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Paper No. 8
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CELLTRION, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-01140
Patent 7,371,379 B2

Before ZHENYU YANG, CHRISTOPHER G. PAULRAJ, and ROBERT A. POLLOCK, *Administrative Patent Judges.*

PAULRAJ, *Administrative Patent Judge.*

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

I. INTRODUCTION

Celltrion, Inc. ("Petitioner") filed a Petition (Paper 1, "Pet."), requesting institution of an *inter partes* review of claims 1–3, 5, 7, 9–11, 16–28, and 30–40 of U.S. Patent No. 7,371,379 B2 (Ex. 1001, "the '379 patent"). Genentech, Inc. ("Patent Owner") timely filed a Preliminary Response (Paper 7, "Prelim. Resp.").

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Upon consideration of the Petition and the Preliminary Response, and for the reasons explained below, we determine that Petitioner has shown that there is a reasonable likelihood that it would prevail with respect to at least one of the challenged claims. We, thus, institute an *inter partes* review of claims 1–3, 5, 7, 9–11, 16–28, and 30–40 of the '379 patent.

A. Related Proceedings

Petitioner has filed a separate petition for an *inter partes* review for a related patent, U.S. Patent 6,627,196 ("the '196 patent") in IPR2017-01139. Additionally, in IPR2017-00804 and IPR2017-00805, we previously instituted *inter partes* reviews of the '196 patent and '379 patent, respectively, based on petitions filed by Hospira, Inc.

B. The '379 Patent (Ex. 1001)

The '379 patent issued on May 13, 2008, with Sharon A. Baughman and Steven Shak as the listed co-inventors. Ex. 1001, (45), (75). The '379 patent claims priority as the divisional of an application filed December 25, 2000, as

well as to provisional applications filed June 23, 2000 and August 27, 1999. *Id.* at (22), (60).

The '379 patent relates generally to dosages for the treatment of anti-ErbB2 antibodies. *Id.* at (54). The overexpression of ErbB2 has been associated with cancer. *Id.* at 1:20–25. As noted in the '379 patent, a recombinant humanized anti-ErbB2 monoclonal antibody (alternatively referred to as "rhuMab HER2," "trastuzumab," or by its tradename "Herceptin") had been clinically tested and approved for patients with ErbB2-overexpressing metastatic breast cancers who received prior anti-cancer therapy. *Id.* at 3:59–65. The recommended initial "loading dose" for Herceptin was 4 mg/kg administered as a 90-minute infusion, and the recommended weekly "maintenance dose" was 2 mg/kg, which could be administered as a 30-minute infusion if the initial loading dose was well-tolerated. *Id.* at 3:66–4:3.

The invention described in the '379 patent "concerns the discovery that an early attainment of an efficacious target trough serum concentration by providing an initial dose or doses of anti-ErbB2 antibodies followed by subsequent doses of equal or smaller amounts of antibody (greater front loading) is more efficacious than conventional treatments." *Id.* at 4:26–31. The method of treatment, according to the invention described in the patent, "involves administration of an initial dose of anti-ErbB2 antibody of more than approximately 4 mg/kg, preferably more than approximately 5 mg/kg," with the maximum dose not to exceed 50 mg/kg. *Id.* at 4:51–55. "[T]he initial dose or doses is/are followed by subsequent doses of equal or smaller amounts of antibody at intervals sufficiently close to maintain the trough serum concentration of antibody at or above an efficacious target level." Ex. 1001,

4:65–5:2. Preferably, "the amount of drug administered is sufficient to maintain the target trough serum concentration such that the interval between administration cycles is at least one week," and "the trough serum concentration does not exceed 2500 µg/ml and does not fall below 0.01 µg/ml during treatment." *Id.* at 5:4–9. The patent explains that "[t]he front loading drug treatment method of the invention has the advantage of increased efficacy by reaching a target serum drug concentration early in treatment." *Id.* at 5:9–12. As a result, "[t]he efficacious target trough serum concentration is reached in 4 weeks or less . . . and most preferably 1 week or less, including 1 day or less." *Id.* at 4:31–34. Additionally, the patent states that the method of therapy may involve "infrequent dosing" of the anti-ErbB2 antibody, wherein the first and second dose are separated by at least two weeks, and optionally at least about three weeks. *Id.* at 6:23–36.

