Trials@uspto.gov
Tel: 571-272-7822

Paper 16
Entered: July 27, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HOSPIRA, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-00739
Patent 7,892,549 B2

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

POLLOCK, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 325(d) and 37 C.F.R. § 42.108

I. INTRODUCTION

Hospira, Inc. ("Petitioner")[1] filed a Petition requesting an *inter partes* review of claims 1–11 and 14–17 of U.S. Patent No. 7,892,549 B2 (Ex. 1101, "the '549 patent"). Paper 1 ("Pet."). Genentech, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). Based on the particular circumstances of this case, we exercise our discretion under 35 U.S.C. § 325(d) and 37 C.F.R. § 42.108 and do not institute an *inter partes* review of the challenged claims.

A. Related Applications and Proceedings

In addition to this proceeding, Petitioner has challenged claims 1–17 of the '549 Patent in IPR2017-00737. The '549 Patent shares substantially the same specification with U.S. Patent No. 7,846,441 B2 ("the '441 Patent), and is related as follows. The '549 Patent issued from Application No. 10/356,824, filed February 3, 2003 ("the '824 Application"), which is a continuation of Application No. 09/208,649, filed Dec. 10, 1998 ("the '649 Application"), and claims benefit of priority to Provisional Application No. 60/069,346, filed Dec. 12, 1997 ("the '346 Provisional Application"). Ex. 1101, [21], [63], [60], 1:4–9. The '441 Patent issued from the '649 Application and is presently the subject of IPR2017-00731.

Petitioner has also filed IPR2017-00804 and IPR2017-00805 involving the claims of U.S. Patent Nos. 6,627,196 and 7,371,379, respectively. These two patents are not in the chain of priority of the '549 and '441 Patents but relate to subject matter similar to that at issue here. Petitioner also directs us to invalidation and revocation proceedings involving European Patent EP 1,037,926, which also

[1] Petitioner identifies Pfizer, Inc. as "the real party in interest for Petitioner." Paper 10, 2.

claims benefit of priority to the '346 Provisional Application. *See* Pet. 1–2 (citing Ex. 1104, 1126, and 1149).

B. The '549 Patent and Relevant Background

According to the Specification, 25% to 30% of human breast cancer patients overexpress a 185-kD transmembrane glycoprotein receptor ($p185^{HER2}$), also known as HER2 (human epidermal growth factor receptor-2) or ErbB2. Ex. 1101, 1:21–32, 5:16–21. These HER2-positive cancers are associated with poor prognoses and resistance to many chemotherapeutic regimens including anthracyclines (e.g., doxorubicin or epirubicin). *Id*. at 3:43–52, 4:11–12, 11:41–45. Conversely, patients with HER2-positive cancers are three times more likely to respond to treatment with taxanes than those with HER2 negative tumors. *Id*. at 3:52–56 (citing Baselga '97 (Ex. 1107)).

Although "ErbB2 overexpression is commonly regarded as a predictor of poor prognosis," "a humanized version of the murine anti-ErbB2 antibody 4D5, referred to as rhuMAb HER2 or HERCEPTIN® [or trastuzumab] has been clinically active in patients with ErbB2-overexpressing metastatic breast cancers that had received extensive prior anti-cancer therapy." Ex. 1001, 3:35–61 (citing Baselga '96 (Ex. 1105)). Anti-ErbB2 4D5 antibodies also "enhance the activity of paclitaxel (TAXOL®) and doxorubicin against breast cancer xenographs in nude mice injected with BT-474 human breast adenocarcinoma cells, which express high levels of HER2." *Id*. at 3:56–61 (citing Baselga '94 (Ex. 1106)).

According to the Specification,

> The present invention concerns the treatment of disorders characterized by overexpression of ErbB2, and is based on the recognition that while treatment with anti-ErbB2 antibodies markedly enhances the clinical benefit of the use of chemotherapeutic agents in general, a syndrome of myocardial dysfunction that has been observed

> as a side-effect of anthracycline derivatives is increased by the administration of anti-ErbB2 antibodies.

