

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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HOSPIRA, INC.,  
Petitioner,

v.

GENENTECH, INC.,  
Patent Owner.

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Case IPR2017-00731  
Patent 7,846,441 B1

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

YANG, Administrative Patent Judge.

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

## INTRODUCTION

Hospira, Inc. (“Petitioner”)<sup>1</sup> filed a Petition requesting an *inter partes* review of claims 1–14 of U.S. Patent No. 7,846,441 B1 (Ex. 1001, “the ’441 patent”) on two asserted grounds of unpatentability. Paper 1 (“Pet.”). Genentech, Inc. (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 9 (“Prelim. Resp.”).

We deny institution of an *inter partes* review because on this record, we determine Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim based on one asserted ground. *See* 35 U.S.C. § 314(a). Also on this record, we exercise our discretion under § 325(d) and decline to institute *inter partes* review on the other asserted ground.

### *Related Proceedings*

The ’441 patent issued from Application No. 09/208,649 (“the ’649 application”), filed on December 10, 1998, and claims benefit of priority to provisional application No. 60/069,346, filed on December 12, 1997 (“the ’346 provisional”). Ex. 1001, (21), (22), (60). Also claiming benefit of priority to the ’346 provisional is European Patent EP 1 037 926 B1 (“the EP ’926 patent”). Ex. 1002, (30). Petitioner informs us that the EP ’926 patent is a European counterpart to the ’441 patent and has been invalidated and revoked in two separate European proceedings. Pet. 3 (citing Exs. 1003, 1020, 1021).

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<sup>1</sup> Petitioner identifies Pfizer, Inc. as “the real party in interest for Petitioner.” Paper 13.

Petitioner has concurrently filed IPR2017-000737 and IPR2017-00739, challenging certain claims of U.S. Patent No. 7,892,549, a patent in the same family of the '441 patent. Pet. 3–4; Paper 8, 2–3.

*The '441 Patent*

The '441 patent relates to the treatment of disorders characterized by the overexpression of ErbB2. Ex. 1001, Abstract, 1:11–12.

According to the Specification, “human ErbB2 gene (erbB2, also known as her2, or c-erbB-2), which encodes a 185-kd transmembrane glycoprotein receptor (p185<sup>HER2</sup>) related to the epidermal growth factor receptor (EGFR), is overexpressed in about 25% to 30% of human breast cancer.” *Id.* at 1:23–27. Before the '441 patent, a recombinant humanized anti-ErbB2 monoclonal antibody (a humanized version of the murine anti-ErbB2 antibody 4D5, also referred to as rhuMAb HER2, trastuzumab, or HERCEPTIN®) had been approved to treat patients with ErbB2-overexpressing metastatic breast cancers. *Id.* at 3:34–39.

According to the '441 patent, ErbB2 overexpression was known to be linked to resistance to chemotherapeutic regimens, including anthracyclines. *Id.* at 3:41–49. On the other hand, “the odds of HER2-positive patients responding clinically to treatment with taxanes were greater than three times those of HER2-negative patients.” *Id.* at 3:51–54.

The '441 patent states that

[T]he invention concerns a method for the treatment of a human patient susceptible to or diagnosed with a disorder characterized by overexpression of ErbB2 receptor comprising administering a therapeutically effective amount of a combination of an anti-ErbB2 antibody and a chemotherapeutic agent other than an anthracycline derivative, e.g. doxorubicin or epirubicin, in the absence of an anthracycline derivative, to the human patient.

*Id.* at 4:4–11.

*Illustrative Claim*

Among the challenged claims, claims 1, 11, 13, and 14 are independent. Claim 1 is representative and is reproduced below:

1. A method for the treatment of a human patient with a malignant progressing tumor or cancer characterized by overexpression of ErbB2 receptor, comprising administering a combination of an intact antibody which binds to epitope 4D5 within the ErbB2 extracellular domain sequence and a taxoid, in the absence of an anthracycline derivative, to the human patient in an amount effective to extend the time to disease progression in said human patient, without increase in overall severe adverse events.

*Asserted Grounds of Unpatentability*

Petitioner asserts the following grounds, each of which challenges the patentability of claims 1–14:

<b>Basis</b>	<b>References</b>
§ 103	Baselga '97 <sup>2</sup> and Baselga '94, <sup>3</sup>
§ 103	Baselga '96 <sup>4</sup> and Baselga '94

In support of its patentability challenges, Petitioner relies on the Declaration of Dr. Allan Lipton (Ex. 1007).

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<sup>2</sup> Baselga et al., HER2 Overexpression and Paclitaxel Sensitivity in Breast Cancer: Therapeutic Implications, 11(3) (Suppl. 2) ONCOLOGY 43–48 (1997) (Ex. 1006).

