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 ROBERT P. SCHLEIMER, PH.D.

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1. I, Robert P. Schleimer, have been retained by Defendants Apotex, Inc., and Apotex Corp. as an expert to analyze certain claims 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. I have been asked to respond to the report of Dr. Michael Kaliner submitted by plaintiffs on July 29, 2016, in rebuttal to my opening report. I do so below, and incorporate the contents of my previous reports here, as if set forth verbatim.

3. I reserve the right to amend or supplement my opinions in light of evidence presented by or on behalf of the plaintiffs, or in connection with additional information that may later be made available to me. At trial, I may use demonstrative exhibits if useful for explaining and understanding the opinions in this report, and I may testify about background scientific concepts related to pharmacology to explain as necessary the context of the claims.

4. I am being compensated for my time on this matter at a rate of $400/hour for consulting and $600/hour for testimony. Those are my standard consulting rates. My compensation is in no way dependent on the outcome of this case.

5. My professional background and the bases for my opinions are set forth in my previous reports.

I. SUMMARY OF OPINIONS

6. In paragraph 31 of his report, Dr. Kaliner succinctly states the basis for his disagreements with my opinion that it would have been obvious to a POSA to combine intranasal azelastine and intranasal fluticasone. He offers six grounds for disagreement. He alleges: (1) there were dozens of available allergic rhinitis treatments, yielding hundreds of possible two-

drug pairings; (2) many of these drugs had activity in both the early and late phases of the allergic response, and thus a POSA would not have sought to combine an early-phase drug with a late-phase drug; (3) studies of antihistamine/steroid pairings showed no benefit over steroids alone; (4) experts at the time concluded from these studies that there is no benefit to combining an antihistamine and a steroid; (5) a clinician would have been discouraged from combining the two drugs to minimize patients' drug exposure; and (6) a POSA would have been discouraged by FDA's combination rule requiring superior results over either monotherapy, in light of the antihistamine/steroid studies suggesting no improvement over steroids. Points (3), (4), and (6) all generally rely on the combination studies to which Dr. Kaliner refers and may be treated together. None of these points are correct or cause me to change my opinions.

7. To the first point, it is not true that a POSA would have had to wade through hundreds of possible pairings in 2002 in coming to an obvious decision about what drugs to combine into a single product. As explained in my opening report, my rebuttal report, and in the rebuttal report of Dr. James Wedner, there were only a handful of treatments that doctors routinely used for the treatment of allergic rhinitis. Dr. Kaliner himself admits that intranasal steroids were the most common treatment. Of these, fluticasone propionate was one of only five FDA-approved steroids in 2002 and was a best-selling drug product (known as Flonase®). Antihistamines were the other most common treatment, and although oral antihistamines were and continue to be prescribed, *intranasal* antihistamines were nonetheless a widely used option and were known to be more effective than oral antihistamines. At the time, there were only *two* available intranasal antihistamines—azelastine and levocabastine. Of these, azelastine was shown to be more safe and effective *and* it was far more commonly prescribed (as Astelin®) than levocabastine. What's more, doctors routinely prescribed both Flonase® and Astelin® to patients

who did not respond sufficiently to Flonase® (and occasionally Astelin®) alone.

8. Addressing the second point, it is true that some drugs have effects on both the early-phase allergic response as well as the late phase. I stated no differently in my report. Intranasal steroids have an impact on *all* symptoms, but they have their *strongest*, and more importantly *most timely*, impact on the late phase. Intranasal azelastine, moreover, was known to be effective in part because it also had an effect on late-phase inflammation. But like other antihistamines, its predominant effect was on the early-phase response. It would have been obvious to combine the two, as doctors routinely did by prescribing both Flonase® and Astelin®, for patients with cases of more severe or persistent allergic rhinitis. The fact that they have some overlapping effects does not make it inventive to combine the two, particularly when there is no dispute that they achieve those effects through different mechanisms of action.

9. To the third, fourth, and sixth points, Dr. Kaliner interprets selected studies showing that oral antihistamines combined with intranasal corticosteroids are no better than corticosteroids alone as indicating that any combination of these drugs would have no benefit above that of the steroid monotherapy. I strongly disagree with this interpretation. Even if these studies would be interpreted as Dr. Kaliner says (a proposition with which I disagree), they are of relatively little importance to a POSA's decision in 2002 whether to combine intranasal azelastine and intranasal fluticasone. As discussed in some detail in my opening report, in my rebuttal report, and in the rebuttal report of Dr. McCulloch, these studies were all of *oral* antihistamines combined with intranasal steroids—none studied a combination of an *intranasal* antihistamine with an intranasal steroid. As explained repeatedly, intranasal antihistamines were known to be significantly more effective than oral antihistamines. Additionally, all but one of these studies reported results only after at least a week of treatment—a time point at which the

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