Id. at 3:65–4:5.

The '549 Patent thus relates to the treatment of breast cancers that overexpress HER2/ErbB2 "comprising administering a therapeutically effective amount[2] 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 4:6–13. In some embodiments, the anti-ERbB2 antibody of the combination is Herceptin and the chemotherapeutic agent "is a taxoid, such as TAXOL® (paclitaxel) or a TAXOL® derivative." *Id*. at 4:23–25. The combination may further include one or more additional anti-ErbB2 antibodies, "antibodies which bind to the EGFR . . . ErbB3, ErbB4, or vascular endothelial factor (VEGF)," "one or more cytokines,"or "a growth inhibitory agent." *Id*. at 23:60–24:5, 25:20–34; *see also id.* at 11:4–40 (defining "chemotherapeutic agent" and "growth inhibitory agent").

The '549 Patent also provides an Example disclosing the conduct and results of a clinical trial involving 469 women with metastatic HER2-positive breast cancer *Id*. at 26:34–30:25. All patients were treated with one of two chemotherapy regimens (CRx) designated either "AC" for anthracycline (doxorubicin or epirubicin) and cyclophosphamide, or "T" for Taxol (paclitaxel). *See id*. at 28:5–47; 29:13–30:12. Half of the patients were also treated with the anti-ERbB2 antibody Herceptin, designated "H". *Id*. The Specification discloses

---

[2] The Specification defines a "therapeutically effective amount" of the combination as "an amount having an antiproliferative effect," which can be measured by assessing the time to disease progression (TTP) or determining the response rates (RR)." *Id*. at 10:41–50.

that "[a]t a median follow-up of 10.5 months, assessments of time to disease progression (TTP in months) and response rates (RR) showed a significant augmentation of the chemotherapeutic effect by HERCEPTIN®, without increase in overall severe adverse events (AE)." *Id*. at 29:13–18. According to the inventors:

> These data indicate that the combination of anti-ErbB2 antibody treatment with chemotherapy markedly increases the clinical benefit, as assessed by response rates and the evaluation of disease progression. However, due to the increased cardiac side-effects of doxorubicin or epirubicin, the combined use of anthracyclines with anti-ErbB2 antibody therapy is contraindicated. The results, taking into account risk and benefit, favor the combined treatment with HERCEPTIN® and paclitaxel (TAXOL®).

Id. at 30:17–25.

C. Challenged Claims

Petitioner challenges claims 1–11 and 14–17. Pet. 4. Claims 1, 5, and 16 are independent. Claim 1 requires "administering a combination" of three agents—an anti-ErbB2 antibody, a taxoid, and "a further growth inhibitory agent"—"in an amount effective to extend the time to disease progression:"

> 1. A method for the treatment of a human patient with breast cancer that overexpresses ErbB2 receptor, comprising administering a combination of an antibody that binds ErbB2, a taxoid, and a further growth inhibitory agent to the human patient in an amount effective to extend the time to disease progression in the human patient, wherein the antibody binds to epitope 4D5 within the ErbB2 extracellular domain sequence.

Independent claim 16 is similar to claim 1, but further includes a negative limitation requiring the administration of the three agents "in the absence of an anthracycline derivative."

Independent claim 5 is also similar to claim 1, but specifies that the taxoid is paclitaxel. Depending from claims 1 and 5, respectively, claims 2 and 7 require that the 4D5 anti-ErB2 antibody is humanized.

Claim 5 also differs from claims 1 and 16 in reciting a "further therapeutic agent," rather than the "further growth inhibitory agent" of claims 1 and 16. Claims depending from claim 5 variously specify that this "further therapeutic agent" is "another ErbB2 antibody, EGFR antibody, ErbB3 antibody, ErbB4 antibody, vascular endothelial growth factor (VEGF) antibody, cytokine, [or] growth inhibitory agent" (claim 11; *see* claims 12–14)[3], wherein the growth inhibitory agent may be "a DNA alkylating agent" (claim 15).