<sup>3</sup> Baselga et al., Anti-HER2 Humanized Monoclonal Antibody (MAb) Alone and in Combination with Chemotherapy Against Human Breast Carcinoma Xenografts, 13 Proc. AM. SOC. CLIN. ONCOL. 63 (Abstract 53) (1994) (Ex. 1005).

<sup>4</sup> Baselga et al., Phase II Study of Weekly Intravenous Recombinant Humanized Anti-p185<sup>HER2</sup> Monoclonal Antibody in Patients with HER2/*neu*-Overexpressing Metastatic Breast Cancer, 14 J. CLIN. ONCOL. 737–44 (1996) (Ex. 1004).

## 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); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). 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). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to expressly construe any claim terms.

### *Disclosures of Asserted Prior Art*

#### Baselga '94

Baselga '94 teaches that HER2 overexpressing tumors were grown in nude mice followed by treatment with the 4D5-antibody in combination with paclitaxel. Ex. 1005, 4. Although the antibody or paclitaxel alone produced 35% growth inhibition, the combination of the two resulted in 93% growth inhibition without increasing toxicity. *Id.*

Baselga '96

Baselga '96 reports the results of a phase II clinical trial in patients with ErbB2-overexpressing metastatic breast cancer who had received extensive prior therapy. Ex. 1004, 9. Each patient received a loading dose of 250 mg of intravenous rhuMAb HER2, followed by 10 weekly doses of 100 mg. *Id.* at 10. According to Baselga '96, “[a]dequate pharmacokinetic levels of rhuMAb HER2 were obtained in 90% of the patients. Toxicity was minimal and no antibodies against rhuMAb HER2 were detected in any patients.” *Id.* at 9. Objective responses were seen with an 11.6% remission rate. *Id.* In addition, “[t]he median time to progression for the patients with either minor or stable disease was 5.1 months.” *Id.* at 12.

Baselga '97

Baselga '97 states that HER2 positive tumors “have increased resistance to adjuvant CMF (cyclophosphamide, methotrexate, and fluorouracil)-based therapy and, conversely, increased dose-response effects to an anthracycline-containing regimen.” Ex.1006, 7. But, according to Baselga '97, “despite the association of HER2 overexpression with poor prognosis, the odds of HER2-positive patients responding clinically to taxanes were greater than three times those of HER2-negative patients.” *Id.* at 6.

Baselga '97 reviews the results of Baselga '94 and Baselga '96. *Id.* at 9. According to Baselga '97:

Results from the phase II studies and the activity of rhuMoAb HER2 against xenografts when given in combination with doxorubicin and paclitaxel have been encouraging. These positive results have led to the design of a phase III multinational study of chemotherapy in combination with rhuMoAb HER2 in patients with HER2-overexpressing breast tumors who have not

received prior chemotherapy for metastatic disease.

*Id.* at 10.

In Baselga '97, patients received either cytotoxic chemotherapy alone or rhuMoAb HER2 in combination with chemotherapy. *Id.* at 10. The chemotherapy regimen was selected based on whether the patients had been previously treated with anthracyclines (e.g., doxorubicin or epirubicin). *Id.* Patients not previously treated with anthracyclines were administered a combination of cyclophosphamide and doxorubicin or epirubicin, whereas patients received anthracycline therapy in the adjuvant setting were treated with paclitaxel. *Id.* Baselga '97 comments that “[b]ecause anthracyclines are widely used in the adjuvant setting, it is likely that a significant number of patients will be treated with paclitaxel ± rhuMoAb HER2.” *Id.*

*Asserted Obviousness over Baselga '97 and Baselga '94*

Petitioner contends that claims 1–14 would have been obvious over the teachings of Baselga '97 and Baselga '94. Pet. 25–41. Because, during the prosecution of the '649 application, which issued as the challenged '441 patent, the applicant successfully antedated Baselga '97, we exercise our discretion under 35 U.S.C. § 325(d) and decline to institute *inter partes* review on this ground.

Institution of an *inter partes* review is discretionary. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that under § 314(a), “the PTO is permitted, but never compelled, to institute an IPR proceeding”). Under 35 U.S.C. § 325(d), in determining whether to institute an *inter partes* review, we “may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.”

In this case, in an office action dated December 7, 1999, the examiner rejected the then-pending claims as anticipated by Baselga '97. Ex. 1011, vol. 1, 379. In response, the applicant attempted to distinguish over the reference. *Id.* at 398. The applicant later submitted a declaration by the inventor under 37 C.F.R. §1.131, together with certain evidence, to antedate Baselga '97. Ex. 1011, vol. 2, 37, 118–47. In an office action dated January 9, 2001, the examiner found that neither the argument nor the declaration was persuasive. *Id.* at 213–14. As a result, the examiner continued to reject the claims as unpatentable over Baselga '97. *Id.* at 212–14. In response, the applicant submitted another declaration by the inventor under 37 C.F.R. §1.131, accompanied by additional evidence, to antedate Baselga '97. *Id.* at 230–31, 237–312. Thereafter, the examiner withdrew the rejection based on Baselga '97, stating that “[t]he declaration filed on 5/07/2001 under 37 CFR 1.131 is sufficient to overcome the Baselga (1997).” *Id.* at 324. Petitioner does not present additional evidence or persuasive arguments in this proceeding for us to reach a different conclusion with respect to Baselga '97.

