IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LUPIN LIMITED
Petitioner

v.

JANSSEN SCIENCES IRELAND UC
Patent Owner, based on Public Filings
JANSSEN R&D IRELAND
Patent Owner, based on Electronic Records of PTO
U.S. Patent No. 8,518,987 B2 to Vermeersch et al.
Issue Date: August 27, 2013
Title: Pseudopolymorphic Forms of a HIV Inhibitor

Inter Partes Review Trial No. TBD

Declaration of Frederick J. Northrup, Ph.D. In Support of Lupin Ltd.'s Petition for *Inter Partes Review* of U.S. Patent No. 8,518,987 B2

I, Frederick J. Northrup, declare as follows:

I. INTRODUCTION

1. I have been retained by counsel for Lupin Limited ("Lupin") in connection with a petition Lupin intends on filing for *inter partes* review of U.S. Patent No. 8,518,987 B2 ("the '987 patent") (Ex. 1001). Specifically, I have been advised that Lupin intends on requesting that the United States Patent and Trademark Office ("PTO") cancel Claims 1-19 of the '987 patent as unpatentable on anticipation and/or obviousness grounds. I understand that this Declaration will be used to support unpatentability in any trial proceeding initiated in connection with these grounds.

II. QUALIFICATIONS AND BACKGROUND.

2. I am currently a Distinguished Senior Lecturer and Director of Undergraduate Studies in the Department of Chemistry at Northwestern University in Evanston, Illinois. I have held both positions since September 2008. From September 1998 to August 2008, I held the position of Senior Lecturer and from September 1995 to August 2006, I held the position of Director of the Analytical Services Laboratory. From 1990 through 1998, I was a Lecturer in the Department of Chemistry at Northwestern University. I have also served as a Research Associate for the Brookhaven National Laboratory and as a Faculty Research Participant for Argonne National Laboratory.

3. My current responsibilities include teaching various undergraduate laboratory courses in instrumental analysis, spectroscopy and advanced physical chemistry. I also advise 15-17 freshman students and 15-20 students in the chemistry major program each year, and I supervise undergraduate students in independent research projects. As the Director of Undergraduate Studies, I oversee all aspects of the undergraduate chemistry major program at Northwestern University. As the former Director of the Analytical Services Laboratory, I was responsible for management of Analytical Services Laboratory's instrumentation, which included optical spectroscopy, NMR spectroscopy, mass spectrometry, and X-ray diffraction equipment, and supervision of the laboratory staff.

4. Attached as Exhibit 1070 is my curriculum vitae setting forth my educational experience, employment history, professional affiliations, and publications.

5. I have relied upon my education, background, and experience in conducting the testing and in forming the opinions set forth herein.

III. SUMMARY OF ANALYSES.

6. I have been asked to review the '987 patent and the test methods disclosed therein for the characterization of the purported pseudopolymorphic forms set forth therein.

7. In accordance with these disclosures, I have also been asked to conduct testing on three samples sent to me by Dr. Aris G. Kalivretenos from Aurora Analytics on behalf of counsel for Lupin Limited. The samples were identified as Darunavir, 0.5 g, Lot No. C13-040215-2; Darunavir, ethanol recrystallized, 0.5 g; Lot No. C13-040415-E; and Darunavir, isopropanol recrystallized, 0.4 g, Lot No. C13-040415-I. The sample vials were further labeled as "Compound 13," "Compound 13 EtOH recrystallized," and "Compound 13 iPrOH recrystallized," respectively.

8. I specifically conducted Powder X-Ray Diffraction (XRPD) and Thermogravimetric Analysis coupled with Mass Spectrometry (TGA/MS) on such samples. Based on my review of the XRPD data, the results showed "Compound 13" is consistent with a predominantly amorphous material and "Compound 13 EtOH recrystallized" and "Compound 13 iPrOH recrystallized" are consistent with predominantly crystalline materials that I conclude are most likely solvated and isostructural. Based on my review of the TGA/MS data, all three samples showed results consistent with the presence of water and other solvents such as alcohols.

IV. BACKGROUND.

A. XRPD.

9. XRPD is a scientific technique which employs diffraction of X-ray radiation from powdered, typically crystalline, samples in order to structurally

characterize such samples. In XRPD (also commonly known as PXRD), an incident monochromatic beam of X-rays is diffracted from multiple crystals in the powdered sample. For each crystal in the mixture, the spacing between the planes in the crystal lattice is comparable to the wavelength of the incident beam. The diffraction occurs according to Bragg's Law: $n*\lambda = 2d*\sin\theta$. The resulting diffraction pattern is presented as a plot of diffracted X-ray intensity against the angle "two-theta" measured in degrees. The term "two-theta" is used because the diffracted X-rays are detected at twice the angle of the incident irradiating beam.

10. "Powder X-ray diffraction is the most powerful method for detecting polymorphs" because it specifically analyzes the packing pattern of atoms. (Ex. 1071, REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY 710 (Daniel Limmer et al. eds., 20th ed. 2000). Since polymorphs have different crystal structures, the packing patterns will therefore also be different. *Id.* However, closely related crystal structures can produce X-ray scattering at similar angles. As noted above, polymorphs consist of the same molecules stacked in different ways and consequently several reflections or peaks in the XRPD pattern may appear at the same or very similar two-theta values. Consequently, one cannot discern a specific polymorphic form based on a small number of scattering angles; the entire scattering pattern must be considered.

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