Trials@uspto.gov
571-272-7822

Paper 39
Entered: October 27, 2015

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.*

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

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."). Thereafter, we determined that the information presented in the Petition demonstrated that there was a reasonable likelihood that Petitioner would prevail in showing claims 1–8 as unpatentable. Paper 11 ("Dec. to Inst."), 2, 23. Pursuant to 35 U.S.C. § 314, we instituted this proceeding on October 29, 2014, to review whether claims 1–8 of the '856 patent would have been obvious under 35 U.S.C. § 103 over Chari 1992[1] in view of the HERCEPTIN® Label,[2] further in view of Rosenblum 1999[3] and Pegram 1999.[4] *Id*. at 23.

After institution of trial, Patent Owner filed a Patent Owner Response. Paper 18 ("PO Resp."), and Petitioner filed a Reply to the Response. Paper

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[1] Chari et al., *Immunoconjugates Containing Novel Maytansinoids: Promising Anticancer Drugs*, 52 CANCER RES.127–131 (1992) ("Chari 1992") (Ex. 1012).

[2] HERCEPTIN® (Trastuzumab) Label, dated September 1998 ("the HERCEPTIN® Label") (Ex. 1008).

[3] 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) ("Rosenblum 1999") (Ex. 1018).

[4] 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) ("Pegram 1999") (Ex. 1020).

24 ("Reply"). Petitioner also filed a Motion to Exclude certain evidence submitted by Patent Owner. Paper 28. Patent Owner responded by filing an Opposition to the Motion to Exclude (Paper 29), as well as an unopposed Motion to Seal two exhibits filed by Patent Owner in connection with the Opposition (Paper 31, 1). Petitioner filed a Reply to the Opposition to the Motion to Exclude. Paper 35.

An oral hearing was held on July 9, 2015. A transcript of the hearing has been entered into the record. Paper 38 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6(c). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine that Petitioner has not shown by a preponderance of the evidence that claims 1–8 of the '856 patent are unpatentable. We deny Petitioner's Motion to Exclude Evidence, and we grant Patent Owner's Motion to Seal.

A. Related Proceeding

About a month 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. On December 9, 2014, we declined to institute review in that case. *Phigenix, Inc. v. Genentech, Inc. and ImmunoGen, Inc.*, Case IPR2014-00842 (PTAB Dec. 9, 2014) (Paper 10).

The ’748 patent, at issue in that case, 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.

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

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