D. The Asserted Prior Art and Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability (Pet. 4):

Ground	Reference	Basis	Claims
1	Nabholtz[4]	102(b)	1–8, 10–11, and 14–17
2	Leyland-Jones[5]	102(a)	1–11 and 14–17

[3] Claims 12 and 13, respectively, recite that the further therapeutic agent is "another ErbB3 antibody" and "a vascular endothelial growth factor (VEGF) antibody." As set forth in section II(D), below, Petitioner does not assert that these claims are unpatentable in this Petition.

[4] Nabholtz et al., *Results of Two Open-Label Multicentre Pilot Phase II Trials with Herceptin® in Combination with Docetaxel and Platinum Salts (Cis- or Carboplatin) (TCH) as Therapy for Advanced Breast Cancer In Women with Tumors Over-Expressing HER2*, 64(1) BREAST CANCER RESEARCH AND TREATMENT 82 (Abstract 327) (2000). Ex. 1114.

[5] Leyland-Jones et al., *Phase III Comparative Study of Trastuzumab and Paclitaxel With and Without Carboplatin in Patients with HER-2/neu Positive Advanced Breast Cance*r, 76(Suppl. 1) BREAST CANCER RESEARCH AND TREATMENT S37 (Abstract 35) (2002). Ex. 1150.

Ground	Reference	Basis	Claims
3	Yardley[6]	102(a)	1–11 and 14–17

Petitioner also relies on Ex. 1111, the declaration of its technical expert, Allan Lipton, MD.

II. ANALYSIS

Petitioner challenges claims 1–11 and 14–17 as anticipated by one or more of Nabholtz, Leyland-Jones, and Yardley. *See* Pet. 4, 24–55. Petitioner contends that each of the asserted references qualifies as prior art under 35 U.S.C. § 102(a) or (b) because the challenged claims are not entitled to an earlier priority date with respect to the three-part combinations such that, "the date of the claimed invention is no earlier than February 3, 2003 (the filing date of the '549 patent's claims)." *Id*. at 19; *see id*. at 4–5, 15–19.

Patent Owner responds that, "[d]uring prosecution, the examiner determined that the challenged claims are entitled to priority to the provisional application filed on December 12, 1997, and therefore withdrew a rejection based upon the same Nabholtz reference (Ex. 1114) that Petitioner asserts in Ground 1." Prelim. Resp. 1. Patent Owner argues that the Board should deny the instant Petition under 35 U.S.C. § 325(d) because "[t]he Patent Office has already decided the dispositive issue for this petition" as neither Nabholtz nor the later-published Leyland-Jones and Yardley references qualify as prior art with respect to the '549 Patent. *Id*. For the reasons that follow, we agree with Patent Owner.

---

[6] Yardley et al., *Final Results of the Minnie Pearl Cancer Research Network First-Line Trial of Weekly Paclitaxel/Carboplatin/Trastuzumab in Metastatic Breast Cancer*, 76 (Suppl. 1) BREAST CANCER RESEARCH AND TREATMENT S113 (Abstract 439) (2002). Ex. 1153.

Before addressing the details of parties' arguments, we discuss the relevant portions of the prosecution history.

A. Relevant Prosecution History.

As indicated in section I(B), above, the '549 Patent issued from the '824 Application, filed February 3, 2003, which is a continuation of the '649 Application, filed Dec. 10, 1998. The '649 Application claims benefit of priority to the '346 Provisional Application, filed Dec. 12, 1997. *See* e.g., Ex. 1101, 1:4–8. The Specifications of both the '649 Application and the '346 Provisional Application are substantially identical to that of the '549 Patent. *See, e.g.*, Prelim. Resp. 3. Because Nabholtz, Leyland-Jones, and Yardley were published after the filing date of the '649 Application, we focus our attention on the disclosure of '649 Application.