The '379 patent describes embodiments in which the initial dose of anti-ErbB2 is 6 mg/kg, 8 mg/kg, or 12 mg/kg, followed by subsequent maintenance doses of 6 mg/kg or 8 mg/kg administered once every 2 or 3 weeks, in a manner such that the trough serum concentration is maintained at approximately 10–20 µg/ml during the treatment period. *Id.* at 5:19–43, 45:19–45. The treatment regimen according to the invention may further comprise administration of a chemotherapeutic agent, such as a taxoid, along with the anti-ErbB2 antibody. *Id.* at 6:6–10, 7:26–32, 46:28–58.

C. Illustrative Claim

Petitioner challenges claims 1–3, 5, 7, 9–11, 16–28, and 30–40 of the '379 Patent. Independent claim 1 is illustrative, and is reproduced below:

> 1. A method for the treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor,

comprising administering an effective amount of an anti-ErbB2 antibody to the human patient, the method comprising:
administering to the patient an initial dose of at least approximately 5 mg/kg of the anti-ErbB2 antibody; and
administering to the patient a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose, wherein the subsequent doses are separated in time from each other by at least two weeks; and
further comprising administering an effective amount of a chemotherapeutic agent to the patient.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of the claims of the '379 Patent based on the following ground:

References	**Basis**	**Claims challenged**
Slamon,[1] Watanabe,[2] Baselga '96,[3] and Pegram '98[4]	§ 103(a)	1–3, 5, 7, 9–11, 16–28, and 30–40

[1] D. Slamon et al., *Addition of Herceptin(™) (Humanized Anti-HER2 Antibody) to First Line Chemotherapy for HER2 Overexpressing Metastatic Breast Cancer (HER2 +/MBC) Markedly Increases Anticancer Activity: A Randomized Multinational Controlled Phase III Trial*, 17 JOURNAL OF CLINICAL ONCOLOGY 98a, Abstract *377 (1998) (hereinafter "Slamon") (Ex. 1005).
[2] T. Watanabe et al., *Pharmacokinetically Guided Dose Escalation Study of Anti-HER2 Monoclonal Antibody in Patients with HER2/NEU-Overexpressing Metastatic Breast Cancer*, 17 JOURNAL OF CLINICAL ONCOLOGY 182a, Abstract *702 (1998) (hereinafter "Watanabe") (Ex. 1006).
[3] Jose Baselga, *Phase ll Study of Weekly Intravenous Recombinant Humanized Anti-p185^{HER2} Monoclonal Antibody in Patients With HER2/neu-Overexpressing Metastatic Breast Cancer*, 14 JOURNAL OF CLINICAL ONCOLOGY 737–744 (1996) (hereinafter "Baselga '96") (Ex. 1013).
[4] Mark D. Pegram, *Phase ll Study of Receptor-Enhanced Chemosensitivity Using Recombinant Humanized Anti-p185^{HER21neu} Monoclonal Antibody Plus Cisplatin in Patients With HER2/neu-Overexpressing Metastatic Breast Cancer Refractory to Chemotherapy Treatment*, 16 JOURNAL OF CLINICAL ONCOLOGY 2659–71 (1998) (hereinafter "Pegram '98") (Ex. 1014).

Petitioner further relies upon the declaration of Mark Ratain, M.D. (Ex. 1003).

II. ANALYSIS

A. Claim Construction

We interpret claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see also Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable construction standard, claim terms are generally given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner adopts constructions for "ErbB2 receptor," "Epitope 4D5," "antibody," "treatment," "cancer," "chemotherapeutic agent," and "doxorubicin" based on definitions set forth in the specification. *See* Pet. 15–16. Patent Owner separately proposes a construction for "effective amount" based on the specification. *See* Prelim. Resp. 25–26. At this stage of the proceeding, we find that no explicit construction of any claim term is necessary to determine whether to institute a trial in this case. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'"

(quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

B. Level of Skill in the Art

Petitioner contends that a person of ordinary skill in the art for the '379 patent "would have either an M.D. with subspecialty training in oncology and/or a Ph.D. with substantial experience in oncology drug development," and "familiarity with the treatment of breast cancer and substantial experience in the design and/or implementation of oncology clinical trials, as well as expertise in clinical pharmacology, including pharmacokinetics." Pet. 15 (citing Ex. 1003 ¶ 44).[5] Patent Owner does not address the requisite level of skill in its Preliminary Response.

