Paper No. ___
Filed: May 22, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN LABORATIORIES, LTD.,
Petitioner,

v.

AVENTIS PHARMA S.A.,
Patent Owner.

Case IPR2016-00712
Patent 8,927,592

PETITIONER MYLAN LABORATORIES LIMITED'S RESPONSE TO PATENT OWNER'S MOTION FOR OBSERVATIONS ON THE CROSS-EXAMINATION OF DR. RAHUL SETH

Petitioner submits this Response to Patent Owner Aventis's Motion for Observations on the Cross-Examination of Dr. Rahul Seth ("Observations") pursuant to the Scheduling Order (Paper 10) as modified by the parties (Paper 49).

1. Observation 1 omits relevant testimony and mischaracterizes the cited testimony. Dr. Seth explained that the dosage of cabazitaxel ***was*** disclosed (EX2258 at 28:6-9, 142:25-143:9), and that it was only the doses of mitoxantrone and prednisone that were not expressly disclosed in Winquist and TROPIC (*id.* at 143:6-9); accordingly, the ***control arm*** of the TROPIC study could not be perfectly replicated solely based on Winquist and TROPIC. No claim of the '592 patent recites mitoxantrone, and only dependent Claims 14-16 require a dose of prednisone. As Dr. Seth has previously explained, those claims are obvious over Winquist, TROPIC, and Tannock. *See, e.g.*, EX1002, ¶¶152-54, 160; Pet. at 42-45.

2. Regarding Observation 2, Dr. Seth explained that "hope" is the equivalent term that an oncologist would use when deciding to give a drug to a patient. EX2258 at 30:17-31:2. Furthermore, as Dr. Seth pointed out (*id.*), Aventis's questions misapplied a legal term ("expectation of success") to whether the outcome of cabazitaxel treatment could be predicted for every patient. The relevant legal question is whether a POSA would have "reasonable expectation of success" that the prior art references could be combined to arrive at the claimed invention; "reasonable expectation of success" does not depend on whether a prior

art method is efficacious in every patient or is likely to receive FDA approval. *See* Pet. at 53; *see also id.* at 20-21, 28, 33, 52; EX1002, ¶¶89, 112, 120-21, 133. Indeed, as explained by Dr. Seth, in 2009 and today "it is impossible to know on an individual basis whether such a method will work (before treatment)," and physicians routinely administer chemotherapy drugs such as cabazitaxel without such guarantees. EX1043, ¶¶38-39 (citing EX1041 at 115:19-23); *see also* EX1002, ¶220 (cancer drugs working in only 10% of patients considered effective). Furthermore, Dr. Seth clarified the degree of confidence behind the "hope" of cabazitaxel, stating that "when we were thinking about cabazitaxel in 2009, we expected it to get FDA approval and it would increase overall survival. … We felt cabazitaxel was a drug worthwhile to give patients a clinical benefit." EX2258 at 80:12-81:12. When pressed as to the percentage chance, he stated that "I could not say what percentage we would see but I thought we definitely would see a survival benefit," and when asked whether the odds of success were greater than 50 percent, replied "You can say 50. I mean, we would see a definite benefit versus mitoxantrone." *Id.*

3. Observation 3 repeats the same mischaracterizations explained above for response 2, presuming that the use of the term "hope" precludes a "reasonable expectation," even though Dr. Seth explained that he uses the term "hope" as equivalent to "expectation" when describing a decision to treat a patient. EX2258

at 30:17-31:2. As also described in response 2, Aventis misapplies the concept of "reasonable expectation of success" to a question of whether a POSA would recognize inherent properties of a prior art method of treatment.

4. Regarding Observation 4, Dr. Seth's quoted statement was in response to a question regarding the results of future research with no specified time horizon: "There's always a hope we're ***going to*** cure prostate cancer?" EX2258 at 32:17-18 (emphasis added); *see also id.* at 32:21-33:11 (explaining that he was predicting future research progress in the field). Aventis's observations equivocate between "hope" with regard to unknown future research and "hope" with regard to administering a treatment with known anti-cancer activity to a particular patient, and is at any rate not relevant to a reasonable expectation of success. *See* Reply at 2; Pet. at 34.

5. Regarding Observation 5, Dr. Seth explained that he cannot speak as a patient because he never personally had prostate cancer, nor did his family members. EX2258 at 36:24-37:6, 38:4-9. Dr. Seth explained that he hoped to obtain a clinical benefit for the patients he sent to the TROPIC study, that clinicians send patients to clinical studies to live, not die, and that he always intends to increase survival when treating patients with cabazitaxel. *Id.* at 38:4-9, 37:9-15, 31:13-22, 21:22-22:19.

6. Observation 6 misquotes Dr. Seth as saying a POSA "would ***try to***

hope that [dose of] cabazitaxel would work," whereas in fact Dr. Seth stated a POSA would conclude cabazitaxel could work at 20 or 25 mg/m^2. EX2258 at 45:1-20. In particular, Dr. Seth stated with regard to 15 mg/m^2 dose that "I can't really say what a POSA would feel [on that], but 20 to 25 milligrams per meter squared, I feel we would feel that [would] work." *Id.* Mita's example of efficacy at 15 mg/m^2 in mCRPC and 25 mg/m^2 in post-docetaxel mCRPC supports a conclusion that cabazitaxel would likewise be effective at 20 or 25 mg/m^2 in post-docetaxel mCRPC, regardless of whether a dose of 15 mg/m^2 would be equally effective. *See* EX1043, ¶30; EX1002, ¶103, 225; Reply at 9; Pet. at 22, 27, 54. The observation also mischaracterizes the testimony regarding "hope" vs. "expect," as discussed above.

7. As discussed above in Responses 2-4 and 6, Aventis mischaracterizes the testimony regarding an oncologist's "hope" when treating an individual and a POSA's reasonable expectation of success when combining prior art methods. As Dr. Seth has previously pointed out, the '592 patent's data does not specifically prove a survival benefit with the 20 mg/m^2 dose, nor does DeBono. Reply at 16; EX2177 at 72:17-73:23. Despite this lack of data, Dr. Seth explained that based on the prior art "a POSA would think 20 milligrams would probably work close to 25 milligrams per meter squared in giving a patient a benefit." EX2258 at 41:3-7; *see also id.* at 43:17-20 ("the drug was known and was felt to be working" at 20 or 25

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