Filed: August 1, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ACRUX DDS PTY LTD. & ACRUX LIMITED
Petitioners,

v.

KAKEN PHARMACEUTICAL CO., LTD. and
VALEANT PHARMACEUTICALS INTERNATIONAL, INC.
Patent Owner and Licensee

Case: IPR2017-00190
U.S. Patent No. 7,214,506

DECLARATION OF YOSHIYUKI TATSUMI, PH.D.

I, Yoshiyuki Tatsumi, hereby declare and state:

1. I am an inventor of the subject matter described and claimed in U.S. Patent No. 7,214,506 ("the '506 patent"). I submit this Declaration on behalf of Kaken Pharmaceutical Co., Ltd. ("Kaken") in *Inter Partes* Review No. 2017-00190.

2. I am a Group Manager of the Pharmacology Department of the Drug Discovery Center at Kaken Pharmaceutical Co., Ltd. ("Kaken"). I am also the Chairman of the Biosafety Committee and Chairman of the Genetic Recombination Experiment Safety Committee at Kaken.

3. I graduated with a degree in Pharmaceutical Sciences from Kindai University in 1990 before gaining a master's degree in pharmaceutical science from Kindai University Graduate School. I obtained a Ph.D. in Pharmaceutics from Kindai University Graduate School in 2003.

4. In 1992, I joined the Chemotherapy Group of Pharmaceutical Science in the Research Center of Kaken. In general, from 1992-1995, I worked on antibacterial agents, including cephalosporins and quinolones. From 1994-2000, I worked on the treatment of athlete's foot (also known as tinea pedis) using KP-103. I have extensive experience in researching and evaluating the therapeutic effects of KP-103, including for the topical treatment of tinea pedis and onychomycosis.

5. I have been asked to explain the research and development Kaken conducted on KP-103 and to explain the contents of several internal laboratory notebooks, and activity reports relating to that research. This Declaration describes my personal knowledge of each of the events and documents described below.

6. Kaken discovered the compound KP-103 in the early-1990's during its research on a new antifungal agent that could be commercialized to treat tinea pedis. In particular, Kaken hoped to discover an antifungal agent that could be used to treat mycosis and specifically, tinea pedis (commonly called athlete's foot).

7. Kaken considered various topical antifungal agents and focused its attention on triazole derivatives to develop a broad spectrum antifungal agent. We evaluated the differences between triazole and imidazole derivatives and studied the *in vitro* activities of the agents against various microorganisms commonly found in tinea pedis. In the course of this research, KP-103 was discovered.

8. Exhibit 2030 and Exhibit 2033 are pages from lab notebooks during our research. Exhibit 2030 is a laboratory notebook labeled "Fungus" and is dated September 8, 1992 through September 17, 1993. Exhibit 2033 is titled "Antifungal activity of triazole-based compound *in vitro*" and is dated April 26, 1993. I have knowledge of the work recorded on these pages. The compound labeled either "S-32282" or "32282" corresponds to KP-103. *See* Ex. 2030, 2; Ex. 2033, 1. It was the regular practice at Kaken to maintain contemporaneous laboratory notebooks

documenting the research we conducted and the results of those experiments, as reflected in these appendices. To the best of my knowledge, these reports are accurate and reflect data generated during the experiments that led to the discovery of KP-103. Because Kaken was interested in commercializing an antifungal agent, none of the data resulting from the research in the 1992-1993 period was published or otherwise made publicly available at that time. Instead, Kaken continued experimenting with KP-103 and other antifungal agents.

9. Kaken then decided to publish its internal data to determine third-party interest in licensing KP-103 as a treatment for tinea pedis. In September 1996, licensing representatives from Kaken and I attended the 36th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). At the ICAAC, we presented the Kaken Abstracts that are shown in Exhibit 1015 and related Abstracts 790, 792, and 793, which are shown in Exhibit 2036, Exhibit 2037, and Exhibit 2038, respectively. I located Abstracts 790, 792, and 793 in my corporate files. Those were the only materials relating to the conference that I found. I have personal knowledge of the information presented in the Abstracts and personal knowledge of Kaken's commercialization efforts for KP-103.

10. The Kaken Abstracts explained that KP-103 was a novel antifungal that had been developed for topical treatment of tinea pedis and that KP-103 showed broad spectrum antifungal activity and positive cure rates against that

fungal infection. The progression of *in vitro* experiments in the Kaken Abstracts from MIC activity testing, to testing in stripped horny layer, and then on guinea pig skin illustrates our research focus on tinea pedis and the direction of that work.

11. Kaken began phase I clinical trials related to using KP-103 to treat tinea pedis in November 1996. Following the conclusion of the phase I trial in November 1997, the company decided to stop any additional clinical trials or research on KP-103 and the project was subsequently put aside.

12. To my knowledge, the clinical significance of KP-103 for treating onychomycosis had not yet been recognized by Kaken or by anyone at the ICAAC meeting, nor had I heard of anyone else suggesting at that time to use KP-103 for that indication. Once the KP-103 project was put aside, we were permitted to publish the data from our 1992-1993 research evaluating KP-103's efficacy in tinea pedis.

13. We published the data in 1999 in an article entitled "Synthesis and Antifungal Activities of (2R,3R)-2-Aryl-1-azolyl-3-(substituted amino)-2-butanol Derivatives as Topical Antifungal Agents" by Ogura et al. I understand the article has been cited in the *Inter Partes* Review as Exhibit 1012. The article was based in part on the data in Exhibits 2030, 2033, 2036, 2037, and 2038. I am listed as an author on this publication and I have personal knowledge of its contents. To the best of my knowledge, this article accurately describes experiments from 1992-

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