UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.
Petitioner,

v.

ICOS CORP.
Patent Owner.

Patent No. 6,943,166

DECLARATION OF GEORGE GRASS, PHARM.D., PH.D.

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I, George Grass, declare as follows:

I. QUALIFICATIONS

1. My name is George M. Grass IV. I have been working in the drug discovery and biotechnology industries since 1985. I am currently President of a consulting business, G2 Research Inc., and Sr. Vice President of Non-Clinical Development for NeuroVia Inc.

2. I received a Pharm. D. from the University of Nebraska in 1980, a M.S. in Pharmaceutics from the University of Wisconsin in 1983, and a Ph.D. in Pharmaceutics from the University of Wisconsin in 1985.

3. My primary areas of technical expertise are drug development, drug delivery, and pharmacokinetics, including computational simulations and modeling of pharmacokinetic processes.

4. In previous professional roles, I have served as a researcher, an executive, or a consultant for numerous drug development and biotechnology companies, including Sorbent Therapeutics, PDxRx Inc., Trega Biosciences, NaviCyte, Inc., Precision Instrument Design, Inc., and Syntex Research.

5. I have authored over 30 publications related to drug development, drug delivery and pharmacokinetics, including book chapters and peer-reviewed journal articles. I have authored over 30 abstracts for presentation at professional

meetings. I am also an inventor or co-inventor on 12 patent applications, including eight awarded patents.

6. A summary of my experience, education, publications and other qualifications is provided in my CV, a copy of which is submitted separately. EX1003.

II. SCOPE OF WORK

7. I understand that a petition is being filed with the United States Patent and Trademark Office for *Inter Partes Review* of U.S. Patent No. 6,943,166 ("the '166 patent," EX1001). I have been retained by Mylan Pharmaceuticals Inc. as a technical expert to provide analysis and opinions regarding the '166 patent. I have reviewed the '166 patent and sections of its prosecution history in the United States Patent and Trademark Office. EX1006. I have also reviewed and considered various other documents in arriving at my opinions, and I cite them in this declaration. For convenience, documents cited in this declaration are listed in the Appendix in Section XIII.

8. I am compensated at the rate of $575/hour for my work. I have no financial interest in the outcome of this matter.

III. OVERVIEW OF THE '166 PATENT

9. The '166 patent issued on September 13, 2005. The '166 patent is titled "Compositions Comprising Phosphodiesterase Inhibitors for the Treatment of

Sexual Dysfunction." The first page of the patent states that an application for the '166 patent (U.S. Application No. 10/031,556), was filed as a national stage entry application of PCT/US00/11129 and claims priority to provisional U.S. Application No. 60/132,036, filed on April 30, 1999.

10. The '166 patent is generally directed to the treatment of sexual dysfunction, including male erectile dysfunction and female arousal disorder using the compound (6*R*,12a*R*)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, referred to herein for convenience as "tadalafil," and also referred to in the '166 patent as Compound I. EX1001, 2:58-63. Tadalafil is marketed under the trademark Cialis®. Cialis® Approved Label ("Cialis® Label," EX1010).The '166 patent states:

> The biochemical, physiological, and clinical effects of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase (cGMP-specific PDE) inhibitors suggest their utility in a variety of disease states in which modulation of smooth muscle, renal, hemostatic, inflammatory, and/or endocrine function is desired. Type 5 cGMP-specific phosphodiesterase (PDE5) is the major cGMP hydrolyzing enzyme in vascular smooth muscle, and its expression in penile corpus cavernosum has been reported. Thus, PDE5 is an attractive target in the treatment of sexual dysfunction.

Id. at 1:29-40 (citations omitted).

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