On this record, we adopt Petitioner's definition of the level of ordinary skill in the art as it undisputed at this time and consistent with the evidence of record. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d

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[5] In IPR2017-00805, we adopted Hospira's proposed level of skill for purposes of our institution decision in that case. *See Hospira, Inc. v. Genentech, Inc.*, Case IPR2017-00805, Decision on Institution, 7 (PTAB July 27, 2017) (Paper 13). In particular, we adopted Hospira's proposal that

> [A] person of ordinary skill in the art for the '379 patent would be a "team" that includes both (1) a clinical or medical oncologist specializing in breast cancer with several years of experience in breast cancer research or clinical trials, and (2) a person with a Ph.D. in pharmaceutical sciences or a closely related field with an emphasis in pharmacokinetics with three years of relevant experience in protein based drug kinetics.

Id. Although we have adopted a different definition of the level of skill in the art based on the current record in this proceeding, any differences in the level of skill do not materially affect our analysis in this Decision.

1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp*., 755 F.2d 158, 163 (Fed. Cir. 1985)).

C. Patentability Analysis

1. Content of the Prior Art

Petitioner relies primarily upon the following prior art in its challenges.

a. Slamon (Ex. 1005)

Slamon summarizes the results of a Phase III clinical trial in which patients received Herceptin (H) along with chemotherapy (CRx). Ex. 1005, 98a. The chemotherapy (doxorubicin-cyclophosphamide or paclitaxel) was administered once every three weeks. *Id.* The Herceptin was administered intravenously at a 4 kg/mg loading dose, followed by 2 mg/kg weekly doses. Slamon indicates that "[a]t a median follow-up of 10.5 months, investigator assessments of time to disease progression (TTP) and response rates (RR) show a significant augmentation of CRx effect by H, without increase in overall severe adverse events (AE)." *Id.* As such, Slamon concludes that the data from the clinical trial "indicate that addition of Herceptin to CRx markedly increases clinical benefit, as assessed by RR and TTP." *Id.*

b. Watanabe (Ex. 1006)

Watanabe summarizes a phase I dose escalation study of an anti-HER2 monoclonal antibody (MAb 4D5 (MKC-454)) in patients with chemotherapy-resistant metastatic breast cancer. Ex. 1006, 182a. In the study, the first dose of antibody was followed in 3 weeks by 9 weekly doses. *Id.* Doses of 1, 2, 4,

and 8 mg/kg were administered as 90-minute intravenous infusions. *Id.* Watanabe reports the following data:

MKC454 dose	# of Pts	trough level (μg/ml)	toxicity		tumor response
			grade 2	grade 3≤	
1 mg/kg	6	9		1 fever, 1 n/v	
2 mg/kg	3	19	1 fever, 1 pain		1 MR
4 mg/kg	3	102	1 fever		1 PR
8 mg/kg	6	248		1 pain	1 MR, 2 PR

Id. According to Watanabe, "[t]arget trough plasma concentration was achieved with 2 mg/kg weekly intravenous infusions." *Id.* Thus, Watanabe concludes that "[f]urther clinical trials examining the efficacy of MAb 4D5 (MKC-454) with 2–4 mg/kg weekly intravenous infusions is warranted." *Id.*

c. Basegla '96 (Ex. 1007)

Baselga '96 reports the results of a phase II clinical trial in which patients with ErbB2-overexpressing metastatic breast cancer were treated with rhuMAb HER2. Ex. 1013, 737. The pharmacokinetic goal of the trial "was to achieve rhuMAb HER2 trough serum concentrations greater than 10 μg/mL, a level associated with optimal inhibition of cell grown in the preclinical model." *Id.* at 738. Further, the "[s]erum levels of rhuMAb HER2 as a function of time were analyzed for each patient using a one-compartment model." *Id.*

