UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS VIII, LLC
Petitioner,

v.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA
Patent Owner

Case: IPR2015-01836
Patent No. 7,932,268

DECLARATION OF RICHARD E. GREGG, M.D.

PENN EX. 2083
CFAD v. PENN
IPR2015-01836

I, Richard E. Gregg, M.D., am competent to testify regarding the matters set forth herein, which are based on my personal knowledge and experience.

1. I currently serve as the Chief Scientific Officer at Vitae Pharmaceuticals, Inc. ("Vitae"). Prior to joining Vitae in 2008, I spent 19 years at Bristol-Myers Squibb Company ("BMS"), serving in the following positions: Executive Director in the Department of Metabolic Diseases (1988-1996); Vice President of Metabolic Diseases and Drug Discovery (1996-1998); Vice President of Metabolic and Cardiovascular Drug Discovery (1999-2001); and Vice President of Clinical Discovery responsible for Early Clinical Development, Clinical Pharmacology, Translational Medicine, and Biomarker Technologies (2001-2007). Prior to joining BMS, I spent ten years at the National Health Heart, Lung, and Blood Institute, National Institutes of Health ("NHLBI NIH") in Bethesda, Maryland, where I studied disorders of lipid and lipoprotein metabolism. I met Dr. Daniel Rader during my time at NHLBI NIH.

2. I hold a Bachelor of Science degree in biochemistry (1970) and a Master of Science degree in biochemistry (1971) from Iowa State University, and a Doctor of Medicine degree from Stanford University School of Medicine (1976). I completed my internship and residency in Internal Medicine at Strong Memorial

Hospital in Rochester, New York, and completed my fellowship in Endocrinology and Metabolism at the NHLBI NIH. My C.V. is included as Ex. 2055.

3. While at NHLBI NIH, I studied patients who suffer from abetalipoproteinemia, a rare inherited disorder that results in extremely low cholesterol levels. Patients with this disease are not able to make certain lipoproteins, particles that carry fats and fat-like substances (such as cholesterol) in the blood. As a consequence, these patients cannot properly absorb fat and fat-soluble vitamins like vitamin E and vitamin A from food. This, in turn, damages their nervous system and eyes.

4. In the summer of 1990, I went to a conference on lipids & lipoproteins, where I met Dr. John Wetterau. Dr. Wetterau was working at the University of Cincinnati and had been studying the function of microsomal transfer protein (MTP) for about 6-8 years at that time. I realized that MTP was an interesting target to study and that it may be the cause of abetalipoproteinemia, which I studied at NHLBI NIH. I recruited Dr. Wetterau to join BMS to explore the function of MTP, and Dr. Wetterau started working at BMS in 1990 in the Department of Metabolic Diseases.

5. Sometime in late 1990-early 1991, I suggested that BMS initiate an exploratory program to study the function of MTP. Dr. Wetterau and I hypothesized that MTP might be important for assembly and secretion of lipoproteins, although we did not have a definite understanding about the function of MTP. Dr. Wetterau and I further hypothesized that mutations in MTP may be the cause of abetalipoproteinemia and may be important in regulating cholesterol levels. As such, I recognized that understanding the MTP function might assist with efforts to develop treatments for various conditions associated with increased lipid and cholesterol levels, such as hyperlipidemia and hypercholesterolemia. BMS management recognized the potential value of exploring MTP function, and launched an early stage exploratory program in 1991.

6. As the leader of the program, I was responsible for managing the exploratory program, setting the program goals and directions, and helping to coordinate the program activities. I was managing a group of about 15 scientists who were working on the exploratory program. Dr. Wetterau reported to me.

7. During the initial stages of the exploratory program, I worked with Dr. Wetterau and Dr. Rader, who was at NHLBI NIH at the time, to determine the genetic cause of abetalipoproteinemia. Dr. Rader supplied samples obtained from

patients with abetalipoproteinemia that allowed us to perform genetic studies and determine the cause of abetalipoproteinemia. In one study, we investigated the possibility that mutations in MTP may be the cause of abetalipoproteinemia. During our study, we discovered that MTP played an important role in the assembly of very low density lipoprotein (VLDL) in the liver and chylomicrons in the intestine. We postulated that MTP mediated the transfer of triglycerides from their site of synthesis in the endoplasmic reticulum membrane to nascent lipoprotein molecules within the endoplasmic reticulum as they were synthesized. We published our study results in the journal SCIENCE. *See* Ex. 2056.

8. In or around 1992, Dr. Wetterau and I cloned MTP cDNA and were able to correlate the activity of MTP with certain disease states, including hypercholesterolemia and hyperlipidemia. We also discovered that the function of MTP was defective in abetalipoproteinemic patients. These findings led us to hypothesize that inhibition of MTP may lead to lowering cholesterol and lipid levels.

9. Sometime around 1992, Dr. Scott Biller and I initiated a drug discovery program at BMS focused on discovering a class of compounds that could inhibit MTP. At one time, this program was a high priority at BMS. BMS

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