UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS VII, LLC,
Petitioner,

v.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA,
Patent Owner.

Case IPR2015-01836

Patent 7,932,268

PATENT OWNER'S RESPONSE TO PETITIONER'S OBSERVATIONS ON CROSS-EXAMINATION OF DR. THOMAS A. BAILLIE

Patent Owner hereby files its Response to Petitioner's Observations on Cross-Examination of Dr. Thomas A. Baillie. IPR2015-01836, Paper 43.

Response 1: Petitioner mischaracterizes Dr. Baillie's testimony because he specifically identified the "critical feature" of the invention to be the claimed dosing regimen, which produced unexpected results of adaptation or tolerance to toxicities of concern with lomitapide. CFAD Ex. 1057 at 8:16-10:12. Further, the precise dose escalation factor needed to promote biological adaptation with lomitapide is irrelevant. Although Dr. Rader used dose escalation factors that were more aggressive than twofold in his phase II trial, this does not contradict Dr. Baillie's opinion that the claimed twofold escalation was both clinically efficacious and non-routine. *Id.* at 13:14-14:5, 19:20-20-22; *see also* Ex. 2007 at 2. This testimony is consistent with the opinions Dr. Baillie expressed in his Supplemental Declaration (Ex. 2305) at ¶¶ 17, 64-69.

Response 2: The testimony cited by Petitioner does not bear on the question of what caused the amelioration of side effects seen by Dr. Rader. Dr. Baillie has maintained that the improved side effect profiles observed by Dr. Rader in his clinical trials (versus those conducted by BMS) cannot be attributed entirely to a low-fat diet, and were instead due to Dr. Rader's novel dosing regimen. Ex. 1057

at 51:20-54:3; Ex. 2305 at ¶¶ 65-68. Dr. Baillie testified that even if the diets in BMS's and Dr. Rader's clinical trials were not identical, all studies employed low-fat diets, and the incidence and severity of adverse events in the BMS trials were shown to be dose-dependent, indicating that adverse effects are related to dose, not solely diet. Ex. 1057 at 40:20-41:14, 50:15-51:19.

Response 3: Petitioner is incorrect that Dr. Baillie "ignore[d] evidence that amelioration of side effects was due to an aggressive restriction of fat in the diet of subjects taking lomitapide." Dr. Baillie testified that although he considered Exhibit 2079 in forming his opinions, he differed with Petitioner and its experts as to how to interpret the statements in that document. Ex. 1057 at 38:11-40:5. Furthermore, Dr. Baillie did not make "unsubstantiated assumptions" regarding whether the BMS clinical trials with lomitapide employed a low-fat diet. Dr. Baillie based his opinions on internal BMS documents (Ex. 2078 and 2080) that describe the use of low-fat diets in clinical trials that studied the toxicity profile of loimitapide. Ex. 1057 at 30:10-31:7, 32:18-34:17; Ex. 2305 at ¶¶ 67-68; Ex. 2078 at 2-4; Ex. 2080 at 1-2

Response 4: Petitioner mischaracterizes Dr. Baillie's testimony. Dr. Baillie

testified that although a patient undergoing the claimed forced titration method might be subject to a *temporary* dose reduction in the case of toxicity, the patient would still have to complete all of the dosing levels in order to fall within the claims. Ex. 1057 at 10:18-12:23, 44:4-14. Furthermore, Dr. Baillie explained that this forced titration regimen is significantly different from non-forced titrations such as that proposed in Stein (Ex. 1014) and Pink Sheet 2004 (Ex. 1013). *Id.* Dr. Baillie's testimony is consistent with the opinions expressed in his Supplemental Declaration. Penn Ex. 2305 at ¶¶ 15-16, 24-25, 64.

Response 5: Petitioner is incorrect that Dr. Rader's citation of Wetterau in Ex. 2077 "contradicts" Dr. Baillie's opinion regarding lack of reasonable expectation of success. Dr. Baillie testified that in designing his clinical trial, Dr. Rader could not have relied solely on Wetterau's animal data, especially given Dr. Rader's access to proprietary BMS human data regarding lomitapide and its adverse event profile. Ex. 1057 at 55:22-58:17; Ex. 2080 at 1-2. This is consistent with Dr. Baillie's opinion that although Wetterau reports *pharmacodynamic* data, it lacks the necessary *pharmacokinetic* and *toxicology* data a POSA would need to design a safe and effective human dosing regimen for lomitapide. *Id.* at 45:15-47:6; Ex. 2305 at ¶¶ 22-23, 38-39, 52.

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Respectfully submitted,
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