IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MEDA PHARMACEUTICALS, INC. and CIPLA LTD.	)	
Plaintiffs,	)	Civil Action No. 14-1453 (LPS)
v.	)	
APOTEX, INC. and APOTEX CORP.	)	
Defendants.	)	

EXPERT REPLY REPORT OF MAUREEN D. DONOVAN, PH.D.

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1. I, Maureen Donovan, have been retained by Defendants Apotex, Inc., and Apotex Corp. as an expert to analyze certain aspects of U.S. Patent Nos. 8,163,723 ("the '723 patent"); 8,168,620 ("the '620 patent"); and 9,259,428 ("the '428 patent"), in connection with this lawsuit.

2. I submitted an opening expert report on June 30, 2016, opining that the asserted claims of the patents-in-suit are obvious. I also submitted a rebuttal report on July 29, 2016, and I incorporate both reports by reference. I have been asked to respond to the report of Hugh David Charles Smyth, Ph.D., submitted by plaintiffs on July 29, 2016, in rebuttal to my opening report. I reserve the right to amend or supplement my opinions in light of evidence presented by or on behalf of Meda Pharmaceuticals and Cipla Ltd., or in connection with additional information that may be made available to me in the future.

3. In addition to the information, materials and opinions discussed in this report, I may use demonstrative exhibits at trial to the extent useful for explaining and understanding the opinions I set forth in this report.

4. I may testify at trial about background scientific concepts related to my opinions to the extent that is useful for understanding my opinions.

5. I am being compensated for my time on this matter at a rate of $250/hour for general document and background review, $400/hour for preparing reports, and $600/hour for testifying at trial or depositions. Those are my standard consulting rates. My compensation is in no way dependent on the outcome of this case.

6. My professional background and the bases for my opinion are set forth in my opening expert report.

I. SUMMARY OF OPINIONS

7. Dr. Smyth's rebuttal report rests on two fundamental misconceptions. First, he opines that one cannot merely assume that a formulator would have sought to combine azelastine

hydrochloride and fluticasone propionate and then proceed to determine how to go about formulating the two active ingredients. This, he claims, would "be nothing more than hindsight: starting at the end of the process by considering the obvious way a formulator POSA would proceed if she were to make a combination nasal spray that uses azelastine hydrochloride and fluticasone propionate." Smyth ¶ 2. Rather, Dr. Smyth claims, "a formulator first would consider formulation issues when selecting an active ingredient," and by doing so "would be counseled away from trying an intranasal antihistamine and steroid combination." ¶ 3. A formulator would be counseled away, he argues, because "given the formulation challenges of a solution-suspension system, such a combination would not have been obvious to try, and in June 2002, a formulator POSA would not have had a reasonable expectation of success in combining those systems into a new type of nasal dosage form." ¶ 5.

8. Dr. Smyth's hindsight argument, however, assumes the conclusion that a co-formulation would in fact have been difficult to achieve. My opinion, as I explained in my opening report, is that there would be no readily apparent difficulties in such a formulation, and hence it would be obvious for a formulator to combine the two ingredients if that is what was desired. Assuming that such a combination is desired, as Dr. Schleimer opines without the use of hindsight, only then determining how to formulate it is not hindsight on my part or the part of any other expert whose report I have read on behalf of Apotex. Dr. Smyth, on the other hand, relies entirely on hindsight to dig through the literature finding what he says are reasons the claimed combination formula may not have worked. That inquiry makes no sense and is not how scientists work. A formulator tasked with making the combination product would have known that it was fully possible and would have had a reasonable expectation of success—even if not guaranteed success—based on the teachings of the prior art.

9. Second, Dr. Smyth's entire report is based on his opinion that formulating azelastine hydrochloride and fluticasone propionate would be difficult because it would require creating "a new dosage form: a solution/suspension" (¶ 61)—or as he puts it elsewhere, a "dosage form that is both a solution and suspension" (¶ 50). *See also, e.g.*, ¶¶ 1, 4, 5, 23, 37, 59, 68, 69, 74–78, 84, 88, 104, 105, 107 (making similar statements). This is incorrect. Every suspension is a "dosage form that is both a solution and suspension." ¶ 50. That is because every suspension includes materials that are in solution as well as materials that are undissolved. Flonase®, for example, is actually ~99.95% fluid vehicle with dissolved materials and less than 0.05% undissolved particles in suspension. Opening Report ¶ 93. Hence Dymista® is actually properly categorized—as Dr. Smyth notes in paragraph 55—as an "aqueous suspension" and not as some hybrid, "new" dosage form.

10. The question for a POSA as of June 2002—just as it would be for a POSA today when making any formulation with similar goals—is whether adding azelastine hydrochloride to the Flonase® formulation would be expected to be incompatible with fluticasone propionate or any of the excipients in Flonase®. That is the question that would have determined, as of June 2002, whether formulating a combined azelastine hydrochloride-fluticasone propionate product would have been obvious to a POSA. Dr. Smyth does not give a single example of such an incompatibility. His report fails to show that a POSA would foresee any difficulty in formulating a suspension of fluticasone propionate that includes dissolved azelastine hydrochloride.

11. As I explained in my opening report, a POSA would have expected none. It was known how to formulate azelastine hydrochloride from the Astelin® product, it was known how to formulate fluticasone propionate from the Flonase® product, and a POSA would have

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