According to the results reported in Basegla '96, "[m]ore than 90% of the examined population (41 patients) had rhuMAb HER2 trough levels above the targeted 10 μg/mL level." *Id.* at 739. Moreover, the treatment "was remarkably well tolerated." *Id.* "Toxicity [from rhuMAb HER2] was minimal," and no immune response against the antibody was detected. *Id.* at 737. Out of the 768 times rhuMAb HER2 was administered, "only 11 events occurred that were considered to be related to the use of the antibody." *Id.* at 739. Baselga '96 also teaches that in preclinical studies (both in vitro and in

xenografts), rhuMAb HER2 "markedly potentiated the antitumor effects of several chemotherapeutic agents, including cisplatin, doxorubicin, and paclitaxel, without increasing their toxicity." *Id.* at 743.

d. Pegram '98 (Ex. 1009)

Pegram '98 reports the results of a phase II clinical trial using a combination of rhuMAb HER2 plus cisplatin. Ex. 1014, 2659. Pegram '98 states that "[t]hese studies showed that the pharmacokinetics of rhuMAb HER2 were predictable, and that the doses delivered achieved a target trough serum concentration of 10 to 20 μg/mL, which is associated with antitumor activity in preclinical models." *Id.* at 2660. Pegram '98 also reports a toxicity profile of the combination that paralleled the toxicity of cisplatin alone, which led to the conclusion that rhuMAb HER2 did not increase toxicity. *Id.* at 2668.

2. Obviousness Based on Slamon, Watanabe, Baselga '96, and Pegram '98

Petitioner has provided a claim-by-claim explanation for the basis of its contention that claims 1–3, 5, 7, 9–11, 16–28, and 30–40 are obvious over the combination of Slamon, Watanabe, Baselga '96, and Pegram '98. Pet. 42–59.

We focus our analysis primarily on the method of treatment recited in independent claim 1. The challenged claims are directed to a dosing regimen for the treatment of cancer in which an anti-ErbB2 antibody is administered at an initial dose, followed by administration of the antibody at subsequent doses that are the same or less than the initial dose and separated in time by at least about two weeks. Independent claim 1 specifies an initial dose of approximately 5 mg/kg, while certain dependent claims specify higher initial doses of 6 mg/kg, 8 mg/kg, or 12 mg/kg (e.g., cls. 2, 3, 9, respectively), whereas other dependent claims specify that the subsequent doses are separated

in time by at least three weeks (e.g., cl. 10). The challenged claims further require administering an effective amount of chemotherapy to the patient.

Petitioner's obviousness contention starts with the teaching in Slamon of a treatment regimen that combined Herceptin with chemotherapy, wherein the Herceptin was administered at a loading dose of 4 mg/kg followed by a weekly maintenance dose of 2 mg/kg. Pet. 28. Petitioner contends that the skilled artisan "would have been motivated to administer trastuzumab as disclosed by Slamon, but would have recognized that weekly administration would be inconvenient for patients, who otherwise would need infusions only once every three weeks." *Id.* at 28–29 (citing Ex. 1003 ¶ 89; Ex. 1017, 1–4). As such, Petitioner contends that the skilled artisan "would have sought to reduce the frequency of trastuzumab administration to align it with the less arduous chemotherapy regimen in order to improve patient convenience." *Id.* (citing Ex. 1003 ¶ 90). In doing so, Petitioner contends that the skilled artisan "would have recognized the importance of maintaining dose intensity, i.e., the amount of drug administered over a period of time." *Id.* (citing Ex. 1003 ¶ 91; Ex. 1024, 1–5; Ex. 1029). "Thus, to account for an every-three-week schedule, a [skilled artisan] would have administered an 8 mg/kg loading dose [4 mg/kg + 2 mg/kg + 2mg/kg], followed by 6 mg/kg maintenance doses [2 mg/kg + 2 mg/kg + 2mg/kg], each administered three weeks apart." *Id.* at 30.

