UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MICRO LABS LIMITED AND MICRO LABS USA INC.
Petitioners,

v.

SANTEN PHARMACEUTICAL CO., LTD. AND ASAHI GLASS CO., LTD.
Patent Owners.

Case IPR2017-01434
U.S. Patent No. 5,886,035

PATENT OWNERS' MOTION FOR OBSERVATION

REGARDING CROSS-EXAMINATION OF PETITIONERS' EXPERT,

DR. ARON D. ROSE

Pursuant to the Scheduling Order in this proceeding (Paper 12), and the Office Patent Trial Practice Guide, Patent Owners Santen Pharmaceutical Co., Ltd. and Asahi Glass Co., Ltd. (together, "Patent Owners"), respectfully submit this Motion for Observation Regarding Cross-Examination of Dr. Aron D. Rose, the Reply declarant of Petitioners Micro Labs Limited and Micro Labs USA Inc. (together "Micro Labs" or "Petitioner"). The full transcript of Dr. Rose's July 16, 2018 cross-examination is being filed concurrently as Ex. 2062.

Observation # 1: In Ex. 2062 at 14:19-23 and 15:13-16:13, Dr. Rose testified that, with respect to early $PGF_{2\alpha}$ prostaglandin analogs, Ex. 2015 (a paper titled "Initial Clinical Studies with Prostaglandins and their Analogues") teaches that $PGF_{2\alpha}$ tromethamine salts, $PGF_{2\alpha}$-IE, and 15-propionate-$PGF_{2\alpha}$-IE all "produce unacceptable side effects including conjunctival hyperemia and ocular irritation." Dr. Rose agreed that the authors of Ex. 2015 (Camras and Alm) "were at the forefront of the development of prostaglandin analogs as of December 26, 1996." *Id.* at 15:7-12. Dr. Rose's testimony above contradicts his assertion that early $PGF_{2\alpha}$ analogs were not regarded in the field as "clinically unacceptable." Ex. 1032, ¶¶ 25-26 ("I would not describe $PGF_{2\alpha}$, or its early analogs, as 'clinically unacceptable,' and nothing I have reviewed for this case suggests otherwise."); Dr. Rose's testimony that he had previously reviewed Ex. 2015 (Ex. 2062 at 15:4-6)

also contradicts his assertion that nothing he reviewed for this case suggested otherwise. Ex. 1032, ¶ 26.

Observation # 2: In Ex. 2062 at 18:18-23 and 19:6-23, Dr. Rose testified that Ex. 2058 (a paper titled "Additive Effect of Latanoprost, a Prostaglandin $F_{2\alpha}$ Analogue, and Timolol in Patients with Elevated Intraocular Pressure") "describ[es] PGF2alpha-IE as hampered by clinically unacceptable hyperemia." Dr. Rose acknowledged that the authors of Ex. 2058 cited Ex. 1033 (*id.* at 20:16-25) and Ex. 2013 (*id.* at 21:7-12). And yet, Dr. Rose relied on Ex. 1033 and Ex. 2013 in his Supplemental Declaration for the opposite proposition - that "there were several papers published showing a superior therapeutic profile for the isopropyl ester modified form of $PGF_{2\alpha}$ ('$PGF_{2\alpha}$-IE')." Ex. 1032, ¶ 24. Dr. Rose's testimony contradicts his assertion that early $PGF_{2\alpha}$ analogs were not regarded in the field as "clinically unacceptable." Ex. 1032, ¶¶ 25-26. His testimony also contradicts his position that Exs. 1033 and 2013 teach a "superior therapeutic profile" for $PGF_{2\alpha}$-IE. Ex. 1032, ¶ 24.

Observation # 3: In Ex. 2062 at 22:6-10 and 22:23-23:3, Dr. Rose confirmed that Petitioners' Ex. 1033 (a paper titled "Prostaglandin $F_{2\alpha}$-1-Isopropyl Ester Lowers Intraocular Pressure Without Decreasing Aqueous Humor Flow")

discloses a study in which patients "were receiving increasing doses of the PGF2alpha-isopropyl ester." Dr. Rose testified that Ex. 1033 discloses that two of the 20 patients in the study, *i.e.*, "10 percent of the patients," "could not complete the study for all doses because of marked conjunctival hyperemia." *Id.* at 24:15-23. Dr. Rose's testimony illustrates the significant discontinuation rate caused by conjunctival hyperemia in patients treated with $PGF_{2\alpha}$–IE. Dr. Rose's testimony contradicts his reliance on Ex. 1033 as teaching a "superior therapeutic profile" for $PGF_{2\alpha}$-IE. Ex. 1032, ¶ 24. (Dr. Rose provided further testimony on this subject in re-direct examination, but it was improperly elicited through leading questions and is the subject of a motion to exclude. In any event, Dr. Rose's redirect testimony focused only on technicalities regarding the disclosure in Ex. 1033; Dr. Rose did not withdraw any of his cross-examination testimony detailed above.)

Observation # 4: In Ex. 2062 at 77:8-78:9, Dr. Rose conceded that Stjernschantz (Ex. 2017) at 2:45-52 discloses "that it's clinically impossible to use the PGF2alpha-IE compound in the amount that would give maximum pressure reduction." *See also id.* at 79:3-8 (Q. "So PGF2alpha-IE in its current form, unmodified, presented challenges for continued use; correct?" A. "That's what Stjernschantz is writing here."). Dr. Rose's testimony further contradicts his

assertion that early $PGF_{2\alpha}$ analogs were not regarded in the field as "clinically unacceptable." Ex. 1032, ¶¶ 25-26.

Observation # 5: In Ex. 2062 at 101:8-12, Dr. Rose agreed that Figure 3 of Ex. 2003 reports "differences in IOP between treated and control eyes . . . over time for four different doses of drug." Dr. Rose agreed that the highest dose Figure 3 discloses is 200 µg (*id.* at 101:13-15), and, at 200 µg, $PGF_{2\alpha}$ exhibits a 7 to 8 mmHg increase in IOP shortly after administration (*id.* at 102:4-11). Dr. Rose agreed that this 200 µg dose of $PGF_{2\alpha}$ "provide[s] IOP-lowering activity for at least about 24 hours." *Id.* at 102:12-15. Dr. Rose also agreed that the next highest dose of $PGF_{2\alpha}$ in Figure 3—50 µg—shows an initial increase in IOP of 10 mmHg shortly after administration. *Id.* at 102:16-25. Dr. Rose further agreed that the next highest dose of $PGF_{2\alpha}$ in Figure 3—5 µg—"is the highest dose studied that [does] not exhibit a clear initial increase in IOP." *Id.* at 103:2-13. Dr. Rose conceded that "although lowering the dose from 200 to 5 micrograms eliminated that initial increase in IOP, the duration of IOP lowering was decreased to less than 24 hours [specifically, to approximately 15 hours or less] with 5 micrograms of PGF2alpha." *Id.* at 103:14-24. Dr. Rose's testimony contradicts Petitioners' and Dr. deLong's argument that an undesirable initial increase in IOP could be addressed by simply decreasing the dose. Reply (Paper 24) at 12-13; Ex. 1031,

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