UNITED STATES PATENT AND TRADEMARK OFFICE ————— BEFORE THE PATENT TRIAL AND APPEAL BOARD ———— MICRO LABS LIMITED AND MICRO LABS USA INC., Petitioner,

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

V.

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

PATENT OWNER RESPONSE

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TABLE OF AUTHORITIES

Cases

Eli Lilly and Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369 (Fed. Cir. 2006)	49
Otsuka Pharm. Co. v. Sandoz, Inc., 678 F.3d 1280 (Fed. Cir. 2012)	27, 28, 30
Pfizer Inc. v. Teva Pharm. USA, Inc., 555 F. App'x 961 (Fed. Cir. 2014)	26, 27, 46
PPC Broadband, Inc. v. Corning Optical Commc'ns RF LLC, 815 F.3d 734 (Fed. Cir. 2016)	66
Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350 (Fed. Cir. 2007)	27, 28, 29, 47



LIST OF EXHIBITS

Exhibit			
No.	Document		
2001	Declaration of Timothy L. Macdonald, Ph.D.		
2002	Declaration of Philothy E. Wacdonald, Ph.D. Declaration of Robert D. Fechtner, M.D.		
2003	Camras <i>et al.</i> , "Reduction of intraocular pressure by prostaglandins applied topically to the eyes of conscious rabbits," <i>Invest. Ophthalmol. Vis. Sci.</i> 16:1125-1134 (1977)		
2004	"Pharmacia Cleared To Market Xalatan, Drug for Glaucoma," <i>Wall St. J.</i> B7 (June 7, 1996)		
2005	Fung and Whitson, "An evidence-based review of unoprostone isopropyl ophthalmic solution 0.15% for glaucoma: place in therapy, <i>Clin. Ophthalmol.</i> 8:543-554 (2014)		
2006	Linden and Alm, "Prostaglandin Analogues in the Treatment of Glaucoma," <i>Drug Aging</i> , 14(5):387-398 (1999)		
2007	Coleman <i>et al.</i> , "VIII. International Union of Pharmacology Classification of Prostanoid Receptors: Properties, Distribution, and Structure of the Receptors and Their Subtypes," <i>Pharmacol. Rev.</i> 46(2):205-229 (1994)		
2008	Konturek and Pawlik, "Physiology and pharmacology of prostaglandins," <i>Dig. Dis. Sci.</i> 31(2 Suppl):6S-19S (1986)		
2009	Stjernschantz and Alm, "Latanoprost as a new horizon in the medical management of glaucoma," <i>Curr. Opin. Ophthalmol.</i> 7(2):11-17 (1996)		
2010	Collins and Djuric, "Synthesis of Therapeutically Useful Prostaglandin and Prostacyclin Analogs," <i>Chem. Rev.</i> 93:1533-1564 (1993)		
2011	Giuffrè, "The effects of prostaglandin $F_{2\alpha}$ in the human eye," <i>Graefe's Arch. Clin. Exp. Ophthalmol.</i> 222:139-141 (1985)		
2012	Bito and Baroody, "The ocular pharmacokinetics of eicosanoids and their derivatives: 1. Comparison of ocular eicosanoid penetration and distribution following the topical application of $PGF_{2\alpha}$, $PGF_{2\alpha}$ -1-methyl ester, and $PGF_{2\alpha}$ -1-isopropyl ester," <i>Exp. Eye Res.</i> 44:217-26 (1987)		
2013	Villumsen and Alm, "Prostaglandin $F_{2\alpha}$ -isopropylester eye drops: effects in normal human eyes," <i>Br. J. Ophthalmol.</i> 73:419-26 (1989)		
2014	Villumsen and Alm, "Ocular effects of two different prostaglandin $F_{2\alpha}$ esters: a doublemasked cross-over study on normotensive eyes," <i>Acta Ophthalmol.</i> 68:341-343 (1990)		



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