Declaration of Steven E. Patterson, Ph.D.

Inter-Partes Review _____

Petitioner: Mylan Pharmaceuticals, Inc.

Patent Owner: UCB Pharma GmbH

Patent No.: 6,858,650

Introduction and Background Qualifications

1. I, Steven E. Patterson, Ph.D., have been retained by Kilpatrick Townsend & Stockton, LLP, counsel for Mylan Pharmaceuticals Inc. and Mylan Laboratories Limited ("Mylan"). My curriculum vitae is attached here and is labeled Ex. 1004. I understand that Mylan has petitioned for *inter partes* review of U.S. Patent No. 6,858,650 ("'650 patent") and requests that the United States Patent and Trademark Office cancel Claims 1-5 and 21-24 of the '650 patent as unpatentable. The following discussion and analyses address the bases for Mylan's Petition.

2. I obtained my Ph.D. in Chemistry in 1995 and began a postdoctoral research position at the University of Notre Dame sponsored by Bayer in 1996. As part of my research there, I focused on combinatorial methods to develop selective sensors for carbohydrates and carbohydrate derivatives such as nucleic acid. This work, as could be expected given its sponsorship, was aimed at hopefully finding commercially viable compounds with pharmaceutical applications.

3. Currently, I am professor at the Center for Drug Design at The University of Minnesota. My research focuses on the efficient preparation of novel nucleosides and nucleotide analogs. Much focus in this space is in the prodrug context and is aimed at providing commercially viable pharmaceutical or therapeutic compounds that are either derived from existing, known effective treatments or the discovery of new compounds.

4. As shown in my curriculum vitae, I am listed as author or co-author of over 80 peer reviewed journal articles or publications focused on pharmaceutical and chemical analysis of compounds used in pharmaceutics. I have also served as the Director of the National Science Foundation's Workshop in Medicinal Chemistry in 2012, 2013, 2014, and 2016 (scheduled). I am a member of the American Chemical Society in both the Medicinal and Organic Chemistry Divisions.

5. Also as indicated in my curriculum vitae, I hold a U.S. patent for a novel compound and its preparation of an aklylamino compound – same class of compounds at issue in my analysis here. I have applied for at least four other patents, with at least two of those applications still pending.

6. Much of my granted and focused research at the Center for Drug Design is in the area of structural analogs and improving the bioavailability of compounds

for use in pharmaceuticals or therapeutics. As will be discussed in great detail below, my understanding of how structural analogs are viewed by persons of skill in the art in terms of advancing the pharmaceutical arts is critical in determining which compounds are focused on by artisans in this field.

7. As detailed below, I understand that the relevant period for my analysis is the first half 1998. In 1998 I had experience in drug design and development having specifically researched combinatorial synthesis of heterocyclic libraries as novel drug candidates. Specifically the libraries were focused on discovering potential leads for cancer drugs and *pneumocystis carinii*. This involved obtaining an understanding of what was known about compounds and drug candidates in the area of cancer therapeutics.

8. At that time, I was very familiar with the design and development of prodrug compounds based on known active compounds through literature and my own work on discovery of and structure-activity relationship of a novel class of anti-HIV compounds as a graduate student, some work with rifamycin derivatives, work with amidine-based prodrugs for *pneumocystis carinii*, and my work in discovery at Pharmasset where I was part of the team that discovered PSI-6130, a highly potent anti-HCV compound.

Materials Considered

9. The following table shows the materials that I considered and relied upon in coming to my opinions. I also relied on the understanding that a skilled person in the field of drug design and development was not an automaton and instead possessed reasonable creativity in solving problems known to exist in the field.