With regard to safety concerns, Petitioner contends, based on Watanabe's disclosure that weekly doses as high as 8 mg/kg were safe and well-tolerated, that a skilled artisan "would not have expected an increase in toxicity, or any other safety concerns, for the higher doses required by the every three week regimen." *Id.* at 31 (citing Ex. 1006, 5; Ex. 1003 ¶¶ 72, 92–93). As noted by Petitioner, "the overall number of severe adverse events was

in fact ***lower*** for the six patients treated at the 8 mg/kg dose than Watanabe disclosed for the 1 mg/kg dose." *Id.* Petitioner also cites other prior art references as teaching that trastuzumab was safe at doses as high as 8 mg/kg. *Id.* at 32 (citing Ex. 1014, 4; Ex. 1012, 11:54–56; Ex. 1015, 2:60–61; Ex. 1018, 48:19–52; Ex. 1013, 4; Ex. 1008, 1).

With regard to efficacy, Petitioner relies upon the prior art's disclosure of a target serum concentration (trough concentration) of 10 µg/ml. *Id.* at 33–34 (citing Ex. 1007, 4; Ex. 1009, 3; Ex. 1006, 5; Ex. 1003 ¶ 96). In determining whether the every-three-week regimen would satisfy this trough concentration, Petitioner relies upon the disclosures in Baselga and Pegram that trastuzumab has a mean half-life of at least one week. *Id.* at 34 (citing Ex. 1007, 5; Ex. 1009, 8; Ex. 1003 ¶ 103). Petitioner points out that "Baselga further discloses that trastuzumab has dose-dependent pharmacokinetics, and therefore a POSA would have understood that its half-life would actually be longer at higher doses." *Id.* at 34–35 (citing Ex. 1003 ¶ 102; Ex. 1007, 3). As such, Petitioner contends that the serum concentration would decrease by no more than three times before the next 6 mg/kg maintenance dose is administered. *Id.* at 35 (citing Ex. 1003 ¶¶ 104–105). Based on an initial serum concentration of 169 µg/ml (calculated based on Pegram's disclosure), Petitioner estimates that approximately 21.1 µg/ml would remain after three weeks, which is above the 10 µg/ml trough concentration required for efficacy. *Id.* at 35–36 (citing Ex. 1003 ¶¶ 1000, 104). Petitioner comes to a similar conclusion based on the pharmacokinetic data disclosed in the 1998 Herceptin label. *Id.* at 38–39.

We are persuaded by Petitioner's arguments as set forth in the Petition at this stage of the proceeding. We address Patent Owner's preliminary

arguments below. In its Preliminary Response, Patent Owner does not argue the claims separately.

Patent Owner first argues that we should deny institution pursuant to 35 U.S.C. § 325(d) because the Examiner, during prosecution of the '379 patent's parent and the '379 patent, considered the teachings of Goldenberg '99,[6] a reference that cites the Slamon abstract and discusses the same Phase III clinical trials in more detail. Prelim. Resp. 20–21. We recognize that Goldenberg '99 contains substantially the same teachings as Slamon with regard to the dosing regimen, but we decline to deny consideration of Petitioner's patentability challenge on that basis.

Under § 325(d), we have discretion to deny a petition that raises substantially the same prior art or arguments previously presented to the Office. Here, when taking the expert declaration of Dr. Ratain into account, Petitioner's testimonial evidence presents the prior art in a new light. For example, there is no basis to suggest that the Examiner considered the calculations set forth by Dr. Ratain showing that a tri-weekly dosing regimen would have resulted in an acceptable trough serum concentration above 10 μg/ml. *See* Ex. 1003 ¶¶ 100–106. Based upon these differences in the current record, we exercise our discretion not to deny the Petition as containing "the same or substantially the same prior art or arguments previously were presented to the Office." *See* 35 U.S.C. § 325(d).

[6] Marvin M. Goldenberg, *Trastuzumab, A Recombinant DNA-Derived Humanized Monoclonal Antibody, a Novel for the Treatment of Metastatic Breast Cancer*, 21 CLINICAL THERAPEUTICS (1999) (hereinafter "Goldenberg '99") (Ex. 2001).

