UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC,
Petitioner

v.

CIPLA LTD.,
Patent Owner.

Patent No. 8,168,620
Issue Date: May 1, 2012
Title: COMBINATION OF AZELASTINE AND STEROIDS

Inter Partes Review No.: IPR2017-00807

PETITIONER'S RESPONSE TO PATENT OWNER'S MOTION FOR OBSERVATIONS ON CROSS-EXAMINATION OF PETITIONER'S REPLY WITNESSES: DR. ROBERT SCHLEIMER, DR. MAUREEN DONOVAN, AND JOHN C. STAINES, JR

Petitioner Argentum Pharmaceuticals LLC ("Petitioner") hereby responds to Patent Owner's motion for observations regarding the cross-examinations of Dr. Robert Schleimer, Dr. Maureen Donovan, and John C. Stains, Jr. (Paper 44, hereafter "Mot."). Office Patent Trial Practice Guide, 77 Fed. Reg. 48756 at 48767-68 (August 14, 2012).

Observation #1: Patent Owner's assertion that Dr. Schleimer's testimony is undermined by his adoption of the statements in footnote 1 of his second declaration (EX1144) misapprehends the deposition testimony and the claims. Footnote 1 made clear that Dr. Schleimer did not consider the specific limitations of claims 4 and 42-44 because "[Petitioner] asked a formulation expert to weigh in on them," and that otherwise Dr. Schleimer considers "the combination of azelastine and fluticasone in a formulation suitable for nasal administration to be obvious for claims 4 and 42-44 for the same reasons as all the claims discussed [in the declaration]." EX1144, n.1. Claims 4 and 42-44 all depend from claim 1, making Dr. Schleimer's opinions as to claim 1 relevant to claims 4 and 42-44.

Observation #2: Patent Owner's assertions misapprehend Dr. Schleimer's deposition testimony. Dr. Schleimer explained that from a layperson's perspective, the clinical practice of conjunctive therapy most closely approximates the claimed invention. EX2179, 42:17-44:17. Dr. Schleimer also recognized that in the context of this legal proceeding where "prior art" might be restricted to printed

publications only, Segal and Cramer would be the strongest prior art. *Id*. Dr. Schleimer also noted that adoption of that prior art "does change [his] opinion" relative to his layman consideration of prior clinical use. *Id*.

Observation #3: Patent Owner's assertions based on Dr. Schleimer's testimony regarding Howarth and Nielsen both mischaracterize his testimony and ignore other relevant testimony. As to Howarth (EX2041), Dr. Schleimer explained that Howarth's assertion of lack of clinical benefit was unsupported, and that Howarth overlooked the additivity of azelastine and fluticasone during the first two weeks of administration (EX2179, 66:2-20),which Dr. Schleimer explained in greater detail in his declaration (EX1144, ¶¶32-36). Regarding Nielsen (EX2042), Dr. Schleimer explained that the authors' goal was to "definitively establish that steroids are superior to antihistamines, but when it came to discussing the combination, they kind of gave it short shift" and that "they begrudgingly admit that the combination has some marginal benefits but the cost is an issue" (EX2179, 73:6-9, 12-15), which was also discussed in more detail in Dr. Schleimer's declaration (EX1144, ¶¶37-38). Dr. Schleimer also noted that one of Cipla's own experts disagreed with the conclusions of these papers. *Id*., ¶39.

Observation #4: Patent Owner's assertions regarding what Dr. Schleimer explained in relation to Ratner 2008 (EX1045) grossly mischaracterizes the deposition testimony. The testimony ascribed to Dr. Schleimer only occurred

when he was asked to read aloud a quote from Ratner 2008 (EX2179, 96:13-19)—this was not Dr. Schleimer's own testimony regarding Ratner. Instead, when asked "doesn't this statement imply that six years later the authors were surprised by the efficacy of their regimen?" Dr. Schleimer explained that "[t]o me, as I've testified, a POSA would have anticipated an additivity, and a POSA would have looked at these results and thought, yeah, that makes sense" and "[w]hy they wrote it's unanticipated and to what extent it truly reflects the views of all the authors, I cannot comment." *Id*., 98:2-21.

Observation #5: Patent Owner's assertions that Dr. Schleimer relied on post-invention publications to support his obviousness conclusions mischaracterize the testimony and ignores other relevant testimony. Dr. Schleimer testified that it was well-known before the priority date that azelastine's onset was 15-30 minutes. EX2179, 103:15-104:11, 109:11-13. Dr. Schleimer then explained that because Dr. Carr affirmatively contested the fast onset of azelastine, he felt it was important to find support both before and after the priority date showing that Dr. Carr's arguments were incorrect. *Id*., 104:19-105:22.

Observation #6: Patent Owner's assertion that Dr. Donovan undermined her credibility when she stood by her trial demonstratives is false. Dr. Donovan explained that the purpose of the chart in EX2177 was not to communicate to the Court the advantages and drawbacks of all of the tonicity agents shown. EX2178,

55:11-18. Dr. Donovan also testified on numerous occasions regarding the fact that while all of the listed materials were obvious tonicity agents, there were advantages to glycerine and drawbacks to sodium chloride and dextrose that would cause a POSA to prefer glycerine over the other choices. EX2178, 44:16-45:5; 45:17-46:3; 54:15-55:6; 56:1-19; *see also* EX1145, ¶¶68-70 (same).

Observation #7: Patent Owner's assertion that Dr. Donovan's deposition testimony contradicts her testimony that a motivation existed to "use the three preservatives as recited in claims 42-44" and to "avoid using dextrose" mischaracterizes the testimonial record. When asked if there was no need for dextrose when using the preservatives from Flonase in a combination fluticasone azelastine formulation, Dr. Donovan testified that a "POSA always holds out the possibility that they will have some undesired failure of their system and then the dextrose will serve as a great growth media." EX2178, 66:20-67:13. Dr. Donovan's declaration also explains that "[s]ugars like dextrose are known for aiding bacterial growth when used in low concentrations." EX1145, ¶69. This is further corroborated by Dr. Donovan in her deposition. EX2178, 71:18-72:7. Additionally, Dr. Donovan also testified that there is "always a concern that your antimicrobial preservatives will fail under some use challenge" and that one can "address that concern through the use of adequate antimicrobial preservatives." *Id.*, 67:4-9; 73:5-8.

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