The inventors of the '549 Patent first claimed the administration of a three-part combination with the filing of the '824 Application on February 3, 2003. *Cf.* Ex. 1121, 45–46 and Ex. 1119-1, 47. Representative of those claims, claim 20 of the '824 Application recited "a combination of an antibody that binds ErbB2, a taxoid and *a further chemotherapeutic agent*." *Id*. at 47 (emphasis added).

In the first substantive office action, dated June 2, 2006, the Examiner rejected these claims under 35 U.S.C. § 112, first paragraph, for lack of enablement. Ex. 1119-5, 34, 38–41. According to the Examiner, "it does not appear predictable that all antibodies that bind to Her–2/neu will predictably increase the time to disease progression when combined with paclitaxel and a further chemotherapeutic agent." *Id*. at 39. Thus, according to the Examiner, while the Specification is "enabling for methods comprising the administration of Herceptin®, a taxoid and a further chemotherapeutic agent in amounts to extend time to disease progression," it "does not reasonably provide enablement for

methods comprising the use or administration of all anti-Her-2/neu antibodies in combination with a taxoid and a further chemotherapeutic agent." *Id*. at 38–40; *see id*. at 288.

In determining whether then-pending claim 20 and similar claims were entitled to benefit of priority of an earlier-filed application, the Examiner stated:

> The claims presently under examination are drawn to method comprising the administration of an anti-erbB2 antibody, a taxoid and a further chemotherapeutic agent. *Parent application 09/208,649 provides support for the combination of a anti-erbB2 antibody and a taxoid, and appears to provide support for the combination of an anti-erbB2 antibody and any chemotherapeutic agent and further* a another antibody that may bind to EGFR, ErbB3, ErbB4 or VEGF; or further a cytokine or *a growth inhibitory agent*. However, the specific method of combining an anti-ErbB2 antibody with a taxoid and a further chemotherapeutic agent does not appear to have been contemplated, nor the specific method of combining an anti-ErbB2 antibody with a taxoid and carboplatin [as set forth in then-pending independent claim 32].

Id. at 41–42 (emphasis added). Based on this initial priority determination, the Examiner rejected those claims under § 102(b) as anticipated by Nabholtz (Ex. 1114), which is the same invalidity theory as Ground I of the instant Petition. *Id*. at 42; Pet. 4, 24–35.

In an amendment filed September 12, 2006, Applicants addressed the enablement rejection by amending independent claims 20 and 32 to recite, "wherein the antibody inhibits proliferation of human breast cancer cells that overexpress ErbB2 receptor and induces antibody-dependent cellular cytotoxicity (ADCC)." *See Ex.* 1119-5, 171, 174–178. In accordance with the Examiner's statement that "application 09/208,649 . . . appears to provide support for the combination of an anti-erbB2 antibody and any chemotherapeutic agent and further . . . a growth inhibitory agent," Applicants also amended claim 20 to recite "a combination of an antibody that binds ErbB2, a taxoid and a further *growth*

inhibitory agent." *Id*. at 41–42, 171, 174, 179 (emphasis added). Applicants pointed to support for the latter amendment "at least on page 37, lines 9–18, page 35, lines 6–14, and page 16, lines 11–24" of the '649 Specification." *Id*. at 174. The referenced passages recite:

> A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, especially an ErbB2-overexpressing cancer cell either in vitro or in vivo. Thus, the growth inhibitory agent is one which significantly reduces the percentage of ErbB2 overexpressing cells in S phase. Examples of growth inhibitory agents include agents that block IE cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), TAXOL®, and topo II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C . . . .

