IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PETITION FOR INTER *PARTES* REVIEW

In re *Inter Partes* Review of	U.S. Patent No. 5,856,336
Yoshihiro FUJIKAWA, et al.	Issued: Jan. 5, 1999
Application No.: 07/883,398	Filed: May 15, 1992

For: QUINOLINE TYPE MEVALONOLACTONES

DECLARATION OF DR. MILTON BROWN, M.D., PH.D.

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1. I, Milton Brown, hereby declare and state:

2. THAT I am a citizen of the United States;

3. THAT I received the degree of Ph.D. in synthetic chemistry from University of Alabama at Birmingham in 1995 and a medical degree at the University of Virginia in 1999;

4. I received postdoctoral training in the Department of Chemistry at Virginia, and in 2000 became an assistant professor of chemistry in the same department. In 2003, I was promoted to Associate Professor and tenured at the University of Virgina. In June of 2006, I accepted the position as Director of the Drug Discovery Program (DDP) at the Georgetown University Medical Center (GUMC, or University) which manages and supports the University drug discovery and development efforts. I was appointed as the Edwin H. Richard and Elisabeth Richard von Matsch Endowed Chair in Experimental Therapeutics and Tenured Associate Professor in the Department of Oncology and Associate Director for the experimental therapeutics program in the Lombardi Comprehensive Cancer Center (LCCC). I also hold secondary faculty appointments in the departments of Neuroscience and Biochemistry at GUMC.

5. I have more than 18 years of experience in drug discovery and currently directs the DDP at GUMC. The DDP is a program established in July of 2006 to support translational research at the LCCC at GUMC. The mission of the DDP is to discover new drug treatments and diagnostic tools for cancer using integrated

sciences to improve the healthcare of our patients. As leader of the DDP, I created a new paradigm to catalyze research at GUMC and the LCCC in the area of new experimental therapeutics and personalized medicine. This has led to new initiatives, multi-institutional programs, funded multi-investigator grants, and many scholarly publications and patents.

6. In the DDP, I have directly managed more than 20 staff scientists, including graduate students, technicians, research instructors, post-docs and research assistant professors dedicated to the discovery of new drugs. These individuals have included synthetic chemists, medicinal chemists, pharmacologists, cancer biologists, ADME toxicity specialists, pathologists, and spectroscopists. As director of the DDP, I have managed more than 30 stand-alone drug discovery projects that include more than 40 independent scientific investigators.

7. On a national level, I was appointed by the U.S. Secretary of Health Kathleen Sebelius to serve as a scientific counselor on the National Toxicology Program Board. I have served as a scientific reviewer of grants and programs for the National Institutes of Health (NIH), National Cancer Institute (NCI) Cancer Center Support Grants, Department of Defense (DOD) and the American Association for the Advancement of Science (AAAS). I was elected to the medicinal chemistry long range planning committee for the American Chemical Society (2006-2008) and helped to set the agenda policies for medicinal chemistry

symposia during that time. I have reviewed research articles for nationally and internationally recognized journals. I have given more than 80 invited lectures in the USA, China, Brazil and Europe on developing global strategies for drug discovery and developing pipelines for experimental therapeutics.

8. I am a named inventor on multiple U.S. Patents, as listed in my attached CV.

9. I have been asked by Sawai Pharmaceutical Co., Inc. and Sawai USA (hereinafter "Sawai") to provide my opinion regarding the patentability of claims 1 and 2 of U.S. Patent No. 5,856,336 (hereinafter "the '336 Patent") in view of the cited art raised in the above-captioned *inter partes* review (IPR). For my time spent in connection with this matter, I am being compensated at my standard rate of $500 per hour. My compensation does not depend on the outcome of the IPR.

10. To prepare this Declaration, I reviewed the documents referred to in this Declaration, including:

Document 1: the '336 Patent;

Document 2: the record of the application before the U.S. Patent and Trademark Office for the '336 Patent (the so-called "prosecution history" of the '336 Patent);

Document 3: U.S. Patent No. 4,761,419 (hereinafter "Picard");

Document 4: U.S. Patent No. 4,925,852 (hereinafter "Kesseler");

Document 5: Endo, A. et al., "Competitive Inhibition of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase by ML-236A and ML-236B Fungal Metabolites, Having Hypocholesterolemic Activity," *FEBS Letters* 1976, 72(2), 323-326 (hereinafter "Endo 1976");

Document 6: D.R. Illingsworth, "Lipid Lowering Drugs And Overview Of Indications And Optimal Therapeutic Use," Drugs 1987, 33, 259-279 (hereinafter "Illingsworth 1987");

Document 7: D.R. Illingsworth, "An Overview Of Lipid Lowering Drugs," *Drugs* 1988, 36 (Suppl. 3), 63-71 (hereinafter "Illingsworth 1988");

Document 8: Alfred W. Alberts, "Mevinolin: A Highly Potent Competitive Inhibitor of Hydroxymethylglutaryl-Coenzyme a Reductase and a Cholesterol-Lowering Agent," *77 Proc. Nat'l Acad. Sci. USA,* 1980, 3957 (hereinafter "Alberts 1980");

Document 9: Brown, M., et al., Induction of 3-Hydroxy-3-methylglutaryl Coenzyme A Reductase Activity in Human Fibroblasts Incubates with Compactin "(ML-236B), a Competitive Inhibitor of the Reductase, *Journal of Biological Chemistry,* Vol. 253, NO. 4, 1121-1128 (Feb. 25, 1978)(hereinafter "Brown 1978");

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