We are also unpersuaded by Patent Owner's preliminary arguments on the merits, which focus primarily on whether it would have been obvious to employ the extended dosing interval required by the claimed methods. In particular, Patent Owner argues that the prior art does not support Petitioner's claim that convenience would have motivated skilled artisans to administer trastuzumab at three-week dosing intervals. Prelim. Resp. 38–43. We recognize that the prior art only explicitly described weekly dosing intervals for administration of the antibody. However, Petitioner has presented a sufficient evidentiary basis on this record, supported by expert testimony, to support its argument that the skilled artisan would have been motivated to use a three week dosing interval in order to align both the antibody and chemotherapy infusion treatments on the same schedule. Furthermore, contrary to Patent Owner's arguments, the prior art need not have expressly articulated or suggested patient convenience as a motivation to extend the dosing interval. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("[T]he [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ."); *Hoffman-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1329 (Fed. Cir. 2014) ("A relatively infrequent dosing schedule has long been viewed as a potential solution to the problem of patient compliance.").

Patent Owner also argues the prior art does not suggest the claimed loading and maintenance doses. Prelim. Resp. 44–46. With regard to Petitioner's assertion that the skilled artisan would apply the concept of "dose intensity" to match the total dose amount provided according to Slamon's regimen in an equivalent three week period, Patent Owner argues that this

approach is flawed because 1) the skilled artisan would not have used the chemotherapy dosing strategy of maintaining dose intensity to adjust the antibody dose; and 2) increasing the dose amount and extending the dosing interval was known to cause higher peak and lower trough concentrations as compared to smaller dose amounts administered more frequently. *Id.* We are unpersuaded by this argument at this stage of this proceeding. As discussed above, Petitioner has presented expert testimony indicating that the skilled artisan would have chosen to apply a strategy of maintaining dose intensity, and that applying such a strategy to a triweekly regimen would have resulted in acceptable serum concentration levels for the antibody during the treatment period. Ex. 1003 ¶¶ 91, 100–106. Patent Owner has not presented any expert testimony of its own at this stage of the proceeding to support its argument that the skilled artisan would not have chosen to take such an approach. We, therefore, decline to give Petitioner's arguments based on expert testimony less weight in comparison to Patent Owner's attorney arguments.

Patent Owner further argues that Petitioner has failed to establish a "reasonable expectation of success" with respect to the dosing regimen's efficacy due to the non-linear kinetics of trastuzumab. Prelim. Resp. 46–50. Patent Owner contends that "[d]espite recognizing that the prior art taught that trastuzumab had documented non-linear kinetics, the foundation of Petitioner's analysis is the application of simple equations that apply only to drugs that exhibit linear kinetics." *Id.* at 47 (citing Ex. 1003 ¶¶51–55). We recognize that the desire for patient convenience must be balanced with the desire for efficacy in determining the appropriate dosing interval, but note that "[c]onclusive proof of efficacy is not necessary to show obviousness." *Hoffmann-La Roche Inc.*, 748 F.3d at 1331. In this regard, we have taken into

account Petitioner's contention that a skilled artisan "would have expected the trough serum concentration to be even higher if its non-linear pharmacokinetics were taken into account." Pet. 36–37 n. 8 (citing Ex. 1003 ¶ 102). Again, without the benefit of expert testimony from Patent Owner at this stage of the proceeding, we decline to give Petitioner's arguments based on expert testimony less weight in comparison to Patent Owner's attorney arguments. As such, we determine that, under the reasonable-likelihood standard for instituting trial, Petitioner has shown a reasonable expectation of success based, *inter alia*, on the calculations set forth in Dr. Ratain's declaration.

Accordingly, based on the foregoing analysis, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing with respect to its obviousness challenge based on the combined prior art teachings of Slamon, Watanabe, Baselga '96, and Pegram '98, in combination with the knowledge of the skilled artisan as set in the declaration of Dr. Ratain.

III. CONCLUSION

We conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that claims 1–3, 5, 7, 9–11, 16–28, and 30–40 of the '379 patent are unpatentable as obvious.

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. Thus, our view with regard to any conclusion reached in the foregoing could change upon consideration of Patent Owner's merits response and upon completion of the current record.

IV. ORDER

Accordingly, it is:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted as to claims 1–3, 5, 7, 9–11, 16–28, and 30–40 of U.S. Patent No. 7,371,379 B2 based on the following ground of unpatentability:

A. Claims 1–3, 5, 7, 9–11, 16–28, and 30–40 under 35 U.S.C. § 103(a) as obvious over Slamon, Watanabe, Baselga ’96, and Pegram ’98;

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of the ’379 Patent is hereby instituted commencing on the entry date of this Order, and 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.

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