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

DECLARATION OF LINDA T. VAHDAT, M.D.

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I, Linda T. Vahdat, M.D., do hereby declare as follows:

I. Overview

1. I am a board certified oncologist and Professor of Medicine at Weill Cornell Medical College. This declaration is based on my personal knowledge as an oncologist and my opinions as an expert in the field of cancer research and treatment, including breast cancer. I understand that this declaration is being submitted together with a Patent Owner's Reply to Phigenix, Inc.'s Petition for *inter partes* review ("IPR") of claims 1-8 of U.S. Patent No. 8,337,856 ("the '856 patent," Ex. 1001). I also understand that this declaration is being submitted together with a Declaration by Joyce O'Shaughnessy, M.D. (Ex. 2105). I have read Dr. O'Shaughnessy's Declaration and agree with the facts and opinions expressed therein.

2. I have been retained as an expert witness on behalf of ImmunoGen, Inc. for this IPR. I am being compensated for my time in connection with this declaration at my standard consulting rate of $800 per hour. I have no personal or financial interest in the outcome of this proceeding. I am over the age of eighteen and otherwise competent to make this declaration.

3. Based on the work I have done in this matter and my expertise in this field, I have concluded that:

- T-DM1 filled a long-felt, unmet need for an immunoconjugate capable of targeting delivery of a cytotoxic agent to treat a solid tumor (as discussed in more detail in Section VI, below); and
- T-DM1 received praise in the industry for this path-breaking achievement (as discussed in more detail in Section VII below).

4. In preparing this declaration, I have reviewed the '856 patent (Ex. 1001) as well as each of the other documents listed in the table below or cited herein, in light of general knowledge in the art.

Exhibit #	***Description***
1001	U.S. Patent No. 8,337,856 B2
1008	Herceptin® Label
1012	Chari, R.V.J., *et al*., "Immunoconjugates Containing Novel Maytansinoids: Promising Anticancer Drugs," *Cancer Research* 52: 127-131 (1992)
1015	Chari, R.V.J., "Targeted delivery of chemotherapeutics: tumor activated prodrug therapy," *Advanced Drug Delivery Reviews* 31: 89-104 (1998)
1018	Rosenblum, M.G., "Recombinant Immunotoxins Directed against the *c-erb-2/HER2/neu* Oncogene Product: *In Vitro* Cytotoxicity, Pharmacokinets, and *in Vivo* Efficacy Studies in Xenograft Models," *Clinical Cancer Research* 5: 865-874 (1999)
1020	Pegram M., "Inhibitory effects of combinations of HER-2/*neu* antibody and chemotherapeutic agents used for treatment of human breast cancers," *Oncogene* 18: 2241-2251 (1999)
1028	Trail, P.A., *et al*., "Monoclonal antibody drug conjugates in the treatment of cancer," *Current Opinion in Immunology* 11: 584-588 (1999), Exhibit H to Declaration of Mark X. Sliwkowski, Ph.D., dated on June 30, 2010, filed in U.S. Appl. No. 11/949,351

Exhibit #	***Description***
2006	Walter Blättler, *et al*. "Immunoconjugates," *Cancer Therapeutics: Experimental and Clinical Agents* (Beverly A. Teicher ed., 1997)
2010	Tolcher, A., *et al.*, "Randomized Phase II Study of BR96-Doxorubicin Conjugate in Patients With Metastatic Breast Cancer," *Journal of Clinical Oncology* 17: 478-484 (1999)
2011	Elias, D., *et al.*, "Monoclonal Antibody KS1/4-Methotrexate Immunoconjugate Studies in Non-Small Cell Lung Carcinoma," *American Journal of Respiratory and Critical Care Medicine* 150: 1114-1122 (1994)
2012	Krop, I., *et al.*, "Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): a randomised, open-label, phase 3 trial," *Lancet Oncology* 15: 689-699 (2014)
2015	Cao, Y., *et al.*, "Construction and Characterization of Novel, Completely Human Serine Protease Therapeutics Targeting Her2/neu," *Molecular Cancer Therapeutics* 12: 979-991 (2013)
2016	Cao, Y., and Rosenblum, M.G., "Design, Development, and Characterization of Recombinant Immunotoxins Targeting HER2/neu," in *Antibody-Drug Conjugates and Immunotoxins: From Pre-Clinical Development to Therapeutic Applications*, Chapter 18, pp. 319-348 (2013)
2025	Kadcyla™ Prescribing Information, pp. 1-21(2013)
2029	Pai-Scherf, L., *et al.*, "Hepatotoxicity in Cancer Patients Receiving erb-38, a Recombinant Immunotoxin That Targets the erbB2 Receptor," *Clinical Cancer Research* 5: 2311-2315 (1999)
2030	Pai, L., *et al.*, "Clinical Evaluation of Intraperitoneal *Pseudomonas* Exotoxin Immunoconjugate OVB3-PE in Patients With Ovarian Cancer," *Journal of Clinical Oncology* 9: 2095-2103 (1991)
2031	Gould, B., *et al*., "Phase I Study of an Anti-Breast Cancer Immunotoxin by Continuous Infusion: Report of a Targeted Toxic Effect Not Predicted by Animal Studies," *Journal of the National Cancer Institute* 81: 775-781 (1989)

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