UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PHIGENIX, INC.
Petitioner

v.

IMMUNOGEN, INC.
Patent Owner

Case IPR2014-00676
U.S. Patent No. 8,337,856

PATENT OWNER PRELIMINARY RESPONSE UNDER 37 C.F.R. §42.107(a)

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I. Introduction

Phigenix's IPR petition falls far short of meeting its burden to establish a reasonable likelihood of prevailing with respect to any claim it challenges in U.S. Patent No. 8,337,856 ("the '856 patent"). The challenged patent is directed to an immunoconjugate drug that combines an antibody (huMab4D5-8, also known as trastuzuamb and marketed as Herceptin®) together with a chemotherapeutic agent (a maytansinoid). Phigenix posits that the invention is "no more than a simple substitution of one known element for another to obtain a predictable result." (Petition at 15.)

But one can agree with Phigenix's *prima facie* obviousness arguments only by ignoring extensive evidence in the prosecution history and by ignoring other evidence that would have been readily available to a person of ordinary skill in the art (POSA). As shown in Section II below, Phigenix and its expert ignore evidence showing the serious challenges and unpredictability that researchers in the field faced in developing a therapeutic immunoconjugate drug. Phigenix does not explain how a POSA would have had a reason to combine the art with a reasonable expectation of success in view of the many challenges the prior art presented.

Phigenix and its expert have been willing to ignore such challenges and evidence in their effort to cancel a patent for a ground-breaking cancer drug jointly

developed by ImmunoGen and Genentech. The drug, known as T-DM1, is marketed under the brand name Kadcyla® and has been hailed as revolutionizing the treatment of breast cancers that overexpress HER2. T-DM1 is a conjugate that combines trastuzumab and the highly cytotoxic maytansinoid "DM1."

As discussed in Section III below, one can agree with Phigenix's obviousness assertions only by also disregarding objective indicia of nonobviousness as Phigenix did. Though immunoconjugate therapies have long been viewed as the "holy grail" of cancer treatment, no immunoconjugate before T-DM1 had been proven in a clinical setting for treating solid tumors. Upon learning of T-DM1's clinical results, leaders in the field selected it as one of the top three "game changers in oncology" in 2011, and stated that it is expected to usher in a new era of other cancer therapeutics that simultaneously increase efficacy *and* reduce toxicity. (Ex. 2008 at 4:16-18.) To the surprise of many, T-DM1 showed efficacy in patients that failed to respond to trastuzumab and at least four other therapies, including a taxane chemotherapeutic. And T-DM1's low toxicity was particularly unexpected given that (i) maytansine had demonstrated unacceptable toxicity in previous clinical trials and (ii) normal cells, as well as tumor cells, express the protein to which trastuzumab binds. But, well-regarded practitioners in the field have praised T-DM1's results as ground-breaking.

Phigenix's petition fails to rebut ImmunoGen's objective indicia evidence,

even though extensive evidence is contained right within the prosecution history of the '856 patent. For example, while prosecuting the '856 patent, ImmunoGen presented detailed evidence on unexpected results, including providing expert declarations of Drs. Klencke and Sliwkowski. And after reviewing this evidence, the Examiner indicated the claims were allowable. Phigenix now relies on references that contain the same or substantially the same teachings as the references the Examiner considered. For example, Chari 1992, which is used in the majority of the grounds alleged by Phigenix, was discussed with the Examiner during an interview. (Ex. 2014 at 1.) Certainly, the petition doesn't distinguish between the previously-relied upon references and patentability analysis versus the currently-presented references and analysis. And the petition leaves Drs. Klencke's and Sliwkowski's declarations regarding objective indicia largely unrebutted. For example, as shown below, even Phigenix's expert, Dr. Rosenblum, was apparently unwilling to state that T-DM1's clinical-trial results were expected. Without excuse, neither the petition nor Dr. Rosenblum provides any rebuttal to significant evidence in the prosecution history or readily available in the art showing the invention's praise in the industry, long-felt need, and commercial success. Addressing objective indicia is an essential part of an obviousness inquiry, "not just an afterthought." (*Leo Pharmaceutical v. Rea*, 726 F.3d 1346, 1357 (Fed. Cir. 2013); see also *Omron Oilfield & Marine, Inc. v. MD/Totco*, IPR 2013-00265,

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