Ex. 1121, 20 (16:11–24);

> The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. For example, it may be desirable to further provide antibodies which bind to EGFR, ErbB2 (e.g. an antibody which binds a different epitope on ErbB2), ErbB3, ErbB4, or vascular endothelial factor (VEGF) in the one formulation. Alternatively, or in addition, the composition may comprise a cytotoxic agent, cytokine or growth inhibitory agent, provided that the cytotoxic agent is other than an anthracycline derivative, e.g. doxorubicin, or epirubicin. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

id. at 39 (35:6–14); and

> It may be desirable to also administer antibodies against other tumor associated antigens, such as antibodies which bind to the EGFR, ErbB3, ErbB4, or vascular endothelial factor (VEGF). Alternatively, or in

> addition, two or more anti-ErbB2 antibodies may be co-administered to the patient. Sometimes, it may be beneficial to also administer one or more cytokines to the patient. In a preferred embodiment, the ErbB2 antibody is co-administered with a growth inhibitory agent. For example, the growth inhibitory agent may be administered first, followed by the ErbB2 antibody. However, simultaneous administration or administration of the ErbB2 antibody first is also contemplated. Suitable dosages for the growth inhibitory agent are those presently used and may be lowered due to the combined action (synergy) of the growth inhibitory agent and anti-ErbB2 antibody.

id. at 41 (37:9–18).

Applicants also argued that claim 32, directed to the specific 3-part combination of "an antibody that binds ErbB2, a taxoid and carboplatin" was supported in the '649 Application at:

> - Page 5, lines 4–5 referring to "chemotherapeutic regimens" (emphasis added);
>
> - Page 5, lines 14–17 stating that "treatment with anti-ErbB2 antibodies markedly enhances the clinical benefit of the use of *chemotherapeutic agents in general*" (emphasis added);
>
> - Page 37, line 2 which refers to "dosing schedules for such chemotherapeutic agents" (emphasis added), "such chemotherapeutic agents" being other than an anthracycline derivative (page 36, lines 26–27) and including carboplatin and taxoids (page 16, lines 1–10) . . . .

Ex. 1119-5, 180; *see* Ex. 1121, 9 (5:4–5, 14–17), 41 (37:2). Applicants pointed to additional support for the 3-part combination of anti-ErbB2 antibody, taxoid, and carboplatin, at page 35, line 6 of the '649 Specification, which provides support for combining "more than one active compound." *Id.*; *see* Ex. 1121, 39 (35:6).

In a subsequent office action, dated September 11, 2007,[7] the Examiner maintained that claim 32, directed to a three-drug combination comprising carboplatin, was not supported by the earlier applications; maintained the enablement rejection of claims 20 and 32 because the Specification did not appear to contemplate anti-ErbB2 antibodies other than based on the 4D5 epitope; and further determined that the then-pending claims were not entitled to benefit of priority because they were "drawn to methods of treating human patients with breast cancer that *expresses* ErbB2 receptor, whereas the disclosures of the parent applications teach the treatment of breast cancer that *overexpresses* ErbB2 receptor." Ex. 1119-5, 286, 290–93 (emphasis added). Although the Examiner determined that claim 20 was still not entitled to benefit of priority, she expressly stated that "the specifications of the parent applications . . . generally teach[] combining an anti-ErbB2 antibody with a taxoid and a further agent which is . . . a growth inhibitory agent . . . ." *See id*. at 292–93.

On January 28, 2008, Applicants engaged in an Examiner interview, wherein, according to the Examiner's Interview Summary, the parties "[d]iscussed proposed amendments and arguments, which appear to overcome rejections of record under 112, first, 112, 2nd and 102(b)." Ex. 1119-6, 241. Shortly thereafter, on February 8, 2008, Applicants submitted an amendment cancelling claims 1–33, including claim 32 reciting the three-drug carboplatin combination, and amending certain independent claims to recite methods "for the treatment of a human patient with breast cancer that *over*expresses ErbB2 receptor." Ex. 1119-5, 303–304 (emphasis added). Upon entry of that amendment, then-pending claim 34 was

[7] We note that although Petitioner relies on the Office Action dated December 5, 2006 (*see* Pet. 13–14), the Examiner vacated that Action in the September 11, 2007 Office Action. Ex. 1119-5, 288.

identical to claim 1 of the '549 patent. *Cf. id.* at 303, claim 34 with Ex. 1001, claim 1.