Exhibit No.	Title
1001	U.S.P.N. 6,858,650
1002	File History for Exhibit 1001
1003	Declaration of Dr. Steven Patterson, Ph.D.
1004	C.V. for Dr. Steven Patterson, Ph.D
1005	"Johansson" – WO 94/11337 Filed 6 November 1992 – "Novel 3,3-Diphenylpropylamines, Their Use and Preparation"
1006	"Andersson Review" – BJU International (1999), 84, 923-947 – "The Pharmacological Treatment of Urinary Incontinence"; K-E Andersson, R. Appell, L.D. Cardozo, C. Chapple, H.P. Drutz, A.E. Finkbeiner, F. Haab, and R. Vela Navarrete.
1007	"Brynne 1997" – International Journal of Clinical Pharmacology and Therapeutics (1997), 35, 287-295 – "Pharmacokinetics and pharmacodynamics of tolterodine in man: a new drug for the treatment of urinary bladder overactivity"; N. Brynne, M.M.S. Stahl, B. Hallen, P.O. Edlund, L. Palmer, P. Hoglund, and J. Gabrielsson.
1008	"Thomas" – British Heart Journal (1995), 74, 53-56 – "Concentration dependent cardiotoxicity of terodine in patients treated for urinary incontinence"; S. Thomas, P. Higham, K Hartigan-Go, F. Kamali, P. Wood, R. Campbell, and G. Ford.
1009	"Detrol® Label" – Pharmacia & Upjohn.
1010	"Postlind" – Drug Metabolism and Disposition (1998), 26 (4), 289-293 – "Tolterodine, A New Muscarinic Receptor Antagonist, Is Metabolized by Cytochromes P450 2D6 and 3A in Human Liver Microsomes"; H. Postlind, A. Danielson, A. Lindgren, and S. Andersson.

1011	"Brynne 1998" – Clinical Pharmacology & Therapeutics (May 1998), 63(5), 529-539 – "Influence of CYP2D6 polymorphism on the pharmacokinetics and pharmacodynamics of tolterodine"; N. Brynne, P. Dalen, G. Alvan, L. Bertilsson, and J. Gabrielsson.
1012	"Bundgaard" – Elsevier Science Publishers (1985) – "Design of Prodrugs"; Hans Bundgaard.
1013	"Berge 1977" – Journal of Pharmaceutical Sciences (1977), 66 (1), 1-19 – "Pharmaceutical Salts"; S. Berge, L., Bighley, and D. Monkhouse.
1014	"Andersson 1998" – Drug Metabolism and Disposition (1998), 26(6), 528-535 – "Biotransformation of tolterodine, a new muscarinic receptor antagonist, in mice, rats, and dogs"; S. Andersson, A. Lindgren, and H. Postlind.
1015	"Nilvebrant" – Pharmacology and Toxicology (1997), 81, 169-172 – "Antimuscarinic Potency and Bladder Selectivity of PNU-200577, a Major Metabolite of Tolterodine"; L. Nilvebrant, P. Gillberg, and B. Sparf.
1016	"DeMaagd" – P&T (2012), 37(6), 345-361 – "Management of Urinary Incontinence"; G. DeMaagd and T. Davenport.
1017	"Appell" – Urology (1997), 50, 90-96 – "Clinical efficacy and safety of tolterodine in the treatment of overactive balder: a pooled analysis"; R. Appell.
1018	"Ashworth" – Home Care Provider (1997), 2(3), 117-120 – "Is My Antihistamine Safe?"; L. Ashworth.
1019	"Lipinski" – Advanced Drug Delivery Reviews
1020	"Bundgaard PCT" – WO 92/08459 Filed 11 November 1991 – "Topical Compositions for Transdermal Delivery of Prodrug Derivatives of Morphine"
1021	"AUA Guideline" – American Urological Association Eductatio and Research (2014) – "Diagnosis and Treatment of Overactive Bladder (Non-Neorogenic) in Adults: AUA/SUFU Guideline"; E. Gormley, et al.
1022	"Pfizer 2012 Press Release" – Aug. 2, 2012 "Study Shows Toviaz is Effective in Reducing Urge Urinary Incontinence in Patients with Overactive Bladder After Suboptimal Response to Detrol LA" – www.pfizer.com
1023	"PM360" – April 1, 2012 "Overactive Bladder Market: Managing the Future" – www. pm360online.com

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