IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Review of:	)
U.S. Patent No. 5,665,772	)
Issued: Sep. 9, 1997	)
Application No.: 08/416,673	)
U.S. Filing Date: April 7, 1995	)

For: **O-alkylated rapamycin derivatives and their use, particularly as immunosuppressants**

FILED VIA PRPS

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 5,665,772

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

Table of Contents

I. OVERVIEW 1

II. REQUIREMENTS FOR PETITION FOR *INTER PARTES* REVIEW 3

A. Grounds for Standing (37 C.F.R. § 42.104(a)) 3
B. Notice of Lead and Backup Counsel and Service Information 4
C. Notice of Real-Parties-in-Interest (37 C.F.R. § 42.8(b)(1)) 4
D. Notice of Related Matters (37 C.F.R. § 42.8(b)(2)) 5
E. Fee for *Inter Partes* Review 6
F. Proof of Service 6

III. SUMMARY OF ISSUE PRESENTED 6

IV. INTRODUCTION 7

V. IDENTIFICATION OF CLAIMS BEING CHALLENGED (§ 42.104(B)) 12

VI. DESCRIPTION OF THE PURPORTED INVENTION 12

VII. CLAIM CONSTRUCTION 15

A. Applicable Law 15
B. Construction of Claim Terms 17

VIII. PERSON HAVING ORDINARY SKILL IN THE ART 18

IX. TECHNICAL BACKGROUND AND STATE OF THE ART 19

A. Rapamycin Was Known as a Powerful Immunosuppressant with Limited Solubility 19
B. Rapamycin Derivatives at C40 Had Been Synthesized and Shown to Have Immunosuppressant Activity 20
C. Rapamycin's Interactions With Its Targets Were Known 21
D. Solubility-Enhancing Modifications Were Well-Known 25
E. Standard Assays Were Available to Evaluate Immunosuppressant Activity of Rapamycin Derivatives 27

X. THE SCOPE AND CONTENT OF THE PRIOR ART 27

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

A. Morris Teaches that Rapamycin Is a Promising Lead Compound with Limited Solubility 27
B. Rossmann Teaches How to Obtain Three-Dimensional Coordinates from Stereo Diagrams 29
C. Van Duyne Revealed the Structural Interactions Between Rapamycin and FKBP-12....29
D. The Full Coordinates of the Van Duyne Structure Show that C40 of Rapamycin Is the Optimal Position for Modification....33
E. Flexible Side Chains Were Known to Improve Solubility 34
F. The Addition of Solubilizing Substituents Was Well-Known....35
G. Rapamycin Derivatives at C40 Were Shown to Have Immunosuppressant Activity and Were Evaluated in Standard Assays....36

XI. MOTIVATIONS TO COMBINE THE PRIOR ART REFERENCES....38

XII. PRECISE REASONS FOR THE RELIEF REQUESTED 39

A. Ground 1: Claim 7 Is Invalid under 35 U.S.C. § 103 on the Ground That They Are Rendered Obvious in View of Morris, Van Duyne, Rossmann, Lemke, Yalkowsky, and Hughes 41

XIII. Secondary Considerations Do Not Render Claim 7 Nonobvious 53

XIV. CONCLUSION....54

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

Exhibit List

1001	U.S. Patent No. 5,665,772 ("the '772 Patent")
1002	File History for the '772 Patent
1003	Declaration of William L. Jorgensen, Ph.D. in Support of Petition for *Inter Partes* Review of U.S. Patent No. 5,665,772
1004	Curriculum Vitae of William L. Jorgensen
1005	Randall Ellis Morris, *Rapamycins: Antifungal, Antitumor, Antiproliferative, and Immunosuppressive Macrolides*, 6 TRANSPLANTATION REVIEWS 39 (1992) ("Morris")
1006	Gregory D. Van Duyne *et al.*, *Atomic Structure of the Rapamycin Human Immunophilin FKBP-12 Complex*, 113 J. AM. CHEMICAL SOC'Y 7433 (1991) ("Van Duyne")
1007	Samuel H. Yalkowsky, *Estimation of Entropies of Fusion of Organic Compounds*, 18 INDUS. & ENG'G CHEMISTRY FUNDAMENTALS 108 (1979) ("Yalkowsky")
1008	Thomas L. Lemke, *Chapter 16: Predicting Water Solubility*, REVIEW OF ORGANIC FUNCTIONAL GROUPS 113 (2d ed. 1988)
1009	U.S. Patent No. 5,233,036 ("Hughes")
1010	U.S. Patent No. 4,650,803 ("Stella")
1011	U.S. Patent No. 5,100,883 ("Scheihser")
1012	Stuart L. Schreiber, *Chemistry and Biology of the Immunophilins and Their Immunosuppressive Ligands*, 251 SCI. 283 (1991) ("Schreiber")
1013	Joseph B. Moon & W. Jeffrey Howe, *Computer Design of Bioactive Molecules: A Method for Receptor-Based de Novo Ligand Design*, 11 PROTEINS: STRUCTURE, FUNCTION, & GENETICS 314 (1991) ("Moon")

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

1014	Hans-Joachim Böhm, *LUDI: rule-based automatic design of new substituents for enzyme inhibitor leads*, 6 J. COMPUTER-AIDED MOLECULAR DESIGN 593 (1992) ("Böhm")
1015	Silverman, *Chapter 2: Drug Discovery, Design, and Development*, THE ORGANIC CHEMISTRY OF DRUG DESIGN & ACTION 4 (1992) ("Silverman")
1016	Julianto Pranata & William L. Jorgensen, *Computational Studies on FK506: Conformational Search and Molecular Dynamics Simulation in Water*, 113 J. AM. CHEMICAL SOC'Y 9483 (1991)
1017	William L. Jorgensen, *Rusting of the Lock and Key Model for Protein-Ligand Binding*, 254 SCI. 954 (1991)
1018	Modesto Orozco *et al.*, *Mechanism for the Rotamase Activity of FK506 Binding Protein from Molecular Dynamics Simulations*, 32 BIOCHEMISTRY 12864 (1993)
1019	Michelle L. Lamb & William L. Jorgensen, *Investigations of Neurotrophic Inhibitors of FK506 Binding Protein via Monte Carlo Simulations*, 41 J. MED. CHEMISTRY 3928 (1998)
1020	Michelle L. Lamb *et al.*, *Estimation of Binding Affinities of FKBP12 Inhibitors Using a Linear Response Method*, 7 BIOORGANIC & MEDICINAL CHEMISTRY 851 (1999)
1021	Thomas W. Bell, *Construction of a Soluble Heptacyclic Terpyridine*, 51 J. ORGANIC CHEMISTRY 764 (1986) ("Bell")
1022	M. Ballauff, *Phase Equilibria in Rodlike Systems with Flexible Side Chains*, 19 MACROMOLECULES 1366 (1986) ("Ballauff")
1023	R. Stern *et al.*, *Rigid rod polymers with flexible side chains*, 32 POLYMER 2096 (1991) ("Stern")
1024	Michael G. Rossmann *et al.*, *Three-Dimensional Coordinates from Stereodiagrams of Molecular Structures*, B36 ACTA CRYSTALLOGRAPHICA 819 (1980) ("Rossmann")

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

DOCKET ALARM

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.