UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

AQUESTIVE THERAPEUTICS, INC.

Petitioner

v.

ICOS CORPORATION,

Patent Owner

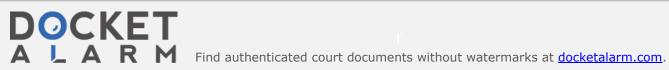
Case: IPR2018-01183 Patent 6,943,166

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 6,943,166



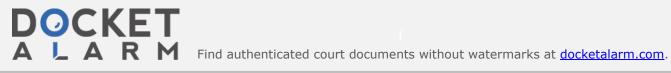
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PETITIONERS' EXHIBIT LIST

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U.S. Patent 6,087,362	1004
WO 9703675	1005
VIAGRA® (sildenafil citrate) label	1006
CIALIS® (tadalafil) label	1007
D. Eros, et al., Structure-Activity Relationships of PDE5 Inhibitors, Current	1008
Medicinal Chemistry, 2008 (15), 1570-1585.	
Prosecution History for U.S. Patent No. 6,943,166	1009
Expert Declaration of Roger Williams, M.D. Regarding U.S. Patent No.	1010
6,943,166	
Sildenafil Citrate (VIAGRA®) Approval Package for New Drug	1011
Application No. 020895 ("SNDA")	
Filloon, Estimating the minimum therapeutically effective dose of a	1012
compound via regression modelling and percentile estimation, Stat Med.	
1995 May 15-30;14(9-10):925-32 ("Filloon")	
Effects of sildenafil citrate on human hemodynamics, Am. J. of Cardiology,	1013
83(5), Supp. 1, pp. 13-20 (March 4, 1999)	
The Guideline for Industry, Dose Response Information to Support Drug	1014
Registration ("FDA Guideline")	
Petition To Add Information About Sildenafil's Danger's To The Drug	1015
Label	
Cutler, et al., Defining the Maximum Tolerated Dose: Investigator,	1016
Academic, Industry and Regulatory Perspectives, J. Clin. Pharmacol. 1997;	
37:767-783 ("Cutler")	
ICOS 10K FY 1998	1017
Ruberg, Stephen J. Ph.D., <i>Dose response studies l. some design considerations</i> , Journal of Biopharmaceutical Statistics, 5:1, 1-14 (1995)	1018
("Ruberg")	
Sildenafil NDA Access Data (indicating the files were created on March 27, 1998)	1019
FDA Approval Letter, Sildenafil (Viagra®) NDA 020895, March 27, 1998 ("Sildenafil Approval Letter)	1020
CNNMoney.com, March 27, 1998 ("CNN Article")	1021
Dow Jones Online News, March 27, 1998 ("Dow Jones Article")	1022
Boolell, M., et al., Sildenafil: an orally active type 5 cyclic GMP-specific	1023



phosphodiesterase inhibitor for the treatment of penile erectile dysfunction, 8 Int. J. Impot. Res., (1996) 47-52 ("Boolell")	
Terrett, N. K., et al., Sildenafil (Viagra ^{IM}), a Potent and Selective Inhibitor of Type 5 cGMP Phosphodiesterase with Utility for the Treatment of Male Erectile Dysfunction, 6 Bioorg. Med. Chem. Lett. (1996) 1819-1824 ("Terrett")	1024
Licht, M.R., Sildenafil (Viagra) for treating male erectile dysfunction, 65 CLEVE. CLIN. J. MED., (1998) 301-304 ("Licht")	1025
Gingell, C. J. C., et al., UK-92,480: A New Oral Treatment for Erectile Dysfunction: A Double-Blind, Placebo-Controlled, Once Daily Dose Response Study, 155 Suppl 5 J. UROL. (1996) Abstract No. 738 ("Gingell")	1026
Goldstein, I., et al., Oral Sildenafil in the Treatment of Erectile Dysfunction, 338 N. Engl. J. Med., (1998) 1397-1404 ("Goldstein")	1027
Morales, A., et al., Clinical safety of oral sildenafil citrate (VIAGRA TM) in the treatment of erectile dysfunction, 10 Int. J. Impot. Res., (1998) 69-74 ("Morales")	1028
de Mey, C., Opportunities for the Treatment of Erectile Dysfunction by Modulation of the NO Axis-Alternatives to Sildenafil Citrate, 14 Curr. Med. Res. Opin., (1998) 187-202 ("de Mey")	1029
Cheitlin, M.D., et al, Use of Sildenafil (Viagra) in Patients with Cardiovascular Disease, 33 J. Am. Coll. Cardiol. (1999) 273-282 ("Cheitlin,")	1030
Lilly and ICOS Establish a Joint Venture to Develop and Market PDE5 Compounds to Treat Sexual Dysfunction Eli Lilly and Company PRESS RELEASE 1998 October 1 ("Lilly Press Release")	1031
Norman, P., IC-351 ICOS Corp, 1 Curr. Opin. Cpns Invest. Drugs (1999) 268-271 ("Norman,")	1032
Bourne, H. R., and Roberts, J. M., Drug Receptors & Pharmacodynamics, BASIC & CLINICAL PHARMACOLOGY (Katzung, B. G. ed., 6th Ed. 1995) 9-32 ("Bourne")	1033
Rowland and Tozer's Clinical Pharmacokinetics (1995 Third Edition) at Section 5.20 'Pharmacologic Response' page 340-341.	1034



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