IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re <i>Inter Partes</i> 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 immu-

nosuppressants

FILED VIA PRPS

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

For ease of reference, Petitioner refers to this petition as the "'772 Petition" challenging claims 1-3 and 8-10.



Table of Contents

I.	REQUIREMENTS FOR PETITION FOR <i>INTER PARTES</i> REV		1
	A. B. C. D. E. F.	Grounds for Standing (37 C.F.R. § 42.104(a))	1 3 3
II.	SUM	IMARY OF ISSUE PRESENTED	3
III.	INTE	RODUCTION	4
IV.		NTIFICATION OF CLAIMS BEING CHALLENGED	10
V.	DES	CRIPTION OF THE PURPORTED INVENTION	11
VI. CLAIM CONSTRUCTION		13	
	A. B.	Applicable Law	
VII.	PER	SON HAVING ORDINARY SKILL IN THE ART	16
VIII.	TEC	HNICAL BACKGROUND AND STATE OF THE ART	16
	A. B.	Rapamycin Was Known as a Powerful Immunosuppressant with Limited Solubility	16
	C.	Shown to Have Immunosuppressant Activity	
	D. E.	Solubility-Enhancing Modifications Were Well-Known	
	F.	Immunosuppressant Activity of Rapamycin Derivatives Computer-Aided Drug Design Provided Quantitative	24
	1.	Assessment of Modifications to Known Compounds	25
IX	THE	SCOPE AND CONTENT OF THE PRIOR ART	26



	Α.	Morris Teaches that Rapamycin Is a Promising Lead	
		Compound with Limited Solubility	26
	B.	Rossmann Teaches How to Obtain Three-Dimensional	
		Coordinates from Stereo Diagrams	27
	C.	Van Duyne Revealed the Structural Interactions Between	
		Rapamycin and FKBP-12	27
	D.	The Full Coordinates of the Van Duyne Structure Show that	
		C40 of Rapamycin Is the Optimal Position for Modification	31
	E.	Flexible Side Chains Were Known to Improve Solubility	32
	F.	The Addition of Solubilizing Substituents Was Well-Known	33
	G.	Rapamycin Derivatives at C40 Were Shown to Have	
		Immunosuppressant Activity and Were Evaluated in Standard	
		Assays	34
	H.	Computer-Aided Design Allowed For the Screening of	
		Potential Modifications to Determine Promising Derivatives to	
		Synthesize and Evaluate	35
X.	МОТ	TIVATIONS TO COMBINE THE PRIOR ART REFERENCES	37
XI.	PRE	CISE REASONS FOR THE RELIEF REQUESTED	38
	A.	Ground 1: Claims 1-3 and 10 are Invalid under 35 U.S.C. § 103 on the Ground That They Are Rendered Obvious in View of Morris, Van Duyne, Rossmann, Lemke, and Yalkowsky	40
	В.	Ground 2: Claims 8 and 9 are 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 in further view of Hughes	48
	C.	Ground 3: Claims 1-3 and 10 of the '772 Patent Would Have Been Obvious Over Routine Use of Computer-Aided Drug Design Software In View of Morris, Van Duyne, Lemke, and Yalkowsky	51
	D.	Ground 4: Claims 8 and 9 are Invalid under 35 U.S.C. § 103 on the Ground That They Are Rendered Obvious Over Routine Use of Computer-Aided Drug Design Software In View of Morris, Van Duyne, Lemke, and Yalkowsky, and in further view of Hughes	54
XII.		ndary Considerations Do Not Render Claims 1-3 and 8-10	
	None	physique	5/



	Petition for Inter Partes	Review of USP 5,665,772
XIII CONCLUSION		55



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 <i>Inter Partes</i> Review of U.S. Patent No. 5,665,772
1004	Curriculum Vitae of William L. Jorgensen
1005	Randall Ellis Morris, <i>Rapamycins: Antifungal, Antitumor, Antiproliferative, and Immunosuppressive Macrolides</i> , 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, <i>Estimation of Entropies of Fusion of Organic Compounds</i> , 18 INDUS. & ENG'G CHEMISTRY FUNDAMENTALS 108 (1979) ("Yalkowsky")
1008	Thomas L. Lemke, <i>Chapter 16: Predicting Water Solubility</i> , 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, <i>Chemistry and Biology of the Immunophilins and Their Immunosuppressive Ligands</i> , 251 Sci. 283 (1991) ("Schreiber")
1013	Joseph B. Moon & W. Jeffrey Howe, <i>Computer Design of Bioactive Molecules: A Method for Receptor-Based de Novo Ligand Design</i> , 11 PROTEINS: STRUCTURE, FUNCTION, & GENETICS 314 (1991) ("Moon")



DOCKET

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.