Under these circumstances, we exercise our discretion under § 325(d) and decline to institute *inter partes* review based on the combination of Baselga '97 and Baselga '94.

*Asserted Obviousness over Baselga '96 and Baselga '94*

Petitioner contends that claims 1–14 would have been obvious over the teachings of Baselga '96 and Baselga '94. Pet. 42–58. Based on the current record, we determine Petitioner has not established a reasonable likelihood that it would prevail on this assertion.

Each challenged claim recites a treatment method comprising administering the combination of an anti-ErbB2 antibody and a taxoid, and



“in the absence of an anthracycline derivative.” To account for this limitation, Petitioner argues that (1) the cardiotoxicity of anthracycline derivatives was well known in the prior art; (2) both preclinical and clinical studies employed the combination of an anti-ErbB2 antibody “with paclitaxel *or* anthracycline, *not* together;” and (3) Baselga ’94 shows that the combination with paclitaxel was superior to the combination with doxorubicin, an anthracycline derivative. Pet. 45–46. Patent Owner counters that Petitioner has not shown an ordinary artisan would have avoided anthracyclines when pursuing the combination therapy of anti-ErbB2 antibody with a taxoid. Prelim. Resp. 52. We agree with Patent Owner.

Petitioner is correct that cardiotoxicity of anthracyclines was well known at the time of the ’441 patent invention. *See, e.g.*, Ex. 1033. Yet, Petitioner concedes that “[a]nthracyclines were and remain common first-line chemotherapies for breast cancer.” Pet. 13. Thus, cardiotoxicity does not appear to have motivated an ordinary artisan to avoid anthracyclines in treating breast cancer.

Indeed, Baselga ’94 reports preclinical data combining anti-ErbB2 antibody with either paclitaxel or an anthracycline. Ex. 1005, 4. Here, Petitioner is correct that Baselga ’94 shows the combination with paclitaxel resulted in 93% inhibition of tumor growth, more than the 70% inhibition achieved by the combination with doxorubicin. *Id.* Baselga ’94, however, does not appear to accord much significance to this alleged superiority of the anti-ErbB2 antibody/paclitaxel combination. Instead, it concludes that “anti HER2 MAbs can eradicate well established tumors and enhance the activity of paclitaxel and doxorubicin against human breast cancer xenografts.” *Id.*

Even two years later, when referring to this study, Baselga '96 similarly does not suggest that an ordinary artisan would have avoided anthracyclines. *See* Ex. 1004, 15 (“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. Laboratory studies of the mechanism of this effect and clinical trials of such combination therapy are currently in progress.”).

We acknowledge that Baselga '94 teaches a pre-clinical study using mice that combined anti-ErbB2 antibody with *either* paclitaxel or an anthracycline, but not the anti-ErbB2 antibody with *both* paclitaxel and an anthracycline. Without additional credible evidence<sup>5</sup> or persuasive argument, however, this fact is insufficient to suggest that an ordinary artisan would have avoided anthracyclines while pursuing the combination therapy with anti-ErbB2 antibody and a taxoid in a treatment regimen for humans. As a result, based on the current record, we conclude Petitioner has

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<sup>5</sup> In the concurrently issued decision to institute trial in IPR2017-00737, we conclude that Petitioner has made a sufficient showing regarding the limitation “in the absence of an anthracycline derivative.” IPR2017-00737, Paper 17, 21–23. There, we take into consideration the disclosures of Baselga '97 and a second prior-art reference. *Id.* We also find the testimony of Dr. Litton on this issue persuasive. *Id.* The record in the present proceeding, however, is different. As explained above, Baselga '97 was removed from consideration as prior art for the two-drug combination treatment recited in the claims of the '441 patent during prosecution and, as we do not revisit the antedating issue here, it is not part of our analysis. Also, the second prior art reference in IPR2017-00737 is not of record in this proceeding and Petitioner does not present persuasive expert testimony on this issue.

not established a reasonable likelihood it would prevail in showing that any challenged claim would have been obvious over the teachings of Baselga '96 and Baselga '94.

#### CONCLUSION

On this record, Petitioner has not demonstrated a reasonable likelihood of prevailing on its challenges to the patentability of any challenged claim of the '441 patent based on the combination of Baselga '96 and Baselga '94. Also on this record, we exercise our discretion under § 325(d) and decline to institute *inter partes* review based on the combination of Baselga '97 and Baselga '94.

#### ORDER

Accordingly, it is

ORDERED that Petitioner's request for an *inter partes* review of claims 1–14 of the '441 patent is *denied* and no *inter partes* review is instituted.

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