

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-1-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).

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