Applicants also amended then-pending claim 38 to recite the three-part combination of "an anti-ErbB2 antibody which binds to epitope 4D5 within the ErbB2 extracellular domain sequence, a taxoid, and a further therapeutic agent." Ex, 1119-5, 303. With respect to support for the claimed "further therapeutic agent" (as is recited in claim 16 of the '549 Patent), Applicants cited

> [P]age 37, lines 7-29 which provides support for the inclusion of a genus of further therapeutic agents in addition to the anti-ErbB2 antibody and chemotherapeutic agent (*e.g.* the taxoid), such as another ErbB2 antibody, EGFR antibody, ErbB3 antibody, ErbB4 antibody, vascular endothelial growth factor (VEGF) antibody, cytokine, or growth inhibitory agent.

Id. at 306; *see also* Ex. 1121, 40–41 (36:26–37:18) (corresponding passage from '649 Application).

In response to the February 8, 2008 amendments, the Examiner withdrew all rejections under 35 U.S.C. § 112, and determined that the then-pending claims have priority to the '346 Provisional Application (and, thus, to the substantially identical '649 Application). *See* Ex. 1119-6, 244–45. The Examiner then withdrew the § 102(b) rejection over Nabholtz "in view of the amendment to the claims so that now the claims have priority to parent application 60/069,346 (filed 12/12/1997)." *Id*. at 245.

The '649 Patent ultimately issued after further arguments and amendments not directly relevant this Decision. *See e.g.*, Ex. 1119-7, 93 (Notice of Allowability dated October 8, 2010).

B. The Parties' Arguments

Petitioner argues that the '739 Patent is not entitled to benefit of priority of the '649 Application because the challenged claims fail to satisfy the written

description and enablement requirements of 35 U.S.C. § 112, first paragraph. *See* Pet. 15–19. We address those contentions in turn.

a. *Written Description*

With respect to written description, Petitioner argues that, "[t]here is no disclosure of any method of treatment in which the claimed three-drug combination is administered." *Id*. at 16. Patent Owner responds that during prosecution leading to the issuance of the 549 Patent, Applicants

> established priority for those claims based upon the parent application's specific disclosure of using growth inhibitory agents as part of the present invention. (Ex. 1119-5 at 179 (citing Ex. 1121 at 20 (16:11-24), 39 (35:6-14), 41 (37:9-18).) Based upon that disclosure, the examiner agreed that the claims reciting a combination with "a further growth inhibitory agent" were supported by, and thus entitled to priority to, the parent applications. (Ex. 1119-5 at 41; *id*. at 292-93; Ex. 1119-6 at 245.)

Prelim. Resp. 10–11; *see also id*. 11, n.3 (arguing that Applicant demonstrated support for a three-part combination comprising a "further therapeutic agent"). Having considered the Specification of the '649 Application and the arguments raised during prosecution, as discussed section II(B), above, Petitioner has not presented any further evidence in this proceeding that would persuade us to reach a conclusion different from the Examiner's position that the challenged claims are adequately disclosed in the priority document.

b. *Enablement*

Petitioner further argues that the challenged method claims involving the three-drug combinations are not entitled to benefit of priority because the earlier applications do not disclose clinical results demonstrating that the use of those combinations were enabled. *See* Pet. 17–19; Ex. 1111 ¶¶ 53–55. Petitioner argues that Applicant's statement to the Examiner "that '**data from clinical trials of the**

