Trials@uspto.gov
571-272-7822

Paper 11
Entered: October 29, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PHIGENIX, INC,
Petitioner,

v.

IMMUNOGEN, INC.,
Patent Owner.

Case IPR2014-00676
Patent 8,337,856 B2

Before FRANCISCO C. PRATS, JACQUELINE WRIGHT BONILLA, and ZHENYU YANG, *Administrative Patent Judges*.

BONILLA, *Administrative Patent Judge.*

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

I. INTRODUCTION

Phigenix Inc. ("Petitioner") filed a Petition requesting *inter partes* review of claims 1-8 of U.S. Patent No. 8,337,856 ("the '856 patent"). Paper 5 ("Pet."). Immunogen, Inc. ("Patent Owner") filed a Preliminary Response. Paper 10 ("Prelim. Resp."). We have jurisdiction under 35 U.S.C. § 314(a), 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 institute an *inter partes* review of claims 1-8 of the '856 patent.

A. Related Proceeding

On May 29, 2014, five weeks after filing the current Petition, Petitioner filed a Petition requesting *inter partes* review of claims 1-20 and 25-27 of U.S. Patent No. 7,575,748 ("the '748 patent") in Case No. IPR2014-00842. Patent Owner of the '748 patent, Genentech, Inc., a real party-in-interest in the current proceeding, filed a Preliminary Response. IPR2014-00842, Paper 9. The '748 patent is a continuation application of U.S. Patent No. 7,097,840 ("the '840 patent"). IPR2014-00842, Ex. 1001. The '856 patent, at issue here, is a divisional application of a continuation application of the '840 patent. Ex. 1001. Claims of the '748 patent are directed to methods for treating a tumor comprising administering an immunoconjugate. IPR2014-00842, Ex. 1001, cols. 81-84. As

discussed below, the claims of the '856 patent are directed to immunoconjugate compounds.

B. The '856 Patent (Ex. 1001)

The '856 patent relates to immunoconjugates comprising an anti-ErbB antibody, such as the humanized anti-ErbB2 antibody known as HERCEPTIN® (huMAb4D5-8), linked to a maytansinoid toxin. Ex. 1001, 1:20-52, 35:47-36:39; *see also id*. at 3:6-16 (discussing HERCEPTIN®), 6:50-67 (defining "ErbB2"), 10:40-52 (defining "humanized"), 16:23-28 (defining "epitope 4D5").

The term "ErbB2" is synonymous with "HER2," "$p185^{neu}$", or "*neu*," and refers to a member of the ErbB family of receptor tyrosine kinases, which mediate cell growth, differentiation, and survival. *Id*. at 1:45-60, 6:50-58. Overexpression of ErbB2 on cell surfaces can lead to cancer in humans, such as certain breast and ovarian cancers. *Id*. at 1:54-66, 8:55-60.

The Specification teaches that maytansinoids, such as DM1, are highly cytotoxic, i.e., inhibit or prevent cell function and/or destroy cells, but induce "severe systemic side-effects primarily attributed to their poor selectivity for tumors" when administered alone. *Id*. at 1:38-44, 17:45-52; *see also id.* at 5:7-13 (referring to Figure 3, showing the structure of the maytansinoid designated "DM1"). The Specification describes making anti-ErbB antibody-maytansinoid conjugates using "a variety of bifunctional protein coupling agents," i.e., linkers, such as N-succinimidyl-3-(2-pyridyldithio)propionate ("SPDP"), N-succinimidyl-4-(2-pyridylthio)pentanoate ("SPP"), and succinimidyl-4-(N-maleimidomethyl)-cyclohexane-l-carboxylate ("SMCC"). *Id*. at 36:13-31.

The Specification states that the "present invention is based on results obtained in a novel murine HER2-transgenic tumor model in which HERCEPTIN® or the murine antibody 4D5 from which HERCEPTIN® was derived, had little effect on tumor growth." *Id*. at 21:65-22:1. In this context, the Specification states that "it was surprisingly found that while the transplanted tumor obtained from such transgenic mice responded poorly to HERCEPTIN® treatment, the HERCEPTIN®-maytansinoid conjugates were highly efficacious." *Id*. at 22:2-7.

C. The Challenged Claims

Petitioner challenges claims 1-8 of the '856 patent. Of those, only claim 1 is independent, which recites:

> 1. An immunoconjugate comprising an anti-ErbB2 antibody conjugated to a maytansinoid, wherein the antibody is huMAb4D5-8.

Id. at 81:28-31. Dependent claim 2 recites that the maytansinoid is DM1 having a specific structure, where the antibody is linked to the maytansinoid via a disulfide or thioether group at "R" shown in the structure. *Id*. at 81:31-53. Dependent claim 3 requires that the immunoconjugate "comprises from 3 to 5 maytansinoid molecules per antibody molecule." *Id*. at 82:27-30. Dependent claim 5 recites a pharmaceutical composition comprising the immunoconjugate and a pharmaceutically acceptable carrier. *Id*. at 82:37-39. Claims 4 and 6-8, which ultimately depend on claim 1 or 2, recite that the antibody and maytansinoid are conjugated by specific chemical linkers, i.e., SPDP, SPP, or SMCC. *Id*. at 82:30-36, 39-51.

D. Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable under 35 U.S.C. § 103(a) based on the following grounds. Pet. 8.

	References	Basis	Claims Challenged
1	Chari 1992 (Ex. 1012)[1] in view of HERCEPTIN® Label (Ex. 1008)[2]	§ 103	1-8
2	Chari 1992 and HERCEPTIN® Label, further in view of Hudziak 1998 (Ex. 1017)[3] and/or Rosenblum 1999 (Ex. 1018)[4]	§ 103	1-8
3	Chari 1992 and HERCEPTIN® Label, further in view of Hudziak 1998 and/or Rosenblum 1999, and further in view of Baselga 1998 (Ex. 1019)[5] and/or Pegram 1999 (Ex.1020)[6]	§ 103	1-8
4	Chari 1992 and HERCEPTIN® Label, further in view of Morgan 1990 (Ex. 1021)[7]	§ 103	6, 8

[1] Chari et al., "Immunoconjugates Containing Novel Maytansinoids: Promising Anticancer Drugs," 52 CANCER RES.127-131 (1992).
[2] HERCEPTIN® (Trastuzumab) Label, dated September 1998.
[3] U.S. Patent No. 5,770,195 (Hudziak, et al.), issued June 23, 1998.
[4] Rosenblum et al., "Recombinant Immunotoxins Directed against the *c-erbB-2/HER2/neu* Oncogene Product: *In Vitro* Cytotoxicity, Pharmacokinetics, and *In Vivo* Efficacy Studies in Xenograft Models," 5 CLIN. CANCER RES. 865-874 (1999).
[5] Baselga et al., "Recombinant Humanized Anti-HER2 Antibody (Herceptin™) Enhances the Antitumor Activity of Paclitaxel and Doxorubicin against HER2/*neu* Overexpressing Human Breast Cancer Xenografts," 58 CANCER RES. 2825-2831 (1998).
[6] Pegram et al., "Inhibitory effects of combinations of HER-2/*neu* antibody and chemotherapeutic agents used for treatment of human breast cancers," 18 ONCOGENE 2241-2251 (1999).

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.