner further argues that the active molecule in GA is unknown, GA's mechanism of action is unknown, and no PK/PD correlation exists for GA. *Id.* at 11–17. Thus, according to Patent Owner, one of ordinary skill in the art would not have had a reasonable expectation of

success in using a 40 mg GA, three times per week regimen. *Id.* at 34–37. In addition, Patent Owner asserts that prior art suggests decreasing the dosing frequency of GA would decrease the efficacy of the drug. *Id.* at 37. Thus, Patent Owner concludes, a person of ordinary skill in the art would not have been motivated to dose GA three times per week. *Id.* at 37–44. Moreover, Patent Owner argues that a person of ordinary skill in the art would not have been motivated to use a 40 mg dose of GA in light of other clinical trials that allegedly show a 40 mg daily dose was not superior to a 20 mg daily dose. *Id.* at 44–45. Finally, Patent Owner argues that there was no reason to combine the prior-art teachings, and that secondary considerations support a finding of nonobviousness of the claims. Id. at 46–48, 54–58.

At this stage of the proceeding, we find that Petitioner has offered sufficient evidence to institute trial. Although Patent Owner's arguments are not unreasonable, they generally amount to a difference in opinion as to the evidence set forth by Petitioner. As a result, they do not persuade us that we should decline to go forward with a trial.

Based on the current record, we conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that claim 1 is unpatentable as obvious over Pinchasi and 1996 SBOA. We have considered the parties' arguments and evidence with respect to the remaining claims (Pet. 52–55; Prelim. Resp. 49–52), and we determine that Petitioner has made a sufficient showing as to those claims, as well.

Obviousness over Pinchasi and Flechter

Petitioner asserts that claims 1–20 would have been obvious over Pinchasi and Flechter. Pet. 56–57. Based on the current record, we determine that Petitioner has established a reasonable likelihood it would prevail in this assertion.

As explained above, we are persuaded by Petitioner's argument that Pinchasi teaches each of the limitations of the claims, except the requirement of three doses per seven day period. Regarding the dosing frequency, Petitioner contends daily administration was therefore not necessary because Flechter teaches that the regimen of alternate-day injection with 20 mg of GA had similar efficacy as the daily regimen. Pet. 56 (citing Ex. 1008, Abstract). In addition, according to Petitioner, the GA dosage from the claimed regimen with three injections per week falls within the alternate-day 40 mg dosage regimen of Pinchasi and the alternate-day 20 mg dosage regimen of Flechter. *Id.* (citing Ex. 1003 ¶ 146). Petitioner further argues that one of ordinary skill in the art would have been motivated to set a course of treatment for the same day each week to increase compliance with the dosage regimen. *Id.* at 56–57 (citing Ex. 1004 ¶¶ 116, 119).

Patent Owner asserts that data in Fletcher show the mean relapse rate of the alternate-day administration of 20 mg of GA twice as high as that of the daily administration of 20 mg of GA. Prelim. Resp. 37 (citing Ex. 1008, Table 5). In addition, Patent Owner observes that Fletcher itself acknowledges the need of larger studies to confirm its findings. *Id.* (citing

Ex. 1008, 5). Patent Owner's other arguments are the same as those discussed above.

As explained above, at this stage of the proceeding, we find that Petitioner has offered sufficient evidence to institute trial, and Patent Owner's arguments do not persuade us that we should decline to go forward with a trial. Based on the current record, we conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that the challenged claims are unpatentable as obvious over Pinchasi and Fletcher.

Obviousness over Pinchasi

Petitioner also asserts that claims 1–20 are unpatentable as obvious over Pinchasi alone. Pet. 45–51. Because we institute trial to review whether the challenges claims would have been obvious over the combination of Pinchasi and the 1996 SBOA, and the combination of Pinchasi and Flechter, we exercise our discretion not to institute an *inter partes* review on this ground. *See* 37 C.F.R. § 42.108(a).

CONCLUSION

For the foregoing reasons, the information presented in the Petition and accompanying evidence establishes a reasonable likelihood that Petitioner would prevail in showing the unpatentability of claims 1–20 of the '250 patent.

At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim or the construction of any claim term.

ORDER

Accordingly, it is

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on the following grounds:

1. Claims 1–20 as obvious over Pinchasi and 1996 SBOA; and

2. Claims 1–20 as obvious over Pinchasi and Flechter.

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized.

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision.

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