combination are needed to demonstrate that they can be usefully combined,'" flatly contradicts Patent Owner's position that the '649 Application and '346 Provisional Application adequately disclose the claimed invention. Pet. 17–18 (citing Ex. 1119-5, 308–09). We do not find Petitioner's argument persuasive. As an initial matter, Petition fails to address the "*Wands*" factors in its enablement analysis. *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Moreover, considered in context, we read the thrust of Applicants' argument as indicating that clinical trials were necessary to establish that anti-ErbB2 antibodies could be efficaciously combined with known chemotherapies—as was demonstrated in the '549 Patent's Example. *See* Ex. 1101, 29:12–30:25 (showing response rates and time to disease progression for combinations of anti-ErbB2 antibodies with either anthracycline and cyclophosphamide (AC) or taxol (T). In particular, the passage Petitioner cites derives from Applicants' argument that the Perez reference teaches that, although

> both 'paclitaxel and carboplatin have significant single-agent activity' . . . only their ongoing trial of the combination [] would 'answer the question of the potential role of this combination.' In other words, Perez supports the notion that even if individual agents are known for cancer therapy, data from clinical trials of the combination are needed to demonstrate that they can be usefully combined. Moreover, even if Perez provides an invitation to experiment with the combination of paclitaxel/carboplatin, this would not have provided a reasonable prediction as to the efficacy of a biologic such as rhuMAb HER2 with chemotherapy, such as a taxoid, particularly given the state of the art at the filing date at which time no biologic had been approved in the US for therapy of a solid tumor, such as breast cancer.

Ex. 1119-5, 308–309. In that same Response, Applicants also argued that Baselga 1996 "did not reveal whether the addition of rhuMAb HER2 antibody to chemotherapy could extend TTP in patients compared to antibody or chemotherapy alone." Ex. 1119-5, 308. We also note that as of the filing date of

the '649 Application, the combination of paclitaxel and another platinum-based chemotherapeutic (cisplatin) was known to be effective in the treatment of metastatic breast cancer. *See* Ex. 1125; Ex. 1111 ¶¶ 29–30, 73; *see also* copending IPR2017-00739, Paper 1 at 16–17 (Petitioner's arguments that "[d]rug combinations, generally, including two- and three-agent combinations, were routinely used to fight cancer, including breast cancer," and that "the combination of paclitaxel with cisplatin was also known to be synergistic").

Accordingly, we agree with Patent Owner that Applicants' argument was intended to "support[] the patentability of the pending claims, not that the results of clinical trials were necessary to render obvious the claimed three-drug combination." *See* Prelim. Resp. 12.

Petitioner also argues that "to obtain earlier priority for claims directed to an 'effective' use of a cancer drug treatment, the inventor must 'provide experimental proof that his invention could be effective in treating cancer.'" Pet. 18–19 (citing *Rasmusson v. SmithKline Beecham Corp*., 413 F.3d 1318, 1324 (Fed. Cir. 2005). We do not read *Rasmusson* so broadly. The Court in *Rasmusson* noted that,"[t]he Board found that a person of ordinary skill in the art would not have believed that finasteride was effective in treating prostate cancer simply because finasteride was known to be a selective 5αR inhibitor. . . . because the anti-tumor effects shown by published experiments involving multi-active 5αR inhibitors could be attributable to contaminating activities having no relation to 5αR inhibition." 413 F.3d at 1324. Moreover, "Rasmusson did not make any contrary showing that a person of ordinary skill . . . would have recognized that a selective 5αR inhibitor . . . would have been effective in treating prostate cancer. *Id.* Accordingly, in order to obtain an earlier priority date, "Rasmusson needed to provide experimental proof that his invention could be effective in treating cancer." *Id*.

In comparison to *Rasmusson*, the present case is not so lacking in evidence. As discussed in section I(B), above, the '649 Application presents clinical results demonstrating the effectiveness of 2-part combinations comprising anti-ErbB2 antibodies and various chemotherapeutic agents, including paclitaxel. In addition, Petitioner admits in a co-pending Petition involving the same patent, that multi-drug combinations of chemotherapy agents were routinely used to treat breast cancer. *See* IPR2017-00739, Paper 1 at 17.[8]

For these reasons, we find the instant case distinguishable from *Rasmusson* and, based on the facts before us, find that it not unreasonable to infer that "determining an effective amount of a three drug combination is a matter of routine experimentation within the general knowledge and skill set of a POSITA." *See* Ex. 1111 ¶ 52. Accordingly, we determine that Petitioner has not shown that the challenged claims are not entitled the benefit of priority to earlier applications due to lack of enablement.

