

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 Terence L. Threlfall, Ph.D. In Support of Lupin Ltd.'s
Petition for *Inter Partes* Review of U.S. Patent No. 8,518,987 B2**

Table of Contents

I.	INTRODUCTION	1
II.	QUALIFICATIONS AND BACKGROUND.....	1
III.	SUMMARY OF OPINIONS.....	5
	A. The Claims and Disclosures of the '987 Patent.	6
	B. State of the Knowledge in the Art as of May 2003.....	6
IV.	SCIENTIFIC BACKGROUND.	11
	A. Polymorphism and Crystal Forms.....	11
	B. Crystallinity and Hydrogen Bonding.	13
	C. Hydrates and Solvates.	15
	D. Solid-State Forms in Pharmaceutical Compositions.....	19
V.	PERSON OF ORDINARY SKILL IN THE ART.	23
VI.	OVERVIEW OF THE '987 PATENT.	26
	A. General Information.	26
	B. Prosecution History of the '987 Patent.	42
	1. Prosecution History of the '352 Application.	43
	2. Prosecution History of the '807 Application.	45
	3. Van Gyseghem.....	56
	C. Claims of the '987 Patent.....	59
	D. File History of EP 1567529.....	62
VII.	DETAILED BASIS FOR OPINIONS.....	65
	A. Comparison of Claims of '987 Patent with EP '929.....	65

Declaration of Terence L. Threlfall, Ph.D.,
In Support of Lupin Limited’s Petition for *Inter Partes* Review
of U.S. Patent No. 8,518,987 B2

B.	Claim Construction.	69
C.	The Claimed Subject Matter of the ‘987 Patent Would Have Been Anticipated to a Person of Ordinary Skill in the Art.	74
1.	The Presence of Water in Pharmaceutical Processes.	74
2.	Disclosures of Ghosh 1998.	75
3.	Disclosures of the ‘775 patent.....	83
4.	Comparison of the Prior Art to the Claims.	90
a.	The Process of Preparing Darunavir and Its Composition As Described and Tested in Ghosh 1998 Would Produce Darunavir Hydrates and Compositions Thereof with All of the Claimed Features of Claims 1-19.....	94
b.	The Process of Preparing Darunavir and Its Compositions Described in the ‘775 Patent Would Produce Darunavir Hydrates and Compositions Thereof with All of the Claimed Features of Claims 1-19.....	107
D.	The Claimed Subject Matter of the ‘987 Patent Would Have Been Obvious to a Person of Ordinary Skill in the Art.	114
1.	State of the Knowledge as of May 16, 2003.....	114
a.	Darunavir, the Molecule, Was Well-known as of May 2003.	114
b.	A Skilled Artisan Would Have Been Motivated to Study the Crystallisation of Darunavir.	116
c.	A Person of Ordinary Skill in the Art Would Have Understood That Such Crystallisation Screening Was Routine.....	118

Declaration of Terence L. Threlfall, Ph.D.,
In Support of Lupin Limited’s Petition for *Inter Partes* Review
of U.S. Patent No. 8,518,987 B2

d.	A Person of Ordinary Skill in the Art Would Have Reasonably Expected Darunavir Hydrate to Form.....	124
e.	Darunavir Would Have Been Reasonably Expected to Form Hydrates in a Ratio of 0.5 to 3.....	127
2.	Comparison of the Claims to the Art.....	129
a.	Claim 1.....	129
b.	Claim 2.....	132
c.	Claims 3-5.....	134
d.	Claims 6-8.....	138
e.	Claims 9-13.....	140
f.	Claims 14-18.....	141
g.	Claim 19.....	142
E.	Secondary Considerations.....	145
VIII.	STATEMENT.....	155

Declaration of Terence L. Threlfall, Ph.D. (Ex. 1025),
In Support of Lupin Ltd.'s Petition for *Inter Partes* Review
of U.S. Patent No. 8,518,987 B2

I, Terence L. Threlfall, 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 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 Senior Research Fellow in the Crystallography Group within the School of Chemistry at the University of Southampton. I have more than 50 years of experience in my principal fields of interest of crystallisation, crystallography, polymorphism, other aspects of solid state structure and behaviour, and in understanding crystallisation and transformation processes.

3. Specifically, I received a Bachelor of Science degree in chemistry from London University in 1956 and a Ph.D. in organic chemistry from London University in 1971. In 1984, I received the degree of LL.B. from London University.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.