C. Section 325(d)

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"). Accordingly, our rules provide that "the Board may authorize the review to proceed" or "deny some or all grounds for unpatentability for some or all of the challenged claims." 37 C.F.R. § 42.108(a), (b). Our discretionary

[8] We further note that "Petitioner's priority analysis does not cite or discuss the *Wands* factors, or otherwise analyze whether the disclosure of the provisional application would have required undue experimentation by a person of ordinary skill trying to make and use the invention." *See* Prelim. Resp. 15 (citing Pet. 16–19; Ex. 1111 ¶¶ 53–55).

determination of whether to institute review is guided, in part, by 35 U.S.C. § 325(d), which states, in relevant part:

> MULTIPLE PROCEEDINGS -- . . . In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director 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.

35 U.S.C. § 325(d).

Our discretion under § 325(d) involves a balance between several competing interests. *See Neil Ziegman, N.P.Z., Inc. v. Stephens*, Case IPR2015-01860, slip op. at 12–13 (PTAB Feb. 24, 2016) (Paper 11) ("While petitioners may have sound reasons for raising art or arguments similar to those previously considered by the Office, the Board weighs petitioners' desires to be heard against the interests of patent owners, who seek to avoid harassment and enjoy quiet title to their rights.") (citing H. Rep. No. 112-98, pt. 1, at 48 (2011)). "On the one hand, there are the interests in conserving the resources of the Office and granting patent owners repose on issues and prior art that have been considered previously." *Fox Factory, Inc. v. SRAM, LLC*, Case IPR2016-01876, slip op. 7 (PTAB Apr. 3, 2017) (Paper 8). "On the other hand, there are the interests of giving petitioners the opportunity to be heard and correcting any errors by the Office in allowing a patent—in the case of an inter partes review—over prior art patents and printed publications." *Id*.

As discussed in section II(B), above, the Examiner considered fully the written description and enablement issues underlying Applicant's claim to priority in allowing the claims to issue, and Petitioner has not presented new evidence or arguments that would convince us that the Examiner's determination was unreasonable. The Examiner's decision to withdraw the rejection under 35 U.S.C. § 102(b) over Nabholtz was expressly predicated on that priority determination, which removed Nabholtz as prior art. In Ground I of this Petition, Petitioner also

asserts that the claims are unpatentable under § 102(b) over Nabholtz, thus raising "the same or substantially the same prior art or arguments previously [] presented to the Office" as contemplated under 35 U.S.C. § 325(d). Under the circumstances of this case, we exercise our discretion under § 325(d) and decline to institute *inter partes* review based on Ground I.

Because the priority determination with respect to Nabholtz is dispositive with respect to whether the later-published Leyland-Jones and Yardley references qualify as prior art, we likewise exercise our discretion under § 325(d) and decline to institute *inter partes* review based on Grounds II and III.

III. ORDER

In consideration of the foregoing, it is ORDERED that the Petition is denied, and no trial is instituted.

PETITIONER:

Amanda Hollis
Stefan Miller
Karen Younkins
KIRKLAND & ELLIS LLP
Amanda.hollis@kirkland.com
dichromik@gmail.com
Karen.younkins@kirkland.com

PATENT OWNER:

David Cavanaugh
Owen Allen
WILMER CUTLER PICKERING HALE AND DORR LLP
David.cavanaugh@wilmerhale.com
Owen.allen@wilmerhale.com

Adam Brausa
DURIE TANGRI LLP
abrausa@durietangri.com